GERIATRIC NEPHROLOGY

DEVELOPMENTS IN NEPHROLOGY

Cheigh JS, Stenzel KH, Rubin AL: Manual of clinical nephrology of the Rogosin Kidney Center. 1981. ISBN 90-247-2397-3.

Nolph KD ed.: Peritoneal dialysis. 1981. ISBN 90-247-2477-5.

Gruskin AB, Norman ME eds: Pediatric nephrology. 1981.
ISBN 90-247-2514-3.

Schück O ed: Examination of the kidney function. 1981. ISBN 0-89838-565-2.

Strauss J ed: Hypertension, fluid-electrolytes and tubulopathies in pediatric nephrology. 1982. ISBN 90-247-2633-6.

Strauss J ed: Neonatal kidney and fluid-electrolytes. 1983.
ISBN 0-89838-575-X.

Strauss J ed: Acute renal disorders and renal emergencies. 1984.
ISBN 0-89838-663-2.

Didio LJA, Motta PM eds: Basic, clinical, and surgical nephrology. 1985.
ISBN 0-89838-698-5.

Friedman EA, Peterson CM eds: Diabetic nephropathy: Strategy for therapy. 1985. ISBN 0-89838-735-3.

Dzúrik R, Lichardus B, Guder W eds: Kidney metabolism and function. 1985.
ISBN 0-89838-749-3.

DiDio LJA, Motta PM eds: Basic, clinical, and surgical nephrology. 1985.
ISBN 0-89838-698-5.

Oreopoulos DG ed: Geriatric nephrology. 1986. ISBN 0-89838-781-7.

Geriatric Nephrology

The medical, psychosocial, nursing, financial and ethical issues of treating end-stage renal disease in the elderly

edited by

DIMITRIOS G. OREOPOULOS MD
Division of Nephrology
Toronto Western Hospital
Toronto, Ontario, Canada

1986 **MARTINUS NIJHOFF PUBLISHERS**
a member of the KLUWER ACADEMIC PUBLISHERS GROUP
DORDRECHT / BOSTON / LANCASTER

Distributors

for the United States and Canada: Kluwer Academic Publishers, 190 Old Derby Street, Hingham, MA 02043, USA
for the UK and Ireland: Kluwer Academic Publishers, MTP Press Limited, Falcon House, Queen Square, Lancaster LA1 1RN, UK
for all other countries: Kluwer Academic Publishers Group, Distribution Center, P.O. Box 322, 3300 AH Dordrecht, The Netherlands

Book information

ISBN-13: 978-94-010-8389-8 **e-ISBN-13: 978-94-009-4255-4**
DOI: 10.107/978-94-009-4255-4

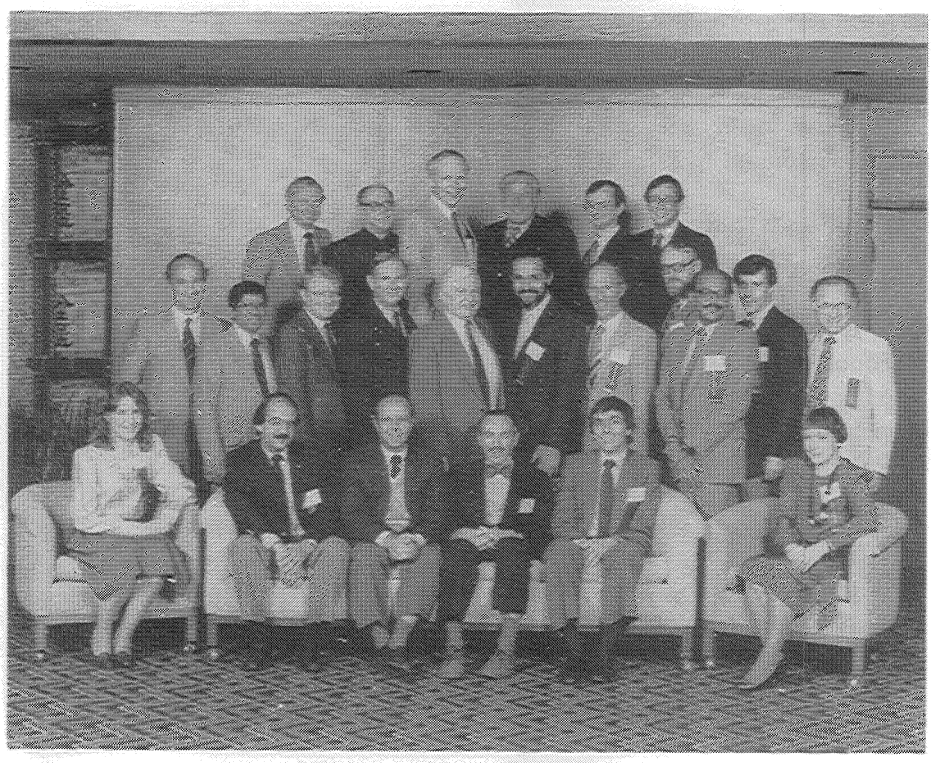
Library of Congress Cataloging in Publication Data

Geriatric nephrology.

(Developments in nephrology)
Papers presented to the First International Symposium on Geriatric Nephrology held in Toronto on May 23-24, 1985.
Includes bibliographies and index.
1. Geriatric nephrology--Congresses. 2. Renal insufficiency--Treatment--Moral and ethical aspects--Congresses. I. Oreopoulos, D. G. (Dimitrios G.)
II. International Symposium on Geriatric Nephrology (1st : 1985 : Toronto, Ont.) [DNLM: 1. Kidney Diseases--in old age--congresses. W1 DE998EB / WJ 300 C3685 1985]
RC903.G48 1986 618.97'661 85-29728
ISBN 0-89838-781-7 (U.S.)

Copyright

TABLE OF CONTENTS



LIST OF CONTRIBUTORS

Cyril I. Gryfe, M.D., F.R.C.P.(C)
Medical Director
Baycrest Centre for Geriatric Care
Associate Professor
Department of Medicine
University of Toronto

H.M. Rosemary Meier, M.B., ChB., MSc., MRCPsych., FRCP(C)
Assistant Professor
University of Toronto
Co-ordinator:Geriatric Psychiatry Service
Toronto Western Hospital
Toronto, Ontario

Richard Ian Ogilvie, M.D., FRCP., FACP
Professor of Medicine and Pharmacology
University of Toronto
Director, Divisions of Cardiology
and Clinical Pharmacology
Toronto Western Hospital
Toronto, Ontario

Robert M. Richardson, M.D., F.R.C.P.(C)
Division of Nephrology
Toronto General Hospital
University of Toronto
Toronto, Ontario

Kamlakar Tripathi,M.D.,D.M.,M.N.A.M.S.
Jawed Ahmed, M.D.
P.K. Srivastava, M.D.,D.C.H.
P.S. Mishra, M.B.B.S.
Division of Nephrology
Department of Medicine
Institute of Medical Sciences
Banaras Hindu University
Varanasi-22 1005
India

Theodore R. Reiff
Professor of Medicine
Tufts University
Boston, MA

Bernard Isaacs, M.D., F.R.C.P.,
Charles Hayward Professor of Geriatric Medicine
University of Birmingham
Hayward Building
Selly Oak Hospital
Birmingham B29 6JD, U.K.

Sharon Anderson, M.D.
Laboratory of Kidney and Electrolyte Physiology
Department of Medicine
Brigham and Women's Hospital and Harvard Medical School
Boston, MA

George E. Schreiner, M.D., F.A.C.P.
Professor of Medicine
Director of Nephrology Division
Georgetown University School of Medicine
Washington, DC

Anastasius S. Dontas, M.D.
Department of Medicine
Accident Hospital, Kifissia and
Center of Studies of Age-Related Changes in Man
Athens, Greece

Norbert Lameire
Associate Professor of Medicine
Renal Division
University Hospital
De Pintelaan, 185, 9000 Gent, Belgium

Karel De Keyzer, M.D.
Resident
University Hospital
De Pintelaan 185, 9000 Gent, Belgium

Walter Pauwels, M.D.
Resident
University Hospital
De Pintelaan, 185, 9000 Gent, Belgium

Erbe Matthys, M.D.
Instructor in Medicine
University Hospital
De Pintelaan, 185, 9000 Gent, Belgium

Raymond Vanholder, M.D.
Instructor in Medicine
University Hospital
De Pintelaan, 185, 9000 Gent, Belgium

Severin Ringoir, M.D.
Professor of Medicine
Head, Renal Division
University Hospital
De Pintelaan, 185, 9000 Gent, Belgium

Christopher R. Blagg, M.D., F.R.C.P.
Executive Director
Northwest Kidney Center
Professor of Medicine
University of Washington
Seattle, Washington

Joel D. Kopple
Mary B. Grosvenor
Charlotte E. Roberts
Department of Medicine and
the Clinical Research Center
Harbor-UCLA Medical Center
Torrance, California and
VA Wadsworth Medical Center
Los Angeles, California

Carl M. Kjellstrand, M.D.,F.A.C.P.
K. Koppy
A. Umen, M.S.
S. Nestrud, B.S., R.N.
L. Westlie, M.D.
Regional Kidney Disease Program
Department of Medicine
Hennepin County Medical Center
701 Park Avenue
Minneapolis, MN 55415

Allen R. Nissenson, M.D., F.A.C.P.
Associate Professor of Medicine
Director, Dialysis Program
UCLA School of Medicine
Chairman, NCC 4

Dominick E. Gentile, M.D.,
Clinical Professor of Medicine
UC Irvine School of Medicine
Chairman, Medical Review Board, NCC 4

Robert E. Soderblom, M.D.,
Associate Professor of Medicine
Loma Linda University

Charlene Brax
Executive Director, NCC 4

Medical Review Board, NCC 4
Los Angeles, California

Bruce G. Sommer, M.D.
David M. Mandelbaum, M.D.
Mitchell L. Henry, M.D.
Ronald M. Ferguson, M.D.
The Ohio State University
Department of Surgery
Division of Transplantation
Room 258, Means Hall
1655 Upham Drive
Columbus, Ohio 43210

Carl J. Cardella, M.D., F.R.C.P.(C)
Director of Transplantation
Toronto Western Hospital
399 Bathurst St.
Suite 526, Edith Cavell Wing
Toronto, Ontario M5T 2S8

Sharron Izatt, R.N.
Renal Supervisor
Toronto Western Hospital
399 Bathurst Street
Toronto, Ontario M5T 2S8

Stephen A. Kline, M.D., F.R.C.P.(C)
Assistant Professor
Department of Psychiatry
University of Toronto, Clinical Director
Department of Psychiatry
Toronto Western Hospital
399 Bathurst Street
Toronto, Ontario M5T 2S8

Howard J. Burton, M.S.W., M.Sc., Dr.P.H.
Associate Professor
Department of Psychiatry
University of Toronto, Associate Director
Division of Rehabilitation Psychiatry
Toronto Western Hospital
399 Bathurst Street
Toronto, Ontario, M5T 2S8

Mumtzar Akhtar, Ph.D.
Research Associate
Department of Psychiatry
Toronto Western Hospital
399 Bathurst Street
Toronto, Ontario M5T 2S8

Bernard M. Dickens, Ph.D., LL.D.
Professor, Faculty of Law and Faculty of Medicine
University of Toronto
78 Queens Park
Toronto, Ontario M5S 2C5

Eli A. Friedman, M.D., D.Sci., (Hon)
Professor of Medicine
Chief, Division of Renal Disease
Downstate Medical Center
450 Clarkson Avenue
Brooklyn, NY 11203

Antony J. Wing
The United Medical and Dental Schools of Guy's
and St. Thomas's Hospitals, London, U.K.

FOREWORD

The year was 1943. As a third-year medical student at Stanford, I was about to witness the beginning of a medical miracle. Dr. Arthur Bloomfield, Professor of Medicine, had selected my patient, a middle aged man, who was dying of acute pneumococcal pneumonia, as one of the first patients to receive miniscule doses (by today's standards) of his meagre supply of a new drug - penicillin. The patient's response amazed everyone especially this impressionable medical student. The rest of the story is history. With one stroke, the introduction of penicillin removed from the medical scene the 'friend of the aged' - lobar pneumonia. The consequences, which no one could have imagined at the time, are still becoming manifest as other 'miracles' such as respirators, artificial kidneys and many potent new antibiotics have come upon the scene.

All of us are aware that these miracles have created a variety of new challenges around the states of dying and near dying. We have no easy answers for these problems. Nevertheless as dialysis techniques, especially CAPD, are applied more widely to the treatment of the elderly, the task of helping the patient meet death with dignity becomes increasingly important and vexing because once begun, dialysis is difficult to terminate. Indeed, in my 1964 Presidential Address to the American Society for Artificial Internal Organs (ASAIO), I predicted that it would prove much more difficult to stop dialysis than to select new patients (1). The major source of difficulty in this area of care is a legal one. Today in most legal jurisdictions, dialysis is regarded as 'routine care' in a class with antibiotic therapy or nutritional support rather than 'extraordinary care' like respirator treatment in an ICU.

This is not the place to discuss this vexing issue in depth. However the danger flags are flying and as nephrologists, we must face this issue sooner rather than later especially now that the cost of medical care has become a major concern to legislators and the public. (Some authorities have estimated that, in the USA, 50% of the entire Medicare budget is spend on patients during their last six months of life).

If we increase our commitment to dialysis of the elderly, we must expect a

marked increase in the number of such patients whose quality of life later will deteriorate because of complications such as myocardial infarctions or cerebrovascular accidents. At that point confusion and conflict begins and at present we can contemplate no fair or humane solutions unless we have prepared the necessary legal steps in advance.

At present two legal options are open in the State of Washington and many other jurisdictions. One is the 'living will'; the other is a new legal instrument called a *durable-power-of-attorney*. Experience to date suggests that the latter mechanism is preferable. With a durable power of attorney, the patient can delegate to a specific relative or friend or his physician the right to discontinue all forms of life support, including dialysis whenever it seems appropriate. The patient does not have to be terminally ill as is necessary to invoke most living wills. I would urge nephrologists to become familiar with this new legal approach to a difficult medical and ethical dilemma.

By focusing on this difficult subject of terminating care, I do not wish to imply that I'm against the use of dialysis in the elderly patient. On the contrary, just as antibiotics are used to prolong the useful lives of elderly patients, so improved dialysis techniques and in some cases transplantation also can be used. At the same time, just as we are becoming more and more concerned about the ethics of using antibiotics to prolong the life of a semi-comatose octogenerian in a nursing home, we now are facing increasingly frequent ethical problems with continuing dialysis in the elderly patient who develops a stroke. I believe that whenever possible, it is wise to anticipate with the patient and family these potential complications and lessen the emotional trauma by planning in advance with the appropriate legal instrument.

Belding H. Scribner, M.D.

Professor of Medicine
School of Medicine
University of Washington
Seattle, WA 98195

REFERENCE

1. Scribner BH. Presidential address. Trans ASAIO 1964;10:209-212.

1. INTRODUCTION

Even five or ten years ago, few dialysis patients were elderly. However, during the past decade most dialysis units have opened their doors to elderly patients with end-stage renal disease.

In Canada during 1983, of new patients with ESRD, 312 (24%) were over the age of 65. Similarly, in Europe, during the years 1980-1982, 25% of all new patients were over the age of 60.

This high percentage of elderly patients on dialysis is a common phenomenon in most North American centers and in most developed countries with the exception of Great Britain. This high percentage of elderly patients on dialysis is due to: 1) The liberalization of criteria for acceptance for dialysis - old age is no longer a contraindication; 2) The increasing success of dialysis which has kept more patients alive longer, and 3) The aging of the population as a whole. As a result and with increasing frequency nephrology teams are encountering the many special problems inherent in the elderly even though many have not had the training which would prepare them to recognize and manage these complex situations.

Since our goal is not only to provide dialysis and extend life but also to give the patient a life of reasonably high quality, it is timely to review existing knowledge in this field with the understanding that a fuller description and recommendations for their management will require the collaboration of other disciplines.

Problems arising in the elderly patient on dialysis may be surveyed under four headings: 1) Medical, 2) Dialysis-related, 3) Psychosocial and 4) Ethical.

Medical-Problems: Usually elderly patients have multiple-system disease, of which cardiovascular lesions are prominent. Frequently they have some degree of mental impairment, which often is aggravated by the side effects of various medications. Most of these patients receive several or even many different medications and the physician should be alert for evidence of synergism, antagonism and side effects.

Dialysis-Related-Problems: An unstable cardiovascular system and the poor

condition of the blood vessels make hemodialysis a difficult procedure and hence some form of peritoneal dialysis seems preferable. Management becomes even more complicated when the elderly patient on dialysis becomes confused or even demented. Then it may be advisable to discontinue dialysis but often this is not an easy decision.

Psychosocial Problems: The main psychological hazards are loneliness and/or depression. In Western society, the bonds between young and the old are so loose that a major disease like ESRD will rupture these bonds almost completely; then the burden of the elderly patient becomes unbearable and the family surrenders the patient to institutional or other public health care. Depression and its consequences reflect the lack of purpose in the patients life, and the perceived lack of concern and care from children and grandchildren. Under these circumstances one might expect the elderly to give up, nevertheless most seem to prefer to live, even on dialysis. Life is worth living for reasons that most may perceive to be small. One day, one of my elderly patients who, in addition to renal failure also had respiratory failure, told me how happy she was because that morning, when she looked out of her window, she saw some blossoming flowers. Again and again I have observed how important family support and care is to the wellbeing and even survival of the elderly. Unfortunately while we are equipped to treat ESRD effectively, we are poorly prepared and get little support from society when we attempt to make the last years of these patients pleasant and meaningful. This problem becomes even more difficult when the family struggles with an additional handicap - poverty.

I am impressed how important it is for the elderly patient to continue to live and eventually die at home amid familiar surroundings. If we can satisfy this desire, we will make each elderly person happier and we will save money because a bed at home is so much less expensive than a bed in an institution. Ironically, society often makes it easier to spend more money and put these patients in an institution than to assist them to stay at home.

Ethical Problems: As a society and as professionals we face a number of agonizing questions: First, should we accept all elderly patients for dialysis? In my view this decision should be based chiefly on the patient's wishes.

Secondly, should we accept for dialysis patients in poor health who have little prospect for improvement but want to continue to live? Of course all would wish to be in a position to grant all such requests, but often funds are not available to offer dialysis to all.

Recently in the USA and Canada health-care professionals have come under increasingly severe financial constraint and the time seems close at hand when doctors will be forced to make the choice 'Who will live? and Who will die?' In that day, the elderly will be the first to suffer and be refused treatment because their management is the least 'cost-effective'.

Finally the physician faces special problems in the demented elderly patient who requires dialysis. If he recognizes the dementia before he considers dialysis,

the physician may be able to convince the relatives that it should not be started. However, once dialysis has been instituted, it is difficult to discontinue it, especially if the family objects.

The physician or other staff members will require much compassion and understanding, if they are to convince the relatives that they should consent to the discontinuation of treatment. When the elderly dialysis patient is in pain or is suffering from complications in other systems, the doctor or the nurse should be prepared to discuss the options with the patient and, from time to time, remind them that they can discontinue dialysis if they so desire. We should make sure that no patient continues dialysis - even though they may be suffering only because they do not want to disappoint their doctors.

The first International Symposium on Geriatric Nephrology was held in Toronto on May 23 and 24 1985 because these problems will become more numerous and more acute as time passes. This course was arranged with the collaboration of an international advisory board - C.R.Blagg, Seattle; E.Friedman, New York; D.Hamburger, Indianapolis; M.Kaye, Montreal; D.Kerr, London; M.Kessel, Berlin; C.M.Kjellstrand, Minneapolis; J.D.Kopple, Los Angeles; N.Lameire, Gent; M.Legrain, Paris; K.D.Nolph, Columbia; F.Parsons, Leeds; J.D.E.Price, Vancouver; G.E.Schreiner, Georgetown; and T.Reiff, Boston, and a local board - S.S.Fenton, W.Williams, B.Goldlist, C.Saiphoo, R.Meier, S.Kline, R.Fisher.

This book includes the papers presented on this conference and the discussion after each presentation. With the publication of the proceedings of this conference, we hope to establish the foundations of the subspecialty of geriatric nephrology, which is urgently need with the increasing numbers of elderly patients with renal disease. I hope subsequent conferences will build on the knowledge accumulated in this conference.

The success of this conference and the prompt publication of its proceedings are the result of hard work by a large team. First I would like to thank the members of the International Advisory Board for their many valuable suggestions. The members of the local organizing committee worked closely together to produce the program. I want also to thank Donald Joseph of Travenol Laboratories who generously guaranteed the expenses of the conference in the event that the registration was not large enough to defray our costs, and Bob Janosko Marketing Services Manager of Travenol, for his expert contributions. Pam Graham, of Congress Canada, and my secretaries - Margarida Silva, Rosa Muhlbacher and Dianna Taylor, provided invaluable help during the organization of the symposium.

This publication would not have been possible without the prompt cooperation of all authors. Dr. J.O. Godden helped immensely by editing all of these papers and my secretaries spent many hours typing the manuscripts. Finally, since a man can do only so much with his time, I thank my wife and our children for surrendering their claim on much of my time during the two years it took to prepare this conference and this book.

D.G. Oreopoulos

2. PHYSIOLOGY OF AGING

C. I. GRYFE, M.D., F.R.C.P.(C)

AGING VS. AILING

Normal aging *is* physiology, and not pathology. This statement may be difficult to reconcile with Comfort's definition of aging (which gives little comfort): A deteriorative process characterized by a decrease in viability and an increase in vulnerability with increasing chronological age (1).

Because the intellectual discipline that we call physiology' is the study of functioning homeostasis (2), it is difficult to perceive a physiological phenomenon as a decremental process. We are conditioned to understand physiology as it represents the optimally functioning young-adult animal. This is the physiology found in the standard textbooks.

The study of disease or pathology is familiar to us as a decremental process. Since both normal aging and the progression of disease diminish vitality and increase vulnerability, and normal aging is not merely the accumulation of diseases, how can we differentiate the two phenomena? For example, how can the clinician decide if the disease diabetes mellitus is present? If traditional standards of glucose tolerance are used, 50% of people over 70 years old might be classified as latent diabetics, but, in this age grouup, the actual prevalence of frank diabetes is probably no greater than 8%. Alternatively, if 'normal' is defined to include those serum glucose values lying within two standard deviations of the mean, then 2.3% would have latent diabetes (3).

CRITERIA OF AGING

Strehler (4) has proposed a set of criteria to define the normal aging process, in distinction to the natural history of disease. The most obvious feature of normal aging is 'deleteriousness' (Strehler's term). That is to say deterioration or degeneration, which also characterize the process of disease and therefore the term does little to differentiate the concepts of physiology and pathology.

However, *rates* of deterioration may be different in two otherwise similar phenomena. Osteoporosis, the progressive loss of bone substance, provides one example. Some old women lose skeletal mass at a rate apparently higher than normal. These individuals may be regarded as having pathological bone loss, while the reference group had physiological bone loss (5). The slopes of the decline curves for the pathological group are clearly steeper than the average slope for the physiological group.

In more general terms, the different slopes may be members of a set of slopes which includes the range between maximum possible, age-specific function, and disuse-atrophic function (Williams 1984). Below the latter lie the slopes of disease-induced dysfunction, and in many instances these steeper slopes demonstrate the combined effects of disuse atrophy and pathology.

Strehler's next criterion, 'intrinsicality' also requires some qualification. Uniformity or sequential predictability of various manifestations of aging imply an inherently programed 'biological clock', that is in genetic material, which becomes exhausted at a predictable rate.

His third criterion, 'universality' clearly distinguishes aging from any known disease entity. No morphological lesion or functional aberration, which we perceive as a disease, can be said to affect every member of a susceptible species. Some possible exceptions spring to mind such as atherosclerosis (7), but, although it is widely prevalent after middle age, atherosclerosis still misses occasional individuals in industrial societies and is rare in some primitive societies. Such reservations on the universality of atherosclerosis are even more meaningful if we focus on site-specific atheromatous lesions.

Also militating against atherosclerosis as a normal aging process is Strehler's fourth criterion of 'progressiveness' or irreversibility. Again, examples are infrequent but atherosclerotic plaques can regress and disappear (8-10). The aging process, being time-determined, cannot be expected to reverse any more than time itself can reverse.

RATES OF AGING

Clinically, there seems to be a time-determined inter-relationship between the normal aging process and the natural history of disease - an interaction which is complex and subtle. Aging proceeds at different rates in different species (men live longer than mice). Also, it has different rates of progression in different organs and tissues.

The per cent loss of tissue mass varies widely among specific organs, ranging from about 5% in lungs to about 48% in spleen during the five decades between 35 and 85 years of age (11-12). As a consequence, the relative masses of major tissue elements are different in older subjects than in their younger counterparts. Especially important are the changes in total body fat, lean muscle and water,

because of their implications for metabolic activity, nutritional management and drug use.

Even within the same organ, such as the skin and its integument, there are variations, e.g. graying of the hair characteristically occurs earlier in the temples than in the eyebrows.

Morphological changes also are seen at the molecular level, particularly those affecting the spatial orientation or racemization of individual protein structures. The ratio of dextro- to levoisomers varies with chronological age (13,14), but whether this has functional consequences is as yet unknown.

Variation in rate is seen most importantly among the different physiological systems. For example, the systems subserved by paired organs, such as respiration and the lungs, or excretion and the kidneys, decline at a faster rate than single-organ functions such as cerebration or cardiomechanics. Another determinant of the rate of decline of physiological functions is the complexity of the system selected. Nerve-conduction velocity involves only the nervous system and declines only about 10% in six decades, but cardiac output involves the endocrine and nervous systems as well as the circulatory system and the overall decrease between 30 and 90 years of age is almost 30%. This principle also is illustrated in testing muscle power if static strength, as measured by dynamometry is compared with the co-ordinated kinetic test of wheel-cranking (15).

Defining the rates of observed decline may be difficult, because Calloway (16) has found at least three different shapes of the regression curves. By definition, simple zero-order mathematical functions produce a linear regression when arithmetic differences in physiological capability are plotted against arithmetic differences in time. Nerve conduction velocity exemplifies such a relationship (17).

First-order mathematical functions produce a linear regression when logarithmic differences in physiological capacity are plotted against arithmetic differences in time, such as with the threshold of vibration perception (18).

The third type of regression, i.e. second-order mathematical function, is linear when logarithmic differences in both function and age are plotted graphically. Many examples have been described, including per cent body water (19), a particularly important clinical consideration.

PHYSIOLOGICAL VARIANCE

To consider only the physiology of the optimally functioning, young-adult animal is the biological equivalent of looking at a still photograph instead of a cinema. There are different physiologies for each period of life: growth, maturity and senescence. But compared to the study of optimal adult function, the study of senescence presents practical and conceptual difficulties, because of the need

to deal with a moving homeostasis, or homeorrhesis (20).

In terms of a systems operational model, aging is the loss of information leading to system deterioration and secondary compensations. In biological terms, there is a consequent failure of adaptation, initially partial and often individually irregular. The deterioration of homeostasis produces a steady increase in variance. Among individuals, there is variation in the system most subject to variance, resulting in even greater variation in surviving compensatory mechanisms.

Genetic determinants specify in which system deterioration will be dominant. These genetic factors determine the primary rate of decline, but system selection and rate of failure are modified by environmental factors. Inversely, environmental determinants may initiate deterioration in a system and determine its decremental rate, while underlying genetic factors influence the process, particularly from the reserve capacity inherent through constitutional endowment.

Many physiological parameters in populations have been analyzed statistically using data acquired in both cross-sectional and longitudinal studies. The analyses have aimed to characterize the general trends in physiological responses with age, and to predict the likelihood of particular changes in particular individuals. In subjects of a given old age, any cross-sectional study of function transects a wide and diverging distribution. The range and variance increase with age, as in age-specific excretion of gonadotrophins (21). This increasing variance makes it necessary to study larger populations in order to assure representative samples. However, there are progressively fewer survivors as a population ages, making it more difficult to obtain samples. The distribution of values may be normal, bimodal or even plurimodal. Increasing variance is illustrated in the diastolic blood pressure; here the mean age-specific value rises in a gentle curve, but the rise in age-specific variance is steeper and the increase in age-specific range proceeds even more steeply (22).

These observations suggest that homeostasis becomes increasingly unstable. Pertubations requiring homeostatic response become larger, while capacity to respond becomes smaller. Incipient failures mobilize fall-back or compensatory mechanisms at all levels and these adaptations initially can mask a shift in the homeostatic balance point.

For example, senescent nephron loss may be compensated by hypertrophy of surviving nephrons, but evenutally these will lose the capacity for further compensation, either inherently or from vascular, interstitial or extrarenal factors, or from a combination of these.

EVOLUTION OF AGING

These adaptive age changes are not random, but appear to have evolved with the

increasing life span characterising those mammals which have a long post-reproductive life (2).

Sacher (23) has developed a mathematical model for the homeostatic process, using a specific point of failure. In reality, each primary physiological process is underpinned by a secondary process, and there may be many more layers of compensation - each with its own point of failure. In essence this is a system of 'overinsurance' (2), of adaptation by the capacity for drift in each major system. Thus in higher animals, homeostatic reliability has been achieved through secondary adaptations rather than by an age-proof primary process. Such overinsurance' probably operates in intracellular as well as in inter-tissue systems. This complex, 'adaptive regulatory' process (20) tends to preserve the organism's vitality and prolong its life span.

Ultimately however, the repertoire of adaptation becomes exhausted. The amplitude of the challenge to homeostasis which can be met effectively, is diminished. The path of homeorrhesis becomes narrowed and the physiology of aging can be summarized in the term 'homeostenosis' (24) - a term probably familiar to every nephrologist. Homeostenosis - the erosion of homeostatic controls, usually is demonstrable during severe stress only. The critical level of homeostatic tolerance has decreased progressively with age but only in very advanced age do minimal insults cause death.

This concept will echo through the discussions regarding chronic renal failure. Increasingly severe degrees of renal insufficiency have their counterparts in phases of senescence. Stages of old age also have been described: The first is that time when one has indeed aged but when he alone is aware that he has grown old; the second is when an individual realizes that he has grown old and the rest of the world also is aware of this; and finally, the third stage of senescence is that time when the individual who has grown old is no longer aware of the fact that he is old, but the rest of the world patently is aware of it (25).

In summary, normal aging is an involuntionary process which is apparent both functionally and morphologically. Senescence may be regarded as the analog of chronic renal insufficiency at a whole body level. The consequent decrease in adaptation strongly resembles the natural history of a disease. The distinction between physiology and pathology is not easy. In our real world, attempts to make this distinction may appropriately evoke a traditional invocation: 'Give me the peace to allow me to accept what I cannot change, to give me courage to change what I can, and to give me the wisdom to distinguish between the two.'

REFERENCES

1. Comfort A (1956). The Biology of Senescence (ed l), London, Routledge and Kegan Paul.
2. Comfort A (1979). The Biology of Senescence (ed. lll), New York, Elsevier.
3. Andres R (1971). Aging and diabetes, Med Clin N Amer 55:835-846.

4. Strehler BL (1977). Time, Cells and Aging, New York, Academic Press, pp. 12-16.
5. Exton-Smith AN, Millard PH, Payne PR, Wheeler EF (1969). Pattern of development and loss of bone with age, Lancet 2:1154-1157.
6. Williams ME (1984). Clinical implications of aging physiology, Am J Med 76:1049-1054.
7. Blumenthal HT (1975). Athero-arteriosclerosis as an aging phenomenon, in Goldman R, Rockstein M (eds). The Physiology and Pathology of Human Aging, New York, Academic Press, pp. 123-147.
8. Wissler RW, Vesselinovitch D (1976). Studies of regression of advanced athersclerosis in experimental animals and man, Ann NY Acad Sci 275:363-378.
9. Gotto AM (1981). Regression of atherosclerosis, Am J Med 70: 989-991.
10. Nash DT (1981). Letter to the editor, Geriatrics 36, 6:158.
11. Calloway NO (1965). Constants of senile decay, J Am Geriat Soc 13:125-142.
12. Rossman I (1971). The Anatomy of Aging, in Rossman I (ed) Glinical Geriatrics, Philadelphia, J.B. Lippincott.
13. Helfman PM, Bada JL (1976). Aspartic acid racemization in dentine as a measure of aging, Nature 262:279-281.
14. Masters PM, Bada JL, Zigler JS (1977). Aspartic acid racemization in the human lens during aging and in cataract formation, Nature 268:71-73.
15. Shock NW (1974). Physiological theories of aging, in Rockstein M (ed) Theoretical Aspects of Aging, New York, Academic Press, pp. 119-136.
16. Calloway NO, Foley CF, Lagerbloom P (1965). Uncertainties in geriatric data II - Organ size, J Am Geriat Soc 13:20-29.
17. Magladery JW (1969). Neurophysiology of aging, in Birren JE (ed) Handbook of Aging and the Individual, Chicago, University of Chicago Press, p.17.
18. Weiss AD (1959) in Birren JE (ed) Handbook of Aging and the Individual, Chicago, University of Chicago Press, p.535.
19. Shock NW, Watkin DM, Yiengst MJ et al (1963). Age differences in the water content of the body as related to basal oxygen consumption in males, J Gerontol 18:1-10.
20. Frolkis VV (1982). Aging and Life-Prolonging Processes, Vienna, Springer-Verlag.
21. Albert A, Randall RV, Smith RA, Johnson CE (1956). Urinary excretion of gonadotropin as a function of age, in Engle ET, Pincus G (eds) Hormones and the Aging Process, New York, Academic Press, p.49.
22. Burger M (1954). Altern und Krankheit, Leipzig, G. Thieme.
23. Sacher GA (1965). Aging and Levels of Biological Organisation, Chicago, University of Chicago Press.
24. Schreiner GE, Seligson DA (1961). in Schreiner GE, Maher JF Uremia: Biochemistry, Pathogenesis and Treatment, Springfield IL, Charles C. Thomas p.140.
25. Loewi O (1975). Cited by Rockstein M, in Goldman R, Rockstein M (eds) The Physiology and Pathology of Human Aging, New York, Academic Press.

3. SENILITY AND MATURITY: PSYCHOSOCIAL ASPECTS OF AGING

H.M. ROSEMARY MEIER, MB, CHB., MSC., MRCPSYCH., FRCP(C)
RICHARD IAN OGILVIE MD, FRCPC, FACP

This meeting has been convened out of concern for the impact on the elderly of end-stage renal disease (ESRD). This paper will present an overview of the psychosocial aspects of aging and will emphasise the theme of development, regarding aging as part of the continuum of life. The perspective is that of a psychiatrist, and the theme echoes Jarvik's salutary reminder that 'elderly designates a heterogeneous group of persons united by chronologic age, but not necessarily by physiologic, psychologic, or social functioning.' (1) We may focus on the development and experience of the individual, but at no age or stage of life is a man 'entire of himself' (2), and any consideration of aging must take into account the context of the society and times in which the man lives. Here 'man' denotes a 'person'; John Donne was referring to mankind, and the human experience. In this context, we may have to distinguish between person, man, or woman, in order to recognise differences in psychological and physiological development, and socio-cultural experience of men and of women. In our day and age, many of the issues of aging -- becoming old, being old, caring for the old -- are women's issues. Planners of health care services and individual care givers are beginning to recognize the importance of the interactions between the individual and society, and the necessity of considering each individual and environment.

William Shakespeare (3) described the seventh age of man as 'last scene of all that ends this strange eventful history'. This view of the aged as 'second childishness, and mere oblivion, sans teeth, sans eyes, sans taste, sans everything' persist even today, even though we recognise several aspects, which are independent of chronological age. 'Vigor' represents biological age, while 'functional age' is an aspect of individual psychological age. Social aging represents the interplay between the individual and society, and the environment in general. Erik Eriksen (4) by describing eight states of development in which each stage has a specific task, has provided a helpful conceptual background to the care of the elderly, which also may be valuable in individual therapy. This epigenetic approach can be accepted only if one recognizes the importance of

factors common to the cohort, or group born at the same time. Many assumptions about aging are confusing because they are based on observations made at the same time but on people of different ages -- cross-sectional slices - these have been interpreted as if they related to change over time, and could be equated with change associated with aging. To extrapolate change over time, one needs to observe a group over time, ideally a prospective longitudinal study. The educational and economic experience of the group depends on the size of birth cohort, and not only on the proportion of the elderly in a population at a particular time.

The concept of adulthood has a strong influence on the experience of aging. Jung (5) reflected that 'a human being would certainly not grow to be 70 or 80 years old if his longevity had no meaning for the species to which he belongs... The afternoon of human life must also have a significance of its own, and cannot be merely a pitiful appendage to life's morning.' In addition to the meaning of an individual's life, the sequence of Eriksen's tasks culminates in the 'acceptance of one's one and only life' and a sense of integrity rather than despair. The concept of 'the stewardship of life' is reminiscent of Kohlberg's (6) theory of moral development. Beginning with primitive ideas of retribution, stages of moral cognition arise which contribute to the establishment of adult moral values and the capacity for mature behaviour. It is important for those who see the consequences of aging chiefly in terms of social or medical pathology to recognize that the process of aging has many dimensions.

PSYCHOSOCIAL CONCEPTS

The development of identity is a function of the integration of personality: it is affected by the wishes, fears, defences and conflicts characteristic of the human condition. Many of the explanations of the life cycle are based on observations of patients, or of those identified as needing help. Normality seems difficult to define in the later stages and the findings are lively but confusing. Mandell and Salk (7) describe the developmental fusion of intuition and reason as 'apparent random processes that self-organise in time, becoming complex, yet stable, structures', implying a 'hidden organization'. Neugarten (8) offers the idea of the 'social clock', according to which life events are either 'on time' or occur unexpectedly, and, being 'off time', represent crises. Freud (9) attributes a vital role to the unconscious, which mediates interactions between biological constitution and psychological experience. 'Timing' is seen in the stages pf psychosexual development, and in the integration of internal psychological forces with external social pressures. Hartmann (10) conceptualizes adaptation as 'primarily a reciprocal relationship between the organism and its environment'. The tasks associated with life stages emphasize that transition and adaptation are part of normal development, rather than pathological crises.

Indeed, like adolescence, aging includes several 'normative crises'.

As in adolescence, the individual's life cycle has to be considered in context of the life cycle of the family. The most rapid increase in any age group 65 and over is among those 85 and over; the children of those 'old-old' are themselves 'young-old' because they are aged 65 or more. Their children in their 40's may be coping with their adolescents, and also keeping an eye on both parents and grandparents. The 'young-old' may also be a 'sandwich generation', finding that the 'empty nest' is inhabited again by middle-aged children returning home after the end of a marriage, or the end of employment. The age range (65 and over), can extend over four decades. The 'frail elderly' aged 85 and over differ from those under 75, even if they are in good health.

SOCIOCULTURAL ASPECTS

The range of life events encountered by an individual has been studied by Holmes and Rahe (11). If an event is anticipated, it causes less stress than if it occurs unexpectedly. Neugarten and her colleagues (8) compared the consequences of an event such as widowhood, when it is anticipated at an appropriate age - in the late 60's or 70's -- and when it is 'off time', for example, in the 30's or 40's.

Social supports help us to cope with 'on time' events, however stressful they are. Often the individual's 'age status' is crucial in the development of a social network at a specific time, particularly if this network is developed because of recognised needs, such as frailty or specific illness. The individual's social role is reflected in the way he accepts, or develops, a place in such a specific social network, which is created often at the instigation of others, such as health-care workers. Throughout life an individual may have 'role portfolio', a multiplicity of attributes and functions; however, usually this becomes progressively depleted and, as life goes on, one's place in society becomes more marginal. Few norms exist to guide behaviour as one grows old and very old, or for determining what is expected or acceptable. The status of the very old is changing because there are more such people, even though society perceives their needs and perhaps their very existence as 'a problem'. As Rosow (12) forthrightly observes, the crucial people in the aging problem are not the old, but the younger groups, because it is the rest of us who determine the status and position of the old person in the social order.

SENSE OF CONTINUITY

The stages of development provide a framework for a sense of continuity of the individual, but it also has relevance for the relationships between generations. An elderly Bernard Berenson (13) asserted that 'difference of age never made any

difference to me at any moment in my life, nor does it now. That is to say, it would not, but for the increasing age consciousness that has crept upon us since I myself was a young person. During my visits to the U.S.A., I began to feel more and more parked into a round where we had to keep turning with our contemporaries in their circle of Dante's inferno, seldom meeting the older, never the young. Indeed, we never saw the children of our best friends at their own table, and seldom knew them by sight'. This wry observation reminds us of the concept of generativity - Eriksen's task of midlife. The literature, professional and more literary, contains many references to the relationship between middle and old age, between maturity and senility. Vida Scudder asserts that 'an energetic middle life is, I think, the only safe precursor of a vitally happy old age'. Janet Baird (17) comments that 'the dangerous and pitiful deterioration of later life is not the product of the aging process, but of a stagnant and inert period of maturity'. Henry Ward Beecher reminds us that 'if you have only two or three things that you can enjoy, and these are things which time and decay remove from you, what are you going to do in old age?'. An important element in the sense of continuity throughout the life cycle is this sense of active participation and commitment beyond work and immediate concerns. It is consolidated in the resilience and responsibility which can mark late adult life -- the epitome of maturity. One marker of the attainment of this stage is the change in perspective, when age is measured not as time since birth -- the candles on the birthday cake -- but in terms of time left to live. Again, the timing and sequence of life events often determine how they can be dealt with. The settings of the biological and social clock tend to coincide.

EPIPHENOMENA OF AGING

Often regarded as synonymous with aging are events which tend to occur because one has lived to a particular age or stage: Blazer and Busse (13) contrast senescence or primary aging with senility or secondary aging (Table I).

Chronic and later end-stage renal disease introduce factors that influence the usual course of senescence and thus contribute to the development of senility. Individual success in coping with these events, which come because one has lived to the later stages of life, depends upon such factors as previous life experience, and how one has prepared for the particular event: perception of the event itself, and the resources available, which include not only state of physical health but cognitive function, state of mind, and socio-economic resources.

We can regard retirement as a normal or expected crisis, although professional workers may see Wilder Penfield's syndrome of retirement neurosis or 'false senility'. To cope with retirement, one tackles the adaptive tasks of later life which have been described by Pfeiffer (14), which include adapting to loss and also reviewing one's identity (one's sense of continuity with life beyond work),

Table I: Aging*

Primary aging:	Senescence
	- Hereditary factors
	- Independent of stress
	Trauma
	Acquired disease
Secondary aging:	Senility
	- Environmental factors
	- Particularly trauma
	Disease

* Busse and Blazer, (13).

and finally remaining active in order to retain function. Here we emphasize the importance of continuing physical activity, social interactions, intellectual and emotional stimulation - all of which reinforce the capacity for self care.

Widowhood, in contrast, follows bereavement. In the weeks following, one needs to do 'grief work' and mourning continues through its stages over many months -- and perhaps is never completed. Kubler-Ross's (15) familiar stages may not be altogether relevant to the elderly. The idea of a sequence of stages is helpful for the bereaved of all ages, and also to those concerned for them. But the vogue has passed for an active working through of the stages of denial, anger, and acceptance; we now adopt a quieter and more experiential approach, particularly if the bereavement is not unexpected. Widowhood may have a profound influence on both biological and psychosocial function, because widows and widowers are more susceptible to physical illness not only in the period immediately following bereavement, but also within the first year (16). Biological vulnerability is increased by such psychosocial factors as increasing social isolation, and poverty. The most disadvantaged group in our society are widows.

With increasing geographic and social mobility, and with divorce, remarriage, and the complexities of reconstituted families, being a grandparent is not what it used to be. As grandparents age, they assume an increasingly peripheral role in the lives of grandchildren. Grandparents seem to have increasingly symbolic and emotional functions, and indeed access to grandchildren depends increasingly upon the goodwill and maturity of the adult children. This access is an aspect of filial maturity - anther stage in the family life cycle. According to Sussman (17), the adult child must assume the help-giving role in such a way that the aging parent experiences that child as dependable, while he or she is not made to feel that they have become a burden. The degree of help required is related not only to the grandparent's health, but also to the quality of the couple's marriage. During the later stages of life household management, care during illness, and emotional gratification are some of the major expectations of

marriage. However, emotional gratification is the vital aspect, and now we are more accepting of the need for emotional and sexual gratification in the elderly. The clinical assessment should enquire about sexual activity even when the assessor may be as young as the patient's children or grandchildren.

SURVIVAL AND LONGEVITY

Contemporary changes in survival and longevity have altered greatly traditional life experiences. Health more than age *per se* determines the place of work and marriage, and intergenerational relationships in individual lives, and declining health forces profound changes in individual functioning. Morale, another key factor, includes a zest for life in the present, a positive self-concept and mood tone, qualities of resolution and fortitude, a sense of congruence of future goals, and a sense of achievement in the past -- similar to the sense of continuity. Neugarten (18) calls the factors contributing to homeostasis in the face of severe crisis an 'adaptive paranoia of old age', reminding one of the adage, 'It's not that one becomes crabby the longer one lives, the crabby live longer'. Lieberman (19), describes this homeostasis as a dimension of maturity, rather than senility, and noted that being aggressive, irritating, narcissistic, and demanding, with a certain amount of magical thinking and perceiving oneself as the centre of the universe, seemed to contribute to homeostasis in the face of crisis. The elderly are helped to deal with changes to come by a sense of active mastery over what has happened before (20). The clinical history taking may serve the function of life review and hence constitute a form of therapy.

With respect to cognitive changes over time, evaluation of cognitive function is a crucial part of clinical assessment, but here one is handicapped by many confounding variables, several of which reflect health status rather than age *per se*. Piaget's (21) scheme of cognitive development provides another epigenetic view of development. These stages have not been studied much beyond early adult life, but it appears that cognitive competence also is lost by stages; the individual regresses toward earlier, more concrete operations, as he loses his higher functions and abstract abilities. Frequently this is manifested in post-operative confusional states, where the patient loses acquired languages and then regains them in the sequence in which they were learned: the mother tongue is retained best. Shaie's (22) concepts of cognitive re-organization across the lifespan, in relation to life experiences also sheds light on the psychosocial aspects of aging.

SENILITY AND MATURITY

This 'age irrelevant but sequence relevant' (23) approach provides a

multidimensional perspective of aging, which views growing older in terms of the ability to adapt to change. Intrapersonal and interpersonal psychological factors contribute to the sense of identity, and to the rhythms of the individual and family life cycle. Socio-cultural factors, including sex roles and marital status, contribute to the individual's sense of continuity, and to his perspective of the life course. At 70, Wilma Donoghue (24) asserted: 'I have more measure of feeling about aging when I see people I was young with, at the University, and all of a sudden I see them in the version of old people. I may not have seen them for a long time, and then I see them after theyve stepped over the threshold, and are now looking old. I have never thought of them as older people, and suddenly I see them as old, and I gather a sense of their being different, and I have thought about this. To them, just like I am to myself, there is a consistent personality. I don't recognize that I was 20,30, 40, 50, 60, and so forth. I just seem to be a consistent personality, that's lived a whole life. I realize I look the same to them, as they look to me. As far as my feeling is concerned, I don't have that sense. I have the same sense of being a whole person, with spirit and interests that are consistent with my life'.

Weinberg (25) emphasizes that aging is associated with a new balance in the world view, with a self assuming a greater importance. There is a greater preoccupation with the inner life, greater concern with satisfaction of one's own needs, and decreased emotional ties to people and objects; this may be because attachments are fewer, following losses and bereavements, than because these attachments are less intense. This process leads the individual to focus on past life experiences, reminiscences, inner affective experiences, and also on health and bodily functions; he meets essential needs by 'exclusion of stimuli' -- being able to restrict attention to the most psychologically relevant stimuli, and apparently ignoring the multitude of details of everyday life which have less psychological relevance. When their well-being is under discussion, deaf older people, for example, may seem to hear what they are not expected to hear. Weinberg associates this exclusion of stimuli with the psychoanalytic concept of subception, and distinguishes it from denial. This mechanism also may help us to understand apparent discrepancies in the individual's understanding, and acceptance of illness or impending death.

The concept of developmental stages in many dimensions of individual life -- psychological, psychosexual, psychosocial, moral and cognitive -- can help us to understand the apparent variability in intellectual and emotional insight, or in the understanding of impending death and 'being ready to die'. Anticipation and preparation for the stages and transitions of life contribute to developing maturity, including the capacity to make choices, and to sustain an adaptive value system. This development of a philosophy of life, whether couched in spiritual or religious terms, includes an acceptance of mortality. Maturity is not necessarily synonymous with wisdom, but is comprised of as series of abilities and biological systems, which peak at different times. Maturity is a phase of

primary aging or senescence. Aging compromised by psychosocial dysfunction or poor health is secondary aging or senility. The great challenge to the individual and to society is senility rather than aging.

REFERENCES

1. Jarvik, LF and Falek, A. 1963. Intellectual Stability & Survival in the Aged. Journal of Gerontology, 18:173-176.
2. Donne, J. 1628. Devotions. ed. Helen Gardner (1957). Penguin Books. Middlesex.
3. Shakespeare, W. 1623. As You Like It. Act II, Scene vii. Line 139.
4. Erikson, EH. 1959. Identity and the Life cycle. W.W. Norton & Co., 1980. New York and London.
5. Jung, CG. 1933. Modern Man in Search of a Soul. Harcourt, Brace, New York.
6. Kohlberg, L and Kramer L. 1969. Continuity and Discontinuity in Childhood and Adult Moral Development. Human Development, 12:93- 120.
7. Mandell, AJ and Salk, J. 1984. Developmental Fusion of Intuition and Reason: A Metabiological Ontogeny. Basic Books, New York.
8. Neugarten, BL and Datann A. 1973. Sociological Perspectives on the Life-Cycle: In Life-Span Developmental Psychology: Personality and Socialisation. ed. PB. Baltes & KW Schaie, New York, Academic Press.
9. Freud, S. 1905. Three Essays on the Theory of Sexuality. Standard Edition, 7:125. London, Hogarth Press.
10. Hartmann, H. 1964. Essays on Ego Psychology. New York. International Universal Press.
11. Holmes, T and Rahe, R. 1967. The Social Readjustment Rating Scale. Journal of Psychosomatic Research, 11:213-18.
12. Rosow, I. 1974. Socialisation to Old Age. Berkeley. University of California Press.
13. Busse, EW and Blazer, D. 1980. The theories and Processes of Ageing. Chapter 1 of Handbook of Geriatric Psychiatry. ed. Busse, E.W. and Blazer. New York, Van Nostrand Reinhold Company.
14. Pfeiffer, E. 1978. Ways of Combining Functional Assessment Data, in Duke-OARS: Multidimensional Functional Assessment: The OARS Methodology. Durham, North Carolina, Duke University Center for the Study of Ageing and Human Development.
15. Kubler-Ross, E. 1969. eath and Dying. New York, MacMillan.
16. Parkes, CM. 1972. Bereavement. International Universities Press. New York.
17. Sussman, M. 1976. The Family Life of Old People. In Handbook of Aging and the Social Sciences. ed. Binstock, RE & Snares, E. New York. Van Nostrand Reinhold.
18. Neugarten, B. 1979. Time, Age & the Life-Cycle. American Journal of Psychiatry, 136:887-94.
19. Lieberman, MA. 1975. Adaptive Processes in Late Life. In Life- Span Developmental Psychology: Normative Life-Crises. ed. Datann, N & Ginsberg, L. New York, Academic Press.
20. Butler, RN. 1936. The Life Review: An Interpretation of Reminiscence in the Aged. Psychiatry, 26:63-76.
21. Piaget, J. 1970. Piaget's Theory in Carmichaels Manual of Child Psychology. 3rd Edition. ed. Mussen, PH. New York, John Wiley and Sons.
22. Schaie, KW. 1977- 8. Toward a State Theory of Adult Cognitive Development. International Journal of Ageing and Human Development, 8:129-38.
23. Offer, D and Sabshin, M. 1984. Normality and the Life Cycle. New York. Basic Books Inc.
24. Weinberg J. 1975. Geriatric Psychiatry in Comprehensive Textbook of Psychiatry. 2nd Ed. Vol. 2. ed. Freedman, AM, Kaplan, EH, & Sadock, BJ. Baltimore, Williams & Williams.
25. Weinberg, J. 1975. ibid.

4. PHARMACOKINETICS AND PHARMACODYNAMICS IN THE ELDERLY

RICHARD IAN OGILVIE MD, FRCPC, FACP

INTRODUCTION

The past 15 years have been marked by a great increase in knowledge about the time course and magnitude of absorption, distribution, biotransformation and elimination of drugs in normal volunteers and in patients with disease. Combined with knowledge of the time course and magnitude of drug effects, we can plan dose schedules, initiate treatment and in many instances follow it by monitoring therapeutic drug concentration to optimize drug efficacy and prevent or reduce drug toxicity.

Adverse drug reactions are common, averaging 10-18% in many studies (1). Although Ogilvie and Ruedy found no increase in incidence in the elderly (1), a study in Northern Ireland found an incidence of 6.3% in 667 patients less than 60 years old and 15.4% in 493 patients more than 60 years of age (2). Another group in Great Britain found that 81.3% of 1998 admissions to departments of geriatric medicine were ingesting prescribed drugs at the time of admission and 15.3% of them had adverse reactions (3). It has been demonstrated that the application of simple kinetic knowledge to the prescribing of digoxin can reduce markedly the incidence of adverse reactions (4). Better knowledge of alterations in kinetics and dynamics of drugs with age may help to reduce adverse drug reactions in the elderly.

Drug kinetic and dynamic information is being assembled for special groups such as neonates, children, pregnant females, patients with renal or liver failure and the elderly. Although the elderly have a disproportionate number of illnesses and receive a disproportionate quantity and number of drugs we do not have adequate data regarding pharmacokinetics and pharmacodynamics in them. Few centers are dedicated to such studies, for example, in Canada, only the University of Manitoba (Drs. P. Mitenko, F. Aoki and D. Sitar) has a geriatric clinical pharmacology unit. Healthy elderly individuals are not ready volunteers for clinical pharmacological studies, often claiming that they have already 'done their bit for society.' The search for information about a single drug in the sick

elderly patient is complicated by the presence of multiple diseases and the variety of drugs that these patients receive. Most studies have too few volunteers or patients, and in addition, the design of all current studies are cross-sectional rather than longitudinal and provide information only about age differences in pharmacokinetics rather than changes with aging. Except for drugs predominantly excreted by the kidney, one cannot easily generalize on the magnitude of age differences in pharmacokinetics. As with other age groups, interindividual differences due to environmental, genetic, or physiological differences are important determinants.

DRUG ABSORPTION

There has been little evidence of altered drug absorption in the elderly compared to younger individuals, despite a reduction in gastric acid production with age, delayed gastric emptying and intestinal motility or a reduction in the number of absorbing cells. Considerable interindividual variation in lag times and the rates and extent of absorption of most drugs at any age, makes it difficult to demonstrate changes with age in small numbers of subjects. For example, Shader *et al* (5) observed a slower apparent first-order half-time of 20 min for chlordiazepoxide in eight elderly subjects compared with an absorption half-time of 6 min in 28 younger subjects. However, variability made it impossible to demonstrate a statistically significant difference. A study by Cusack *et al* (6) showed that the time to peak plasma digoxin concentrations was delayed 60 min in the elderly compared to young subjects but overall bioavailability was similar in both groups. On the other hand, several workers have reported diminished first-pass biotransformation of propranolol (7), labetalol (8), lidocaine (9) and l-dopa (10) and raised the possibility that these drugs would have increased plasma concentrations and effect in the elderly patient.

Decreased absorption of drugs absorbed by active transport mechanisms (eg. iron, thiamin, vitamin B12) has been suggested but not confirmed. As noted earlier, the overall bioavailability of l-dopa is increased because of a decreased first-pass biotransformation in the elderly. Also, the absorption of acid-labile drugs such as potassium penicillin may be increased.

DRUG DISTRIBUTION

Lean body mass as a proportion of total body weight is reduced in the elderly. After comparing age groups 18-25 years of age and 65-85 years, Novak (11) estimated that body fat increased from 18 to 36% of body weight in men and from 33 to 45% in women. The apparent volume of distribution of lipid soluble drugs such as diazepam (12) and lidocaine (9) is increased in the elderly. Total

body water may be reduced some 10-15%, thus, in older subjects the ingestion of drugs such as ethanol, which are distributed in body water, would produce higher peak plasma concentrations although rates of biotransformation are unchanged (13). Their reduced lean body mass results in higher plasma digoxin concentrations because digoxin is largely distributed to skeletal muscle (5,14). This effect is in addition to the delayed elimination caused by impaired renal function (4,6).

Occasionally, the elderly have reduced serum albumin concentrations and hence may have increased plasma clearance of highly bound drugs such as warfarin, phenytoin or phenylbutazone (15-17). However, changes in plasma protein binding of drugs generally have been small and hence a concomitant increased plasma clearance of the free portion would not be expected to alter the clinical effects at steady state. Apparently genetic differences are more important in determining steady state concentrations of a drug like phenytoin than are age, weight, or gender (18). In contrast to the slight reduction in plasma protein binding of acidic drugs, the binding of basic drugs may be increased because alpha 1 - glycoprotein concentrations tend to increase with age.

Bender has estimated that cardiac output decreases some 30% from age 25 to 65 years (19). Cerebral, skeletal and coronary blood flow do not decrease in proportion to the overall decrease in cardiac output. The splanchnic, liver and renal circulations are decreased more than the percentage change in total cardiac output. Thus, the distribution of drugs to the brain and heart may be more efficient in the aged but the distribution of drugs to the liver and kidney is probably less efficient.

Reduced renal blood flow in the elderly reduces the rate of delivery of furosemide to the inner tubular cell - site of action. Its peak effect is less prominent and delayed although the total water and electrolyte loss it produces is similar to that in younger patients (20). A delay in distribution may be responsible inpart for the delayed and blunted blood sugar response to intravenous tolbutamide in the elderly (21) however, this may also reflect a decreased insulin receptor number or responsiveness.

DRUG ELIMINATION

Total body clearance is the estimate of the patient's ability to eliminate the drug either by biotransformation or by excretion. This figure represents a hypothetical volume of blood from which the drug is completely cleared per unit of time. Most drugs are eliminated by hepatic biotransformation or renal excretion. Total clearance cannot exceed the total blood flow to the organ or organs responsible for elimination. Total clearance determines the extent of drug accumulation, that is, the plasma concentration at steady state (Css), during repeated dosing at equal intervals .

$$Css = \frac{\text{dose per interval of time}}{\text{clearance}}$$

This formula assumes complete bioavailability. A reduction in clearance will produce higher steady-state plasma-drug concentrations with the possibility for greater (beneficial or toxic) effects. Obviously, knowledge of the patient's ability to clear a drug is important for rational therapy.

Hepatic biotransformation of drugs: Relative to changes in cardiac output, hepatic blood flow is disproportionately decreased in the elderly (19). Hepatic cell and enzyme activity also are reduced but routine measurements of liver function do not change with age. In spite of these changes, interindividual variation in drug elimination by the liver apparently is more important than aging *per se*, for example, a reduction in hepatic blood flow should lead to a reduction in total clearance of drugs with flow-dependent clearance. However the data are conflicting. Reduced clearance in the elderly has been observed for propranolol (7) but not for lidocaine (9) although both undergo flow-dependent clearance. Antipyrene elimination is reduced in old age (22) suggesting that elimination by phase 1 oxidative mechanisms (hydroxylation and N-dealkylation) may be impaired in the elderly. However, studies of drugs such as the benzodiazepines (23) or theophylline (24) have given conflicting results. Apparently ageing has even a lesser effect on phase II glucuronide-conjugation mechanisms.

Environmental and genetic factors probably have a very large influence, for example, Vestal *et al* (25) reported a sixfold interindividual variation in the hepatic biotransformation of the marker drug-antipyrene, far exceeding the effect of age. In fact, only 3% of the variance in clearance could be attributed to age alone. Hepatic biotransforming enzymes in the elderly are less susceptible to induction by drugs (26) or by environmental factors such as cigarette smoking (27). Thus the average total clearance of a drug like theophylline may be at the upper end of the range for younger subjects due to decreased enzyme induction by protein or smoking in the elderly patient (24,28). The aged may show a decreased total clearance for drugs such as the barbiturates, benzodiazepines, imipramine, nortriptyline, acetaminophen, phenylbutazone, quinidine, theophylline, caffeine and tolbutamide but probably interindividual variation is more important than the effect of aging on liver function.

Renal excretion of drugs: Renal elimination is reduced for drugs eliminated by glomerular filtration because creatinine clearance declines with age. Cockcroft and Gault (29) have provided a formula for estimating changes in creatinine clearance derived from age, weight and serum creatinine.

$$\text{Creatinine clearance} = \frac{(140 - \text{age in years}) \times (1.2) \times (\text{wt in kg})}{\text{serum creatinine in u Mol/L}}$$

for males or (1.0) x (wt in kg) for females to give an estimate in ml/min/1.73 M 2. In severe obesity or malnourishment, one should use ideal body weight for the calculation. In this formula age is important because the decline in muscle mass may result in an unaltered serum creatinine. The physician should make reductions proportional to changes in renal function for the maintenance doses of a large list of drugs that include digoxin, quinidine, cimetidine, aminoglycoside antibiotics, lithium, salicylates, chlorpropamide and several other oral antidiabetic agents.

It is important to recall that many drugs have active metabolites which are eliminated by the kidney. Thus in the elderly decreased renal function may result in significant accumulation of these metabolite(s). For example, the major metabolite of the antiarrhythmic - disopyramide has much greater anticholinergic properties and a longer half-life than the parent compound (30). Accumulation of this metabolite may produce severe mental confusion, psychosis, blurred vision, bladder atony and tachycardia. Monitoring plasma concentrations of the parent drug alone would not detect increased concentrations of the metabolite. Procainamide is excreted partly unchanged by the kidney and is partly biotransformed to N-acetylprocainamide, which is also eliminated by the kidney; it too has a longer half-life than the parent compound. Renal failure can lead to altered proportions of the two compounds (31). In monitoring plasma concentrations, one must be aware of the assay specificity for parent and metabolite, because some assays do not differentiate between them. The metabolites of meperidine can produce hyperexcitability, mood change, tremor, myoclonus or seizures. In addition, meperidine clearance is reduced in the elderly (32). As another example, the active metabolites of diazepam and flurazepam are largely eliminated by the kidneys.

Considerable interindividual differences exist in the changes of renal function with age. Also, congestive heart failure, malnourishment or dehydration may alter renal function. For these reasons it is desirable to measure creatinine clearances by 24-hour urinary collections as well as monitor plasma-drug concentrations.

The elimination of salicylates follows non-linear kinetics after as little as two aspirin tablets which can saturate the hepatic enzymes responsible for conjugation (33). With increasing doses of A.S.A., the kidneys eliminate a greater proportion unchanged as salicylic acid and as a result, the elderly may accumulate salicylates due to renal impairment (34). In addition, one cannot use tinnitus as a guideline in the elderly because they may have coexistent hearing loss and decreased VIII cranial-nerve function.

ALTERED SENSITIVITY TO DRUGS

A major problem in the elderly is altered sensitivity to drugs in the absence of

major alterations in their kinetic disposition. In some instances, this has been related to changes in specific receptor number or affinity. The concentration of receptors for steroids, insulin, glucagon and prolactin are reduced with age (35) whereas the affinity of beta-adrenergic receptors was reduced rather than a change in receptor density (36). Whatever the mechanism, the elderly have a reduced responsiveness to isoproterenol and other beta agonists (37). Also baroreflex sensitivity is reduced in the elderly making them more sensitive to orthostatic hypotension, especially when on antihypertensive, neuropsychiatric or other vascular active agents.

Benzodiazepines are more active in the elderly in spite of lower concentrations (due to an increased volume of distribution) and unaltered clearance (5,23,38,40). Increased responsiveness to analgesics such as morphine (41) may be due to increased distribution to the central nervous system (42) because total clearance is little altered. The minimum alveolar concentration for halothane is the highest in newborns and lowest in the elderly (43). The amount of local anesthetic required to anesthetize a given number of spinal segments by epidural blockade decreases with age (44). Elimination of the neuromuscular blocking agents, pancuronium and d-turbocurarine, is reduced because of reduced renal function (44-45) but this only partly explains the increased responsiveness and prolonged effect in the elderly. Because warfarin kinetics are apparently unaltered in the elderly, their increased bleeding tendency, when on this drug, has been attributed to reduced production of clotting factors, and changes in blood vessels and platelet function (47). There is also increased bleeding in older patients on heparin (48).

IMPLICATIONS FOR DRUG-USE IN THE ELDERLY

This brief review makes it clear that, except for drugs predominantly excreted by the kidney, one cannot generalize concerning the magnitude of age differences in pharmacokinetics. Interindividual variations due to environmental, genetic or physiological differences are important determinants. Knowledge of the route of elimination and active metabolites of the drug is essential for rational therapeutic decisions. Measurement of renal function and plasma drug concentrations can be quite useful. The elderly show an increased responsiveness to drugs that act on CNS regardless of kinetic considerations and often show decreased responsiveness to hormones and agonists to hormonal receptors.
The reader is urged to consult recent reviews and monographs for a more extensive bibliography (49-52).

REFERENCES

1. Ogilvie RI and Ruedy J (1967). Adverse drug reactions during hospitalization Canad Med Assoc J 97:1450-1457.
2. Hurwitz N (1969). Predisposing factors in adverse reactions to drugs. Brit Med J 1:536-539.
3. Williamson J and Chopin JM (1980). Adverse reactions to prescribed drugs in the elderly: a multicentre investigation Age and Aging 9:73-80.
4. Ogilvie RI and Ruedy J (1972). An educational program in digitalis therapy J Amer Med Assoc 222:50-55.
5. Shader RI, Greenblatt DJ, Harmatz JS, Frankie RI, Koch-Weser J (1977). Absorption and disposition of chlordiazepoxide in young and elderly male volunteers J Clin Pharmacol 17:709-718.
6. Cusack B, Kelly J, O'Malley K, Noel J, Lavan J and Horgan J (1979). Digoxin in the elderly: pharmacokinetic consequences of old age Clin Pharmacol Ther 25:772-776.
7. Castleden CM and George CF (1979). The effect of aging on the hepatic clearance of propranolol Brit J Clin Pharmacol 7:49-54.
8. Kelly JG, McGarry K, O'Malley K and OBrien ET (1982). Bioavailability of labetalol increases with age. Brit J Clin Pharmacol 7:79-54.
9. Nation RL, Triggs EJ and Selig M (1977). Lignocaine kinetics in cardiac patients and elderly subjects. Brit J Clin Pharmacol 4:439-448.
10. Evans MA, Broe GA, Triggs EJ, Cheung M, Creasey H and Paull PD (1981). Gastric emptying rate and the systemic availability of levodopa in the elderly parkinsonian patient. Neurology 31:1288-1294.
11. Novak LP (1972). Aging, total body potassium fat-free mass, and cell mass in males and females between ages 18 and 85 years. J of Gerontology 27:438-443.
12. Reidenerg MM, Levy M, Warner H, Coutinho CB, Schwartz MA, Yu G and Cheripko JC (1978). Relationship between diazepam dose, plasma level, age and central nervous system depression. Clin Pharm Ther 23:371-374.
13. Vestal RE, McGuire EA, Tobin JD, Andres R, Norris AH and Mezey E (1978). Aging and ethanol metabolism Clin Pharmacol Ther. 21:343-354.
14. Chamberlain DA, White RJ, Howard MA and Smith TW (1970). Plasma digoxin concentrations in patients with atrial fibrillation. Brit Med J 3:429-432.
15. Hayes MJ, Langman MJS and Short AH (1975). Changes in drug metabolism with increasing age: 1. Warfarin binding and plasma proteins. Brit J Clin Pharmacol 2:69-72.
16. Hayes MJ, Langman MJS and Short AH (1975). Changes in drug metabolism with increasing age: 2. Phenytoin clearance and protein binding. Brit J Clin Pharmacol 2:73-79.
17. Wallace S, Whiting B and Runcie J (1976). Factors affecting drug binding in plasma of elderly patients. Brit J Clin Pharmacol 3:327-330.
18. Houghton GW, Richens A and Leighton M (1975). Effect of age, height, weight and sex on serum phenytoin concentration in epileptic patients. Brit J Clin Pharmacol 2:251-256.
19. Bender AD (1965). The effect of increasing age on the distribution of peripheral blood flow in man. J Amer Geriat Soc 13:192-198.
20. Chaudrey AY, Bing RF, Castleden CM, Swales JD and Napier CJ (1984). The effect of aging on the response to furosemide in normal subjects. Europ J Clin Pharmacol 27:303-306.
21. Swerdoff RS, Pozefsky T, Tobin JD and Andres R (1967). Influence of age on the intravenous tolbutamide response test. Diabetes 15:161-170.
22. O'Malley K, Crooks J, Duke E and Stevenson IH (1971). Effect of age and sex on human drug metabolism. Brit Med J 3:607-609.
23. Meyer RB (1982). Benzodiazepines in the Elderley. Med Clin N Amer 66:1017-1035.
24. Ogilvie RI (1978). Clinical pharmacokinetics of theophylline. Clin Pharmacokin 3:267-293.
25. Vestal RE, Norris AH, Tobin JD, Cohen BH, Shock NW and Andres R (1975). Antipyrene

metabolism in man: influence of age, alcohol, caffeine and smoking. Clin Pharmacol Ther 18:425-432.
26. Salem SAM, Rajjayabun P, Shepherd AMM and Venson IH (1978). Reduced induction of drug metabolism in the elderly. Age and Aging 7:68-73.
27. Vestel RE and Wood AJJ (1980). Influence of age and smoking on drug kinetics in man - studies using model compounds. Clin Pharmacokin 5:309-319.
28. Piafsky KM, Sitar DS, Rangno RE and Ogilvie RI (1977). Theophylline kinetics in acute pulmonary edema. Clin Pharmacol Ther 21:310-316.
29. Cockcroft DW and Gault MH (1976). Prediction of creatinine clearance from serum creatinine. Nephron 16:31-41.
30. Aitio M-L (1981). Plasma concentrations and protein binding of disopyramide and mono-N-dealkyldisopyramide during chronic oral disopyramide therapy. Brit J Clin Pharm 11:369-376.
31. Nattel S, Ogilvie RI, Kreeft JH and Sitar DS (1979). Procainamide acetylation and disposition in dialysis patients. Clin Invest Med 2:5-11.
32. Chan K, Kendall MJK, Mitchard M, Wells WDE and Vickers MD (1975). The effect of aging on plasma pethidine concentration. Brit J Clin Pharmacol 2:297-302.
33. Levy G (1965). Pharmacokinetics of salicylate elimination in man. J Pharmaceut Sci 54:959-967.
34. Cuny G, Royer RJ, Mur JM, Serot JM, Faure G, Netter P, Miallard A and Penin F (1979). Pharmacokinetics of salicylates in the elderly. Gerontology 25:49-55.
35. Roth GS (1979). Hormone receptor changes during adulthood and senescence: significance for aging research. Fed Proc 38:1910- 1914.
36. Feldman RD, Limberg LE, Nadeau J, Robertson D and Wood AJJ (1984). Alterations in leukocyte beta receptor affinity in the elderly. N Eng J Med 310:815-819.
37. Vestal RE, Wood AJJ and Shand DG (1979). Reduced beta- adrenoceptor sensitivity in the elderly. Clin Pharmacol Ther 26:181-186.
38. Greenblatt DJ, Allen MD and Shader RI (1977). Toxicity of high dose flurazepam in the elderly. Clin Pharmacol Ther 21:355-361.
39. Castleden CM, George CF, Marcer D and Hallett C (1977). Increased sensitivity to nitrazepam in old age. Brit Med J 1:10-12.
40. Giles HG, MacLeod SM, Wright JR and Sellers EM (1978). Influence of age and previous use on diazepam dosage required for endoscopy. Canad Med Assoc J 118:513-514.
41. Kaiko RF (1980). Age and morphine analgesia in cancer patients with postoperative pain. Clin Pharmacol Ther 28:823-826.
42. Owen JA, Sitar DS, Berger L, Brownell L, Duke PC and Mitenko PA (1983). Age-related morphine kinetics. Clin Pharmacol Ther 34:364-368.
43. Gregory GA, Eger EI and Munson ES (1969). The relationship between age and halothane requirement in man. Anesthesiol 30:488-491.
44. Bromage PR (1969). Aging and epidural dose requirements. Brit J Anaesth 41:1016-1022.
45. McLeod K, Hull CJ and Watson MJ (1979). Effect of aging on the pharmacokinetics of pancuronium. Brit J Anaesth 51:435-438.
46. Marsh RHK, Chmielewski AT and Goat VA (1980). Recovery from pancuronium. A comparison between old and young patients. Anaesthesia 35:1193-1196.
47. Shepherd AMM, Hewick DS, Moreland TA and Stevenson IH (1977). Age as a determinant of sensitivity to warfarin. Brit J Clin Pharmacol 4:315-320.
48. Jick H, Stone D, Borda IT and Shapiro S (1968). Efficacy and toxicity of heparin in relation to age and sex. N Eng J Med 279:284-286.
49. Ouslander JG (1981). Drug therapy in the elderly. Ann Int Med 95:711-712.
50. Greenblatt DJ, Sellers EM and Shader RI (1982). Drug disposition in old age. N Eng J Med 306:1081-1088.
51. Thompson TL, Moran MG and Nies AS (1983). Psychotropic drug use in the elderly. N. Eng J Med 308:134-138, 194-199.
52. Drug treatment in the elderly. RE Vestal, Editor, ADIS Health Science Press, Sydney, 1984 pp 380.

5. FLUID AND ELECTROLYTE DISORDERS IN THE ELDERLY

ROBERT M.A. RICHARDSON, M.D., F.R.C.P.(C)

INTRODUCTION

Disorders of the volume and composition of body fluids are common in the elderly and are often life-threatening. In part, these disorders are frequent and severe because the elderly are susceptible to illnesses which directly alter body water volume and composition, and in part because of their impaired ability to defend against and correct these alterations. For example, sodium and water losses due to gastrointestinal disturbances are common in them, but the normal defence mechanisms against salt and water deficiency - renal conservation of salt and water, and thirst - become progressively less efficient with age. This chapter will discuss the common fluid-electrolyte disorders in the elderly, emphasizing reasons for their susceptibility and the ways age impairs the normal defence mechanisms.

DISORDERS OF SODIUM BALANCE

Sodium, with the anions chloride and bicarbonate, is the principal extracellular fluid (ECF) osmole, and therefore the quantity of total body sodium determines ECF volume. Excess sodium can lead to peripheral edema, pulmonary edema or hypertension; sodium deficiency may cause hypotension or shock. Table I shows the common causes of disordered sodium balance. The causes of sodium excess, which are similar to those in younger patients, will not be discussed further. Since ECF volume depletion is particularly serious in the elderly, it will be discussed in more detail.

The elderly are particularly prone to developing ECF volume depletion. Frequently they are placed on diuretic drugs for control of edema as in congestive heart failure or for hypertension. Diuretics, particularly the potent loop agents such as furosemide, can induce excessive sodium loss, leading to reductions in central venous pressure, arterial blood pressure and states such as prerenal

Table I: *Common Disorders of Sodium Balance*

Sodium deficiency	*Sodium excess*
Gastrointestinal loss	Congestive heart failure
– Diarrhea	Renal failure
– Vomiting	Nephrotic syndrome
– Pancreatitis	
Renal loss	Cirrhosis of the liver
* – Diuretic drugs	
* – Osmotic diuresis (Hyperglycemia)	
* – Tubulointerstitial disease Aldosterone deficiency	
Sweating burns	
*Reduced intake	

*Discussed in more detail in text.

failure, postural hypotension or even shock. In addition to the frequent use of diuretics in the elderly, sodium loss may be greater in them than in the young. For example, 80 mg of furosemide given intravenously produced a greater sodium loss over 24 hours in eight men aged 60-70 years compared to 10 men aged 29-35 years, although the early response was blunted (1).

Hyperglycemic non-ketotic syndrome is a syndrome seen almost exclusively in the elderly. It is characterized by a slowly progressive, often severe hyperglycemia, by severe ECF volume depletion attributable to the natriuretic effects of the glucose-induced osmotic diuresis, and reduced or inadequate sodium intake; and often by hypernatremia (discussed below). The state of insulin deficiency or resistance which allows hyperglycemia to develop frequently is reversible, and is precipitated by conditions such as stroke, myocardial infarction or sepsis - all of which are more common in the elderly. This syndrome has a high mortality rate, primarily because of the usually serious precipitating illness (2).

Inadequate dietary intake of sodium may aggravate sodium depletion states in the aged. Anorexia due to drugs, such as digoxin and analgesics, neuromuscular disorders or disabling arthritis which impair mobility, and socioeconomic factors may contribute to dietary deficiencies.

Faced with sodium deficit and reduced ECF volume, the elderly are less able than younger persons to reduce urine sodium loss. Epstein and Hollenberg measured the rate at which urine sodium excretion decreased when dietary sodium was reduced from normal to 10 mmol/day (3) (Table II). The half-time for the reduction in urine sodium excretion was significantly prolonged in those over-60, implying that a sodium-depleted elder person would suffer significant

urine sodium loss before balance would occur. The cause of this impairment in renal sodium conservation is unknown. Plasma renin and aldosterone levels tend to be lower in the elderly, but it is not clear if this contributes to the defect in sodium reabsorption (4). Certainly a variety of renal tubulo-interstitial lesions such as urinary tract obstruction or hypertensive nephrosclerosis could impair sodium conservation in elderly patients.

Table II: The effect of age on creatinine clearance and the half-time for the reduction in urinary sodium excretion. Subjects were placed on a 10μmol sodium diet for at least five days and 24 hour urine sodium excretion rates were measured. The Na t 1/2 in individuals over 60 was significantly longer than for those under 30 and those 30-59 years. ($P < .01$). Adapted from reference 3.

	Age (years)				
	<30	30-39	40-49	50-59	>60
No. of subjects	34	8	25	14	8
Na t 1/2 (hours)	−14.6	−23.8	−23.2	−23.5	−30.9
(S.E.M.)	(0.7)	(1.1)	(1.8)	(1.6)	(2.8)
Ccr (mL/min)	112	109	106	89	67
(S.E.M.)	(5)	(7)	(3)	(9)	(4)

Sodium depletion is identified on clinical examination; for example, a useful clue is the reduction in jugular venous pressure, manifested by flat jugular veins with the patient supine. Postural hypotension is a valuable sign, but it may appear in the absence of intravascular volume depletion with autonomic neuropathy in diabetes mellitus or amyloidosis and with antihypertensive drugs. Skin turgor is an unreliable sign in the elderly because skin elastic tissue is greatly reduced. Treatment by oral fluids or intravenous saline should be guided by measurements of blood pressure, jugular venous pressure, examination of lung fields and heart sounds, and by detection of edema. I believe physicians often are too cautious in administering normal saline to severely volume depleted elderly patients, because they are afraid of precipitating congestive heart failure. The best way to prevent this complication is frequent, careful physical examination.

DISORDERS OF WATER BALANCE

Disorders of body-water tonicity (or osmolality) potentially are serious because of their effect on cell volume and brain function. Intracellular volume is inversely proportional to the 'effective' ECF osmolality. As ECF osmolality rises, water is drawn out of cells and cell volume decreases; as ECF osmolality falls, water enters cells and expands their volume. The term 'effective' denotes osmoles which are relatively confined to the ECF space, cross cell membranes poorly and

therefore are active osmotically. The most important effective osmoles are sodium and glucose. Urea is an ineffective osmole, because it readily crosses cell membranes.

When ECF osmolality changes acutely, the volume of all cells including brain exhibit rapid changes. Because changes in brain volume are potentially catastrophic, these cells apparently have the capacity to adjust their volumes to normal when exposed to changes in ECF osmolality over several days (5). They normalize by generating new intracellular solute in hypernatremia, or reducing solute content, in hyponatremia. The cost of adjusting cell volume is abnormal cellular function, so that chronic hyponatremia and hypernatremia are characterized by progressive derangements of central nervous system function (5).

HYPERNATREMIA

Hypernatremia may be due to the ingestion or administration of salt or hypertonic sodium solutions, but more commonly represents water deficiency. Only the latter deficit will be discussed here.

Table III: Hypernatremia - Causes of Water Depletion

Excess Water Loss	*Inadequate Water Intake*
Skin - burns, sweating	Altered level of consciousness
Lungs - hyperventilation	Abnormality of thirst
	- Aging
Gastrointestinal tract	
- vomiting, diarrhea	No access to water
	- bedridden
Urine - diuretics	
- Hyperglycemia, mannitol	
- Interstitial nephritis	
- ADH deficiency	

Table III outlines the pathogenesis of water deficiency. Excessive water loss is common, and may be lost from the gastrointestinal tract, kidneys or skin, or may be insensible from the respiratory tract. Typical causes in the elderly are diarrhea, vomiting, diuretic administration, pneumonia with hyperventilation and fever, obstructive uropathy and uncontrolled diabetes mellitus.

Normally water loss and hypernatremia bring into play two different mechanisms which prevent further losses and correct the water deficit: Namely, the renal concentrating mechanism, which prevents inordinate water losses from

the kidney; and thirst, which stimulates fluid repletion. Both processes are defective in the elderly.

Many studies have shown that the ability to maximally concentrate the urine declines with age (6-8). One such study (Table IV), shows not only that maximal urine osmolality following water deprivation is reduced in the elderly but as well, urine solute excretion is higher (8). In the elderly, the net result is an increase in urine excretion of about 0.5 ml/min, or over 700 ml/day. Obviously, over several days this increase in urine flow would produce significant water depletion. As a result of renal damage, many elderly patients have even lower maximum urinary osmolalites and, when hypernatremic, would have proportionately greater renal water losses.

Table IV: Effect of Age on Urine Concentration

Age	Urine Osmolality mosm/kg	Urine Flow ml/min	Solute Excretion mosm/min
20-39	1,109 ± 27	0.49 ± 0.03	0.54 ± 0.04
40-59	1,051 ± 19	0.63 ± 0.03	0.66 ± 0.03
60-79	882 ± 49*	1.03 ± 0.13*	0.91 ± 0.13*

Subjects were participants in the Baltimore Longitudinal Study of Aging. They were studied after 12 hours of water deprivation. Subjects with renal disease or any systemic illness, which could affect kidney function, were excluded. Results are expressed as mean ± S.E.M.

* Significantly different from 29-39 age group ($P < .01$)
Adapted from reference 8.

The causes of the renal concentrating defect is unknown, although it has been well documented that it is not due to ADH deficiency (9,10). Indeed, ADH levels are higher in the elderly during hypernatremia induced by infusion of hypertonic saline (10). The failure of the kidney to increase urine osmolality normally does not appear to be due to insensitivity of collecting ducts to ADH, because Lindeman, *et al* demonstrated that ADH infusion during water diuresis produced an appropriate decrease in free water clearance (7). Hence, the major abnormality in the aged kidney probably is impaired ability to generate a highly concentrated medullary interstitium - the cause of which is unknown.

Even with large extrarenal or renal losses, hypernatremia will not develop unless fluid intake is inadequate. The normal person becomes thirsty when serum osmolality rises above about 295 mosm/kg, and he drinks water until thirst is relieved. As noted earlier, fluid intake may be reduced in the elderly for several reasons: First, they may suffer from acute or chronic disorders of the central nervous system which impair consciousness, e.g. febrile septic states, stroke, hypotension and dementia. Frequently, the elderly are bedridden and socially

isolated, so that even if they are thirsty they may be unable to gain access to water or control its administration. Some elderly patients, who have had strokes in the past but no alteration in level of consciousness, have defective sensation of thirst (11). Finally, the otherwise normal elderly, when water deprived, ess appreciation of thirst than a younger person with the same degree of water loss and even when it is available, drinks less water (12). This behaviour is seen despite higher levels of ADH so its cause does not appear to be osmoreceptor dysfunction. The exact basis for this thirst disorder is not clear.

The net result of an increased susceptibility to disorders which cause water loss, impaired urinary concentrating ability and impaired thirst response is that the elderly, far more frequently than the young, develop severe water depletion and hypernatremia. Frequently, sodium deficiency also is present, so that severe ECF volume depletion, with hypotension and prerenal failure, often coexists with hypernatremia.

The major defect associated with hypernatremia is central nervous system dysfunction, with progressive obtundation leading to coma and even death. Chronic hypernatremia (more than several days) provokes the accumulation within brain cells of additional solutes, including electrolytes and other unidentified, osmotically active solutes - 'idiogenic osmoles'. These solutes are important because they restore brain volume to normal and disappear slowly when hypernatremia is corrected. Thus, rapid administration to a hypernatremic person of hypotonic fluid may cause rapid brain swelling, seizures, coma and death (5). In treating hypernatremia, one should follow two important guidelines. First, if there is intravascular volume depletion, it should be corrected rapidly with normal saline. Second, hypertonicity should be corrected slowly over two to three days with hypotonic fluid. The water deficit (in litres) is calculated as follows: water deficit $= BW \times 0.6 \frac{(PNa - 140)}{PNa}$ where BW is body weight in kilograms and PNa is the current plasma sodium concentration. This formula is not exact because often the usual body weight is unknown. However, the water deficit calculated by this formula gives a good approximation. In elderly women, the formula should be $BW \times 0.50 \frac{(PNa - 140)}{PNa}$ because elderly women generally have smaller volumes of body water than men. One should exercise caution if using large volumes of 5% glucose as the hypotonic replacement fluid; it may provoke hyperglycemia and an osmotic diuresis, leading to further water loss. If that happens, one-half normal saline should be used. Despite slow correction, altered consciousness may persist for many days. Mortality with severe hypernatremia is high.

HYPONATREMIA

Usually, hyponatremia represents a state of water excess and the basic defect is failure of the kidneys to excrete water and restore osmolality. Other causes include factitious hyponatremia, due to severe hyperlipidemia or hyperproteinemia, both of which are rare, and hyperosmotic hypernatremia, due to hyperglycemia or mannitol administration which is easy to recognize. Because it is essential to make a correct diagnosis of the common forms of hypernatremia, I will focus on the pathophysiology of these disorders.

A normal individual, who ingests water and lowers his serum sodium concentration, responds by suppressing the release of ADH (mediated by the osmoreceptor located in or near the hypothalmus), which allows the kidney to excrete larger volumes of more dilute urine. 'Therefore, failure to excrete water may reflect a failure to adequately suppress ADH release or impaired renal diluting ability. Both are common in the elderly.'

The ADH secretory process has been studied intensively since a reliable radioimmunoassay became available for the hormone. Figure I shows normal osmoreceptor-mediated ADH release. Below a threshold value of serum osmolality - about 280 mosm/kg, plasma ADH is completely suppressed and urine osmolality is minimal, usually less than 100 mosm/kg (13). As serum osmolality rises, ADH levels rise more or less linearly, and urine concentration also rises. When serum osmolality is above about 295 mosm/kg, serum levels of ADH are high enough to induce maximal urine concentration.

Impaired osmoreceptor function does not seem to be a common cause of hyponatremia. Rather, hyponatremia most often is caused by elevated ADH levels associated with stimuli other than osmotic. Table IV lists the non-osmotic stimuli for ADH release. Reductions in blood volume - 'effective circulating volume' probably are the most common causes of hyponatremia. Reductions in central venous pressure, via vagal afferents from atrial stretch receptors, or reductions in arterial pressure, via baroreceptors located in the carotid sinus, both stimulate ADH secretion. Table V lists the common causes of hyponatremia due to volume-mediated ADH release. Note that in these cases, absolute ECF volume may be reduced, normal or increased.

ADH levels may be increased and cause hyponatremia where none of the factors listed in Table V seem to operate. In this case, patients are said to have the 'syndrome of inappropriate ADH' release, (SIADH). This may result from ectopic hormone production by tumors, or from central release of ADH due to central nervous system disorders, intrathoracic disease or drugs (Table VI).

Often, the elderly have disorders which cause ADH release. Frequently they are ECF volume depleted and often they develop heart failure or are using diuretics. They may develop oat-cell carcinoma of the lung, and even pneumonia, so common in the elderly, can cause SIADH (14).

Impaired renal diluting ability may induce or contribute to hyponatremia even

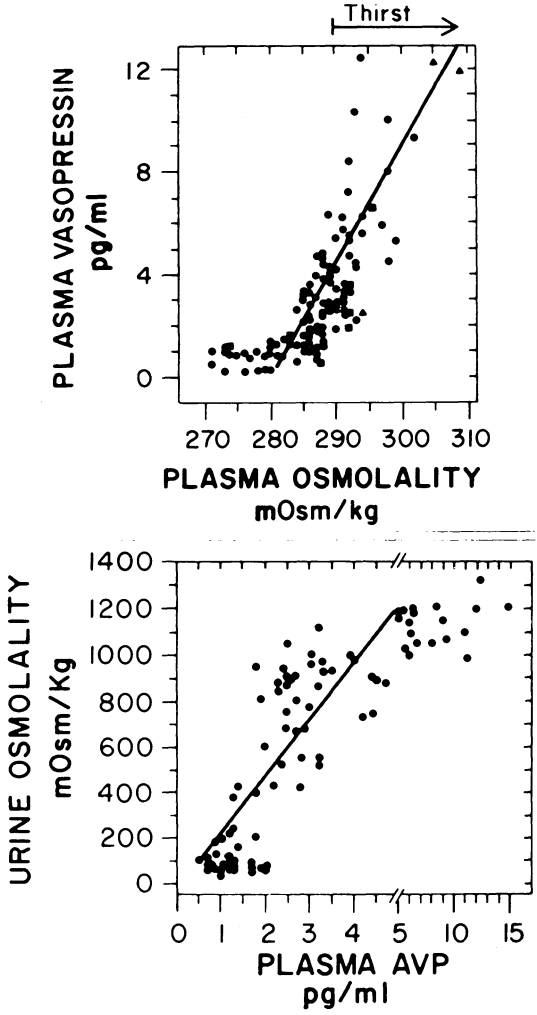


Figure 1: The upper figure shows the normal relationship between plasma vasopressin and plasma osmolality. The lower figure shows the effect of plasma vasopressin levels on urine osmolality. See text for further discussion.

where ADH levels are appropriately suppressed. In severe ECF volume depletion (or reduced effective circulating volume as in heart failure), sodium delivery to the thick ascending limb of the loop of Henle may be sufficiently reduced to limit the excretion of dilute urine. Similarly, renal failure or medullary interstitial diseases, such as obstructive uropathy or pyelonephritis, may impair the kidney's ability to excrete dilute urine.

Usually, the diagnosis of hyponatremia is straightforward, however it may be difficult to differente those with SIADH from those with elevated ADH levels due to a volume stimulus. If ECF volume appears relatively normal on physical

Table V: Non-osmotic Stimuli For ADH Release

Hemodynamic
Reduced absolute or effective blood volume
- Diuretics
- Diarrhea, vomiting
- Congestive heart failure
- Adrenal insufficiency
- Cirrhosis
- Nephrotic syndrome
- Positive pressure breathing
Emetic
- Nausea
- Drugs (cyclophosphamide, morphine, etc.)

Table VI: *Causes of the Syndrome of Inappropriate Anti-diuretic Hormone Secretion (SIADH)*

Carcinomas
- lung, pancreas, thymus etc.
Pulmonary Disorders
- pneumonia
- abscess, tuberculosis
- asthma, etc.
Central Nervous System Disorder
- Encephalitis, meningitis
- Trauma
- Gullain-Barre syndrome, etc.
Drugs
- Vincristine
- Carbamazepine
- Chlorpropamide etc.

examination. Physical assessment of ECF volume may be misleading (15), and probably the best single test is the urine sodium concentration. A value less than 30 mmol/L favors a volume stimulus for ADH release; a value greater than 30 favors SIADH. A high blood urea/serum creatinine ratio or a high serum urate also favors volume mediated ADH release whereas, in SIADH, blood urea and serum urate values typically are very low.

The therapy of hyponatremia depends on the cause and severity. Asymptomatic hyponatremia does not require urgent treatment. If the patient is volume depleted, the treatment of choice is normal saline. Where indicated, measures to improving hemodynamics in heart failure, or reduction in the dose of diuretic may be helpful. Water restriction is effective but often poorly tolerated. In chronic SIADH, demeclocycline, which antagonizes ADH action on

the collecting duct, is helpful. In severe hyponatremia when the patient has such CNS symptoms as obtundation or seizures, hypertonic saline should be given to raise the serum sodium concentration to not more than 125 μmol/L for the first 12 hours. More rapid correction has been associated with permanent neurological damage (5).

REFERENCES

1. Andreasen, F., Hansen, V., Husted, S.E., Magensen, C.E., and Pedersen, E.b., 1984. The influence of age on renal and extrarenal effects of furosemide. Br. J. Clin. Pharmac. 18:65- 74.
2. Halperin, M.L., Goldstein, M.B., Bear, R.A., and Josse, R.G. 1985. Diabetic Comas, in Fluid, Electrolyte and Acid-base Disorders. Arieff AI and DeFronzo, R.A. eds. Churchill Livingstone, New York, pp 933-968.
3. Epstein, M. and Hollenberg, N.K., 1976. Age as a determinant of renal sodium conservation in normal man. J. Lab. Clin. Med. 87:411-417.
4. Hegstad, R., Brown, R.O., Jiang, N., Kao, P., Weinshilboum, R.M., Strong, C. and Wisgerhof, M. 1983. Aging and aldosterone. Am. J. Med. 74:442-448.
5. Arieff, A.I. 1985. Effects of water, acid-base and electrolyte disorders on the central nervous system. In Fluid, Electrolyte and Acid-Base Disorders, Arieff, A.I. and DeFronzo, R.A. eds. Churchill Livingstone, New York, 1985, pp 969-1039.
6. Lewis, W.H. and Alving, A.S. 1938. Changes with age in the renal function of adult men. Clearance of urea, amount of urea nitrogen in blood, concentrating ability of kidneys. Am. J. Physiol. 133:505-515.
7. Lindemann, R.D., Lee, T.D. Jr., Yiengst, M.J., and Shock, N.W. 1966. Influence of age, renal disease, hypertension, diuretics and calcium on the antidiuretic response to suboptimal infusions of vasopressin. J. Lab. Clin. Med. 68:206-223.
8. Rowe, J.W., Shock, N.W. and DeFronzo, R.A. 1976. The influence of age on the renal response to water deprivation in man. Nephron 17:270-278.
9. Kirkland, J., Lye, M., Goddard, C., Vargas, E., and Davies, I. 1984. Plasma arginine vasopressin in dehydrated elderly patients. Clin. Endocrinology 20: 451-456.
10. Helderman, J.H., Vestal, R.E., Rowe, J.W., Tobin, J.D., Andres, R. and Robertson, G.L. 1978. The response of arginine vasopressin to intravenous ethanol and hypertonic saline in man: the impact of aging. J. Gerontology 33:39-47.
11. Miller, P.D., Krebs, R.A., Neal, B.J. and McIntyre, D.O. 1982. Hypodypsia in geriatric patients. Am. J. Med. 73:354-356.
12. Phillips, P.A., Rolls, B.J., Ledingham, J.G.G., Forsling, M.L., Morton, J.J., Crowe, M.J., and Wollner, L. 1984. Reduced thirst after water deprivation in healthy elderly men. N. Eng. J. Med. 311:753-759.
13. Robertson, G.L. 1983. Thirst and vasopressin function in normal and disordered states of water balance. J. Lab. Clin. Med. 101:351-371.
14. Charles R. and Rees J.R. 1975. Inappropriate secretion of antidiuretic hormone in pneumonia. Postgrad. Med. J. 51:663-664.
15. Chung, H.M., Anderson, R.J., Dluger and Schrier R.W. 1984. Is clinical evaluation adequate for assessment of ECF volume status in hyponatremia? Kidney International 27: 135 (Abstract)

6. SODIUM HOMEOSTASIS WITH SPECIAL REFERENCE TO FRACTIONAL EXCRETION OF SODIUM AND PLASMA PROSTAGLANDIN E-1 IN ELDERLY HYPERTENSIVES IN ESSENTIAL AND RENOVASCULAR HYPERTENSION

KAMLAKAR TRIPATHI, M.D.*, D.M. (NEPHROLOGY), M.N.A.M.S. (NEPHROLOGY), JAWED AHMED, M.D.**, P.K. SRIVASTAVA, M.D., D.C.H.*** AND P.S. MISHRA, M.B.B.S.****

INTRODUCTION

Since the kidney plays a dominant role in the maintenance of volume in the body fluid spaces through its influence on sodium and water excretion; it must be involved in all forms of hypertension. As Guyton (1) has indicated renal perfusion pressure is a major determinant of sodium and water excretion and hypertension could not be maintained, unless the relationship had been altered between renal perfusion pressure and its output of sodium and water. Korner *et al* (2) have proposed that excessive activity of sympathetic nervous system and a failure of the kidney to excrete sufficient sodium and water in response to elevation of blood pressure. The presumed relationship between the primary mechanism behind the development of hypertension sodium homeostasis and use of diuretics as antihypertensive agents all over the world, but only recently we have recognized the various hyponatremic syndromes. Little attention has been paid to the special needs of geriatric patients who tend to excrete more sodium because of poor tubular concentration, especially in the tropics. Labeuw *et al* (3) have found that fractional excretion of sodium is a helpful denominator in planning the administration of diuretics. A consideration of these factors led the

* Lecturer in Medicine
** Ex-Resident in Medicine
*** Professor of Medicine
**** Jr. Resident in Medicine

authors to undertake the present study of fractional excretion of sodium and plasma PGE-1 in elderly hypertensives in the tropics.

MATERIALS AND METHODS

At the University Hospital, Division of Nephrology, Banaras Hindu University, we chose for study 20 elderly hypertensives of whom 12 had clinical and biochemical evidence of essential hypertension, the remaining eight were shown to have renal-artery stenosis by angiography. Each had detailed clinical profile with 24 hour urinary sodium, serum sodium and fractional excretion of sodium (FENa) by the method of Espinel *et al* (4). All antihypertensive agents were withdrawn for a week. The patient's were put on uniform salt diet (<0.5 g/day) without diuretics, aspirin or anti-inflammatory drugs during the period of study. Plasma PGE-1 was estimated by the method of Charles *et al* (5).

OBSERVATION

In control patients the mean serum sodium value was $130.01 + 16.1$ whereas the 24-hour urinary excretion was $40.55 + 20.32$. These values were constant throughout the year. However, during summer values do change and the patient tends to lose more sodium in sweat and urinary sodium excretion falls (serum $128 + 10.2$ mEq/L urinary $28 + 0.15$). In essential hypertension the urinary sodium loss did not change much although marked differences were seen in the serum sodium values which is often $110 + 10.33$. These differences do not reach statistical significance. However FENa is about three times higher in essential hypertension and twice as high in those with the renovascular disease. The plasma prostaglandin E-1 also seems to be significantly lower in the renovascular patients than in those with essential hypertension (Table I & II).

In essential hypertension we found a significant positive correlation between age and mean arterial pressure and FENa $r = +0.516$, $p<0.02$ and $r = +0.688$ $p<0.001$ respectively. However, in those with renovascular disease both comparisons were statistically insignificant. Endogenous creatinine clearance also showed a negative correlation between essential hypertension and renovascular hypertension ($p<0.001$).

DISCUSSION

The kidneys have long been seen as the source of arterial hypertension. Peart (6) postulated that kidney exercises a protective function by secreting vasodilator substances in the presence of hypertension. Earlier Muirhead (7) had isolated a

low molecular weight lipid from the renal medulla which demonstrated an antihypertensive property and Lee *et al* (8) identified it as prostaglandin compound.

Earlier Goldring *et al* (9) had shown that in essential hypertension, glomerular filtration rate remains stable and the filtration fraction is increased resulting in natriuresis which ultimately affects the fractional sodium (FENa) excretion. This FENa is a mathematical depiction of tubular sodium reabsorption. Clinical conditions which alter sodium transport along the proximal and distal tubule affect the interpretation of this test. In 1976, Epsinel used it to differentiate between prerenal and acute tubular necrosis. In prerenal azotemia, there is a persistent afferent arteriolar constriction, which leads to a fall in glomerular filtration rate and a decreased delivery of sodium to the tubules.

In 1979, Kikuchi *et al* (10) demonstrated a positive correlation between pressure natriuresis and a FENa. In our study we found an almost similar phenomena, namely a positive correlation between mean arterial pressure and FENa (Table IV). However this does not exist in renovascular hypertension. The validity of these phenomena is supported further by the observation of a significant negative correlation between endogenous creatinine clearance and FENa in both essential and renovascular hypertension both (Table V). Thus FENa becomes an important tool in clinical investigation in elderly hypertensives who tend to lose more urinary sodium than young ones and during the summer often develop symptoms of hyponatremia if there is complete salt restriction. The situation worsens when diuretics are administered to treat the hypertension, because hyponatremia often increases renin secretion.

Also the plasma prostaglandin activity is reduced when serum sodium increases although there is a relative pressure natriuresis. Henceforth, in the tropic's, we should measure serum sodium, urinary sodium, and FENa before starting diuretics and in elderly patients should restrict salt only when there is clinical and laboratory evidence of sodium and water retention. The use of beta blockers, converting-enzyme inhibitors, and minoxidil constitute a more rational approach to the treatment of elderly hypertensive who are sodium-depleted, hyponatremic, and hyperreninemic than that of diuretics.

REFERENCES

1. Guyton AC, Coleman TC, Cowley AW *et al.* A sytem analysis approach to understand long range arterial blood pressure control and hypertension. Circulation Res 1974;35:159-176.
2. Korner PI, Shaw J, Uther JB *et al.* Autonomic and non-atunomic component in essential hypertension. Circulation 1973;48:107-117.
3. Labeuw M, Pozet N, Zeck P *et al.* Furosemide induced natriuresis in advanced renal failure. Nephron 1983;34:71.
4. Espinel CH. Fraction sodium excretion in acute tubular necrosis. J Am Med Assoc 1976;236:578-581.

5. Charles FC, Floyed CM. Quantitative determination of histamine methods of biochemical analysis. D. Glick Eds. Int Sc Pub Inc. New York 1960.
6. Peart WS. Hypertension and the kidney in renal disease. Black DAK eds. FA Davis Company;Philadelphia, PA 1967.
7. Muirhead FE, Jones F, Shairman JA. Antihypertensive property of reno-prival hypertension of extracts of renal medulla. J Lab Clin Med 1960;56:167.
8. Lee JB. Antihypertensive activity of the kidney. The renomedullary prostaglandins. New Engl J Med 1967;277:1073.
9. Goldring W, Chasis H, Ranges HA *et al.* Effective renal blood flow in subject with essential hypertension. J Clin Invest 1941;20:637.
10. Kikuchi K, Limura O, Moriguchi O *et al.* Body fluid balance and fractional excretion of sodium inorganic phosphorus, potassium and water in low renin essential hypertension. Japan Circulation 1979;43:

7. AGING AND BODY WATER

THEODORE R. REIFF, M.D.

INTRODUCTION

We have evolved from the sea and are composed mostly of water. Evidence from phylogeny* and ontogeny** suggest that the amount of water appears to decrease continually as we age. An embryo is about 90% water, a newborn child about 80% water, a mature adult about 70% water, and an older adult about 60% water. Recent work indicates that in senescence the body water is below 60%.

A review of previous work indicates considerable confusion, discrepancy, and disagreement about body water changes with age. Some of the conflicting findings relate to the manner in which water content was measured and how it was expressed, i.e. water/individual, water/total body mass, water/lean body mass.

PREVIOUS WORK AND METHODS

The literature (1-11) draws conflicting conclusions concerning the degree of water loss between intracellular and extracellular compartments. Various experimental methods have been applied in the tracer used to measure body compartments. Although antipyrine has been used (2,5) others believe that deuterium oxide and/or tritium oxide (3,4,11) is superior for the measurement of total body water and, from a physico-chemical point of view, deuterard or tritiated water would appear to be preferable.

Inulin, bromide, sulfate, and thiocyanate have been used to estimate extracellular fluid. Usually intracellular fluid has been calculated from the difference between total body water and extracellular fluid.

* PHYLOGENY: Development of the species.

** ONTOGENY: Development of the individual organism.

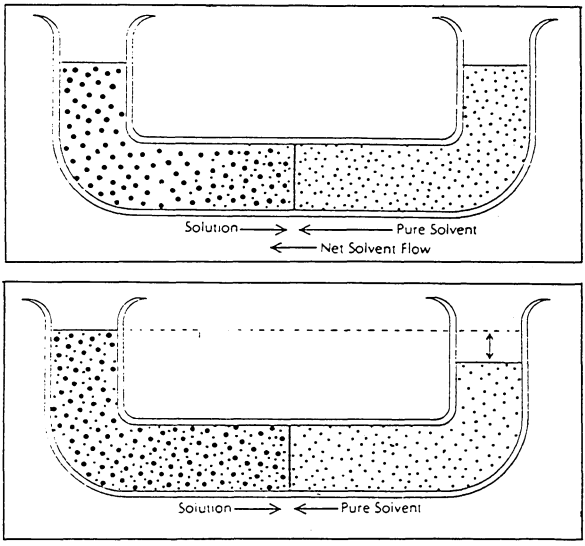


Figure 1: In the osmometer a macromolecular solution is separated from pure solvent by semipermeable membrane, permeable by solvent by not by solute. Net flow of solvent will be toward solution because the chemical potential (concentration) of the solvent is lower on solution side (top). This flow of solvent will be halted by applying a sufficiently high pressure (the osmotic pressure) to the solution. Such equilibrium will be attained when enough solvent has been transported across the membrane to raise the height of the solution sufficiently to exert an osmotic pressure (bottom).

Although earlier studies indicated that the loss in total body water with age was chiefly from the intracellular compartment, Steen *et al* (11) have demonstrated significant decrements in extracellular water as well.

COLLOID OSMOTIC HYPOTHESIS OF SENESCENT WATER LOSS

Theoretically there is good reason to expect profound changes in the chemical potential of intracellular and interstitial water with age, related to increasing macromolecular interaction or aggregation - crosslinking, polymerization, insolubility, etc. The increase in macromolecular solute-solute interaction would be accompanied by a decrease in macromolecular solute-solvent interaction resulting in a higher solvent (water) chemical potential. This would allow for an easier loss of bound water with age.

Water is retained in cells by the oncotic pressure or colloid osmotic pressure exerted by macromolecules, largely protein within the cell. Osmotic pressure can best be explained by reference to the osmometer - a device that measures osmotic pressure. This is a container divided into two sections by a semipermeable membrane, which allows solvent particles (water molecules) to pass through in either direction (Fig. 1). The rates of movement of solvent through the

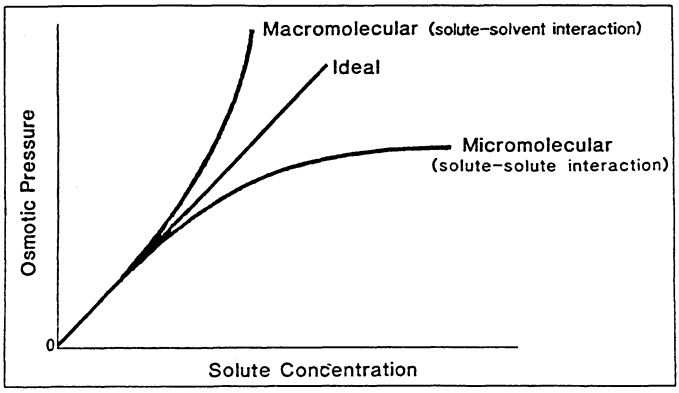


Figure 2: Relationship of osmotic pressure and solute concentration is linear only for 'ideal' solutions of intermediate-size molecules. For solutions of micromoleculr particles, solute-solute interaction predominates, lowering osmotic pressure from the ideal by reducing particle number. For solutions of macromolecules e.g., protein, solute-solvent interaction is predominant, raising osmotic pressure by effectively raising concentration of solute as macromolecular micelles trap solvent.

membrane may be represented by vectors whose length is proportional to the rate of transport of solvent from one side to the other. The algebraic sum i.e. the difference between the two vectors, is the net rate of transport of solvent across the membrane. One side of the container holds pure solvent; the other a solution of macromolecular solute in solvent. The rate of transport of solvent from the solution side is less than the rate from the pure solvent side, because the concentration of solvent on the solution side is less than the concentration of solvent on the pure solvent side. The rate of transport is proportional to the concentration of the material being transported, i.e. the solvent.

Accordingly, net solvent will be transported from the pure solvent to the solution side until the differential pressure is high enough to equalize the rates of transport from one side to the other, resulting in an equilibrium.

The pressure necessary to equalize the rates of solvent transport, resulting in zero net solvent transport, is the osmotic pressure. The relationship of a solution's osmotic pressure to the solute concentration, or number of molecules of solute per unit volume of solution, is linear for 'ideal' solutions (Fig. 2).

With low molecular-weight solutes the osmotic pressure is lower than expected. This is because the solute-solute interaction, which, reduces the concentration of solute particles that have partially combined with each other, lowers solute-solvent interaction, and so reduces the osmotic pressure. Solute-solute interaction can be thought of as making a negative contribution to the ideal line, resulting in a lower than ideal osmotic pressure. For high-molecular-weight solutes such as proteins, the osmotic pressure is higher than expected. This is because of increased solute-solvent interaction, which has the effect of raising the osmotic pressure as if there was a higher concentration of solute.

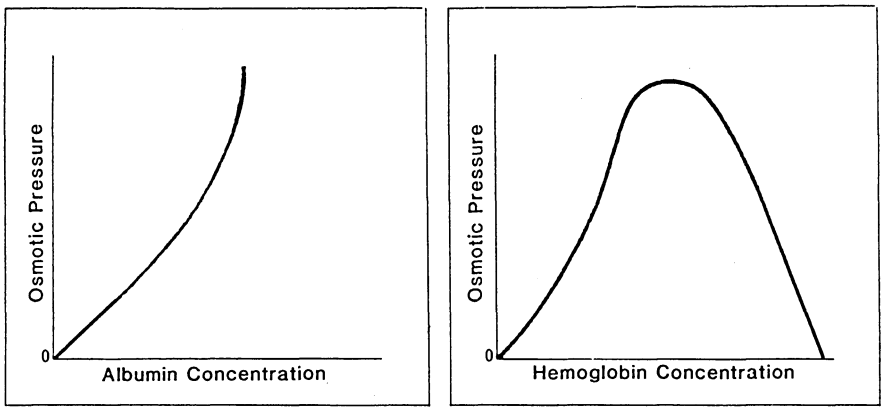


Figure 3: Osmotic pressure curve of extracellular albumin suggests that high concentrations of proteins within the cell would generate intolerably high pressures incompatible with cell viability. (Fig. A) Increased solute-solute interaction at very high solute concentrations may be responsible for less-than-expected intracellular osmotic pressure curve of hemoglobin. (Fig. B)

Increased solute-solvent interaction can be thought of as adding a positive contribution to the ideal line. The increased solute-solvent interaction can be attributed to the trapping of solvent by macromolecular micelles or clusters, which form at high concentrations and to the Gibbs-Donnan effect of charged macromolecules, which produce ionic imbalances and increased solute-solvent interaction.

An alternative, and simpler way of viewing osmotic pressure is to think of two types of attraction or interaction: solute-solvent interaction in which the solute attracts water (the solvent), and solute-solute interaction, in which the solute attracts other solute molecules. When solute-solute interaction predominates, less water interacts with or is bound to the solute resulting in a lower osmotic pressure because the water is more able to transfer across the membrane. When solute-solvent interaction predominates and is greater than one would expect from the concentration of the solute, the osmotic pressure will be higher. The factor responsible for dissolving a solute in a solvent is solute-solvent interaction. In an 'ideal' solution, there is a linear relationship between the solute particles concentration and the osmotic pressure.

Macromolecules, which cannot pass through cell membranes, hold water in the body. Macromolecules manifest increased solute-solvent interaction, resulting in very high osmotic pressures. Figure 3 shows the osmotic pressure-concentration curve for the protein macromolecule albumin which is largely responsible for maintaining plasma volume.

* An 'ideal' solution is one in which colligative properties of the solution are directly proportional to solute concentration.

The oncotic pressure of blood plasma with 5 g/dl albumin is about 25mm Hg. A fivefold increase in concentration to 25 gm/dl will produce a more than 30 fold increase in osmotic pressure - to about 760mm Hg (one atmosphere). Hemoglobin, the major macromolecule in the erythrocyte, has a molecular weight nearly equivalent to that of albumin, about 68,000 Daltons. Thus, it might be presumed that the oncotic pressure of hemoglobin would be about equal to that of albumin. The concentration of hemoglobin within the erythrocyte is about 34 g/dl, which should produce an oncotic pressure of several atmospheres, according to the oncotic pressure concentration curve. Obviously, cell membranes cannot withstand pressures of that magnitude without bursting. What mechanism reduces the intracellular pressure to more reasonable levels? The usual explanation is that the cell membrane has 'active' transport capability and can pump small micromolecules out of the cell to lower internal pressure. Although this undoubtedly is a factor I think that the oncotic pressure within the cell may be considerably less than expected because of increased solute-solute interaction at the high intracellular protein concentration.

The high concentration of solute molecules would result in greater solute-solute interaction and a lowered osmotic pressure. In fact, one could extend that concept to the point where osmotic pressure would begin to decrease as solute concentration increased to very high levels - i.e. when the solute was actually aggregating. The concept could be extended further to the point where osmotic pressure would approach zero, meaning that the solute was no longer in solution, but had precipitated out. One could even visualize a system in which the osmotic pressure would become negative, signifying that solvent was being hydrophobically squeezed out of a precipitating or crystallizing solute; as a result the solvent then might be in a metastable state, in which it would be transiently more reactive chemically than pure solvent. Water of crystallization may be the end result: here the water has been induced to combine in a fixed proportion at certain sites on the crystallized solute. In fact, it has been shown that the osmotic pressure at high hemoglobin concentrations (25 g/dl) does tend to be lower than expected. These experiments have not been extended past 30 g/dl to approach normal intracellular concentrations because of technical difficulties in working with highly viscous solutions.

However, a pathophysiologic model - sickle-cell anemia, demonstrates the phenomenon of decreased osmotic pressure resulting from solute-solvent aggregation in cells, which have protein in high concentration. Hemoglobin S, the abnormal hemoglobin in sickle-cell anemia, has a high degree of solute-solute interaction. When exposed to a low partial pressure of oxygen, the hemoglobin S molecules stick together forming a giant aggregate called a tactoid. Figure 4 illustrates the sequence of events in the sickling phenomenon. The sickling cell initially shows the tactoid with clear space between it and the cell membrane.

As the process continues, the clear space disappears and the membrane collapses around the tactoid. The clear space appears to be cell water, which

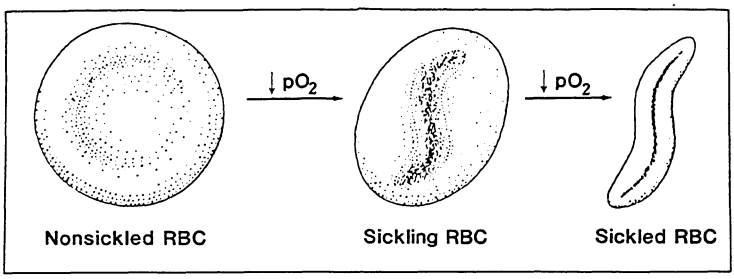


Figure 4: Sickle cell anemia provides a model for osmotic water loss in aging cells. High level of solute-solute interaction of hemoglobin molecules leads, at low oxygen tensions, to aggregation of hemoglobin molecules into a tactoid surrounded by cell water. As aggregation reduces osmotic pressure, water diffuses out of the cell and the cell membrane collapses around the hemoglobin tactoid.

diffuses out of the cell because the solute-solute interaction of the aggregating hemoglobin - taking the hemoglobin out of solution - reduces the internal osmotic pressure to the point where the sickled cell cannot retain the solvent (water).

I postulate that, in aging, the macromolecules within the cells undergo increased solute-solute interaction with a consequent lowering of intracellular oncotic pressure. This could result in water loss from the cell causing a higher concentration of macromolecules which would produce even greater solute-solute interaction, further lowering of the oncotic pressure, and even greater water loss. If we could find ways to reduce this interaction, the cycle might be interrupted.

Obviously a careful investigation is needed of the chemical potential of water and the content of water in individual cells as a function of age.

PHYCIOLOGICAL CONSEQUENCES OF BODY WATER LOSS

When one considers some of the functions of water in the body, it becomes apparent that the loss of water with age can effect many different functions. One of water's prime functions is to dilute water soluble medications. Since the therapeutic effect and toxicity of medication is related to its concentration within body fluids, it is evident that if one gives the same dosage of water-soluble drug to an older person as to a younger, the drug will be distributed in a smaller volume in the former resulting in a higher concentration and greater therapeutic and toxic potential. This can be demonstrated simply by the equation - concentration equals mass of drug administered/volume of distribution'; this implies that older persons may need lower doses of water-soluble drugs to achieve the same therapeutic effects. In addition, other influences tend to make older persons more susceptible to drug toxicity; for example, they may excrete

water soluble drugs more slowly because of decreased renal function with age, and they may metabolize drugs more slowly because of decreased hepatic function and peripheral tissue degradation.

Water in the body also acts as a thermal buffer. Water is well adapted to this function because of its high specific heat, i.e. the number of calories required to be removed or added to effect a change in temperature of one degree centigrade per gram. Water has a specific heat of one calorie per gram degree centigrade. Metals have much lower specific heats. If one places 100g of iron in a glass and 100g of water in another glass and puts both under the windshield of an automobile in the summer, the glasses each receive the same amount of radiant heat from the sun. If one returns in an hour and touches the metal, it will burn him. The water however, will be warm but not hot enough to inflict a burn; in fact it could cool the burn received from the metal. Thus, although both glasses receive the same amount of radiant energy, the temperature of the iron rose much more than that of the water because its specific heat was less. By the same token if an 80-year old and a 30-year old sat in the sun for an hour, only the older person has risked environmental hyperthermia. The older person has less water and therefore less thermal buffering capacity; his body temperature rises more than that of the younger person who has much more body water to absorb radiant energy and prevent an elevation in body temperature. Alternatively if one were to expose the 80-year old and the 30-year old to temperatures below freezing, the older individual would develop environmental hypothermia much more rapidly becasue he doesn't have a large amount of body water to act as a reservoir of body heat. Thus older persons are more susceptable to environmental hypothermia and environmental hyperthermia than are younger persons. There are other reasons for the increased sensitivity of older persons to hyper- and hypothermia namely altered central-nervous-system control, decreased sweating,and other factors.

The diminished total body water of older persons makes them more susceptible to dehydration because they have a smaller reserve. In addition, because they have less capacity to store body water, they are more susceptible to overhydration because they have a smaller volume in which to dilute exogenous water.

Recently, Phillips *et al* (12) showed that healthy elderly men have reduced thirst after water deprivation, compared to younger persons. During 24 hours of water deprivation, they studyied plasma osmolality and plasma vasopressin levels along with urine osmolality and sensations of thirst and mouth dryness. Older persons, although exhibiting slightly higher serum osmolality and vasopressin levels, did not complain of thirst or mouth dryness as did younger persons. This indicates that older persons have a tendency to ingest, and they did ingest, less water in response to water deprivation than did younger persons. This significant study further demonstrates that older persons are at considerably more risk of dehydration, not only due to their decreased body water content, but because

they seem to experience reduced thirst sensations. Earlier Helderman *et al* (13), showed that older persons showed less response to vasopressin, which they believed was due to decreased renal response, presumably because of decreased renal function with age.

Often we neglect these physiologic differences between elderly and younger patients and hence expose them to unnecessary risk. No one would give infants the same dose of medication as adults but relatively few physicians give adequate consideration to the physiological differences of body water and other changes in body composition when prescribing for the elderly.

The decrease in body water with age also makes older persons much more sensitive to and susceptible to hypovolemia and dehydration during diuretic therapy and dialysis. The increased emphasis on treatment of hypertension in the elderly including isolated systolic hypertension tempts us to overprescribe powerful diuretics for older persons. While younger persons may tolerate daily diuretic medication, often systolic hypertension in the elderly can be controlled with a diuretic every other day or every third day. It is incumbent upon the physician to adjust medication assiduously and to monitor the older patient more carefully than is needed with younger patients.

REFERENCES

1. H.M. Hines and G.C. Knowlton, Am. J. Physiol., *120*, 719, 1937.
2. J. M. Steele, E.Y. Berger, M.F. Dunning, B.B. Brodie; American Journal of Physiology, *162*, 313-317, 1950.
3. G. Von Hevesy and E. Hofer, Nature, 134, 879, 1934.
4. N. Pale, L. Kline, H.K. Schachman, M. Harfenist, J. Biol Chem. *168*, 459, 1947.
5. E.Y. Berger, M.F. Dunning, J.M. Steele, R. Jackenthal, B.B. Brodie, Am. J. Physiol. *162*, 318-325, 1950.
6. N.W. Shock, D.M. Watkin, M.J. Yiengst, A.H. Norris, G.W. Gaffney, R.I. Gregerman, J.A. Falzone, J. Gerontol., *18*, 1-8, 1963.
7. O.H. Lowry and A.B. Hastings, chapter 5 in a.I. Lansing (ed) Cowdrys Problems in Aging, Williams & Wilkins Co., Baltimore 3rd Ed. 1962 pp. 105-138.
8. J.E. Cohn and N.W. Shock, Am. J. Med. Sci., *217*, 388, 1949.
9. G. T. Lesser and J. Markofsky, J. Am. Physiol., R 215-220, 1979.
10. CRC Handbook of Physiology in Aging, Ed. E. Masoro, R.D. Lindeman, p. 189.
11. B. Steen, B.K. Lundgren, B. Isaksson (1985). Body composition at Age 40, 45, 49 and 81. A Longitudinal Population Study. In R.K. Chandra (ed.): Nurtrition, Immunity and Illness in the Elderly. Pergamon Press, In press 1985.
12. P.A. Phillips, B.J. Rools, J.G.G. Ledingham, M.L. Forsling J.J. Morton, M.J. Crowe, L. Wollner; New Engl. J. Med., *311*, 12, 753- 759, 1984
13. J.H. Helderman, R.E. Vestal, J.W. Rowe, J. D. Tobin, R. Andres, G. L. Robertson; J. Gerontol., *33*, 39047, 1978.

8. END-STAGE RENAL DISEASE IN THE ELDERLY A GERIATRICIAN'S VIEWPOINT

BERNARD ISAACS, MD., FRCP.

END-STAGE RENAL DISEASE IN THE ELDERLY: A GERIATRICIAN'S VIEWPOINT

A patient aged 70 with end-stage renal failure living in the United Kingdom is unlikely to receive active treatment by renal transplantation or even by dialysis. This happens in a country which has for 40 years enjoyed a 'free' National Health Service and which boasts the most highly developed geriatric service in the world. Is this association fortuitous, or is there some sinister connection?

THE FACTS IN THE UNITED KINGDOM

Ten years ago 82% of renal units imposed an upper age limit on the acceptance of patients for treatment (1). More recently Ross Taylor, *et al* (2) found that, in only three of the eight centres they surveyed, were more than 10% of the treated patients aged 55 or over. At first sight one might explain this age-related reticence to treat by concluding that the results of dialysis were poor or that patients did not have long to live anyway. Neither explanation is correct. Taube, *et al* (3) found that nearly two thirds of a group of patients aged 55 to 72 years who suffered from end-stage renal disease and who were treated actively survived for five years; and two thirds of the survivors continued to lead active independent lives. Moreover a man of 55 can anticipate 20 more years of life, a man of 70 can expect 10 years, and even a man of 80 has, on the average 6 more years to live. For women we can add five years to the lower figure and two years to the higher one (4). We must seek the reason has elsewhere.

THE GERIATRICIAN AND HIS PATIENT

At first sight, it would seem that clinical decision making in geriatric medicine

Table I: Simple model of clinical decision-making

$$\text{Gain} = \text{Risk} + \text{Pain} + \text{Cost}$$

operates, on a fairly simple model (Table 1). On one side of the equation is the gain to be derived from implementing a policy of treatment. On the other side are three factors: the risk the treatment will entail, that is, the chance of some undesired outcome; the pain or discomfort inherent in the treatment itself; and the cost payment by or on behalf of the patient to the private or public purse.

Using this model the geriatrician faced with an elderly patient suffering from end-stage renal disease will analyse the situation as follows:

Gain

The man of 70 belongs to an age group with an average life expectancy of 10 years. He is far below that average because of his renal disease. Without his renal disease what would be his life expectancy? How many years would we obtain for him by active treatment - one year, five or 10 or more than 10 years?

Geriatricians dislike being seen to be in pursuit of added years. Indeed the motto of the British Geriatrics Society states explicitly that its purpose is 'Not to add years to life, but to add life to years'. In considering treatment of end-stage renal disease the geriatrician sees himself, not as adding new years but as restoring lost years. Therefore he likely will conclude that positive intervention will improve the quantity of life.

Physicians working with older people also are concerned about 'quality of life'. There is a general belief that it is a good thing to prolong life only if a certain quality can be assured. Geriatricians accept this view, if the word 'quality' is defined as relative freedom from major illness and disability. There is little point in taking active steps to prolong the life of an old person who would be doomed thereby to a longer period of suffering and dependence. Geriatricians see that as a medical rather than as a moral decision, one they are competent to make, and one that they readily make. It is quite different if the definition of 'quality of life' is extended to non-medical matters, such as the patient's happiness, his family relationships or his financial status. The geriatrician does not see these as legitimate concerns when he makes the decision to treat or not to treat. The geriatrician does not disassociate himself entirely from these matters, however he knows from experience the many traps contained in statements (by patients or their relatives) about happiness and misery; and he is aware that his authority over patients does not extend beyond the bounds of his professional training.

Risk

The concept of 'acceptable risk' influences decision making in geriatric medicine, yet both of these words call for definition. Acceptable to whom? - the surgeon, the nephrologist, the geriatrician, the patient? What of the risk of not taking action? Risk, itself a difficult concept, is based on accumulation of past experience. That the risk of a given operation is 10% means that 10% of patients who have undergone that treatment did not survive. Witinin this field there is scarcely enough experience in any one unit to give any individual a clear idea of what percentage figures should be attached to the risk. Even if this could be done it does not tell the patient what he wants to know: will he survive the operation or will he not? My rule is that I recommend a procedure to my patients if I believe that the risk of undertaking it is less than the risk of not undertaking it; and when the latter approaches 100% the former comes in as a strong chance.

Pain

This concept is better represented by the Latin word 'dolor' - all the grief, suffering, anxiety and discomfort attendant upon a given line of treatment. A natural instinct is to protect the elderly patient against the 'pain' inherent in a procedure. This attitude is widely expressed as a distaste for unnecessary investigations and manipulations. We give much weight to leaving the old person undisturbed; indeed this wish often is expressed by the patient himself, by his family and by his closest advocate, the general practitioner. However the geriatrician must consider 'dolor' as a price often worth paying for long-term gain. He has no hesitation in putting patients through the discomfort of a cataract operation to secure improved vision; or pinning a femur to regain mobility. Elderly patients often are more tolerant of these inflictions than we give them credit for. Just because they may not have long to live does not mean that they are not prepared to pass through a tunnel of pain in order to reach the sunlight beyond.

With respect to cost, most old people are poor, and in a free market they could not afford to purchase intensive kidney treatment. However, in the United Kingdom the National Health Service takes care of the cost; Hence no one of any age need be debarred because he cannot pay.

On the simple model, therefore, the geriatrician favors active treatment of people with end-stage renal failure by dialysis and transplantation. Since this does not happen there must be, obtruding itself upon the decision-making process, another agenda, another system of values.

THE SECOND AGENDA

The geriatrician and his patient are not the only ones making these medical decisions. In the United Kingdom, and in other health care systems, other

Table II: Those involved in the foreground or background of clinical decisions

Decision-Makers	
Patient	Hospital Manager
General Practioner	Health Authority
Consultant Physician	Department of Health
Nephrologist	Cabinet
Geriatrician	Public

interests shape the decision (Table 2). In assigning a role to each player, the description must be speculative, because little research has been done into these issues. In this area I depend largely on experience and intuition.

The Patient

By and large the ancient Briton is a humble, unassertive, uncomplaining chap. He expects little and is grateful for what he gets. I suspect that unless they were told, few aged patients with end-stage renal failure would know, that an operation was available that could add years to their lives or life to their years; and probably they would be the first to question its value. If they believed there was a resource shortage, and that they could receive a kidney or a place on a dialysis machine only at the expense of someone younger, they would be the first to refuse. Many would not wish to be consulted, preferring to leave the decision to their doctors.

I am conscious that here I present a stereotype, not supported by research. I could be very far wrong; and even if I am right the fault, if fault it be, lies not with our old people but with a society that has made them adopt this attitude. But, whether it is true or not, it is believed to be true, and that belief perpetuates complacency and inertia among doctors.

The General Practitioner

The general practitioner is in continuing relationship with his patient and has been so for many years. Many a practitioner sees himself as a trusted counsellor and advisor of the patient and as his protector. Many might see it as their duty to protect patients from what they believe to be *dolorous* procedures of uncertain outcome, involving the introduction of tubes into many body orifices-procedures which the elderly patient does not want.

Consultant Physician

Access to the renal unit is almost always via the consultant physician. After a study of the negative selection of patients for dialysis and transplantation in the United Kingdom Challah *et al* (5) identified low levels of referral to

nephrologists as the major cause of the low rate of active treatment in the United Kingdom.

I suspect that another factor operates here. Nephrologists often are accused of 'playing God' - an unfair charge to level at those whom we force by depriving them of resources to make choices we would rather not make ourselves, but other consultants wish to spare the nephrologist so they take it upon themselves to fix the flow of patients to a level at which the nephrologist does not have to choose whom he will save and whom he will allow to die. Erecting a formal age barrier is the easiest way to avoid the difficulty and the most popular way of solving it. When there is no formal barrier, the consultant physician helps by not pressing too strongly the claims of the oldest patients.

The Geriatrician

In the study of Challah, et al (5), the consultant geriatrician made the following startling statement 'I have no experience whatever in this field....I do not ever have to consider patients for treatment of renal failure.' I would have said much the same. Geriatric medicine in Britain is largely about people aged 75 and over suffering from multiple disease and disability. In that age group we rarely see patients with nice 'clean' renal failure unaccompanied by other life-threatening disease, or when the suitable patient does turn up we are looking the other way. Also the geriatrician often is not called upon to advise others about the relative risks and benefits of treatment. In the future this may increase with the closer integration between departments of geriatric medicine and departments of general medicine in the United Kingdom. However the process is slow.

Also geriatricians have not been active in raising the age barrier in renal transplantation. I asked 20 British geriatricians what they would do if they were given an extra million pounds to spend on developing services for the elderly in their districts. I offered them a range of choices which included developing nephrology services, but none of them chose this option (Table III).

Hospital Manager

The National Health Service is at a virtual standstill and there are limited possibilities of development of new services. Every department in every hospital can make an excellent case for expanding its services, and hospital managers have to avoid supporting unpopular causes. Kidney transplantation is a popular cause; but extending kidney transplantation to treat more old people is a less competitive proposition. One might argue that it is better to spend money on preventing disease in later life than on sustaining chronic disability but this is countered by the argument that it is better to save young lives than older ones. There even may be the unspoken argument that to save an old person's life merely postpones his death; and the financial and resource cost of treatment is but a fraction of the cumulative costs engendered by his prolonged survival.

Local Health Authorities

The Regional and District Health Authorities in England are responsible for resource allocation and resource planning. If they were so minded, they could provide the resources necessary to extend active treatment of kidney disease to the levels seen in other countries. Their failure to do so perhaps reflects the perception that what old people need is community services to sustain them in their own homes. The success of the geriatrician in calling attention to the plight of ill old people and their careers in the community has prompted the government to designate community care for the elderly as a national and local priority for health service expenditure. As a result, old people have good community services. Money can be spent only once, expecially when it is National Health Service money. I do not suppose that a conscious decision was ever made to put the money into incontinence pads rather than into the kidneys which produce the urine that soaks the pads; but the public perception of the needs of old people is that they should be looked after, not that they should be operated on. It is this perception apparently that informs policy.

Department of Health

I daresay international comparisons showing the low level of activity in United Kingdom embarrasses the Department of Health. But the Government insists that it leaves decisions on how to spend Health Service money to the local Health Authorities and would not dream of interfering; at least, I suspect, if there is no great political advantage. The people of Britain are not yet marching to the polls to demand that more kidneys be transplanted.

The Cabinet

Occasionally a voice is heard stating that if the Government spent less on defense there might be more for the National Health Service. Indeed there would; but will they spend less? Even if they did would the money reach the renal units and be used for older patients? I doubt it.

The Public

I do not understand what makes news. Every year we are told that 'thousands of old people will die this winter of hypothermia.' It is untrue but it goes on being repeated. But a headline stating that hundreds of old people will die because they will not receive a kidney is unlikely to be printed prominently. The trouble with our public and our political activists is that they nail their colours to but one mast. They are either all for nuclear disarmament or against vivisection or they want to take the lead out of petrol. Old people's kidneys have not attained the status of a Cause. Maybe it never will.

CONCLUSION

The inverse relationship noted between the intensity and quality of community geriatric services and the level of transplantation and active dialysis for old people may be more than coincidence. Removal of the burden of payment at the time of delivery of service, as in the National Health Service, means that all of us have to pay for each other's treatment, and introduces a whole range of political, psychological and social issues into the question of resource provision. This system also increases our professional perceptions of one another. If the pound can only be spent once it had better be spent on my service, so we all say. Old people with kidney disease have to compete against young people with kidney disease and against old people with other diseases.

We have learned how to make appropriate clinical decisions, but not how to design health care systems, which ensure the adequate implementation of our decisions. Geriatricians are not the only ones who have failed to meet the challenge. Challah, *et al* (5) concluded that many patients with end-stage renal failure are being denied a nephrologist's opinion, but went on to say that it will be of little value to change referral practice unless there is an increase in nephrologists. That is going to take time and money which we do not have.

Decision-making in an organisation as complex in its aims and structures as the United Kingdom National Health Service inevitably creates vast distances between the clinical and the resource decision. An organisation which attempts to do the greatest good for the greatest number will in the process fail to do lesser good for smaller numbers, without sinister intent. The problem is not whether to transplant the older patient or the younger one, but how to organise and finance a service that does both. Equally the problem is not whether to provide kidneys or incontinence pads, but how to organise and finance a service that does both. Until the latter problem is solved we are forced to debate the wrong question.

REFERENCES

1. Wing, A.J., Brunner, F.P., Brynger, H. et al 1977. Combined report on regular dialysis and transplantation in Europe. Proc. Eur. Dial Transplant. Assoc. 15, 4-76.
2. Ross Taylor, R.M., Ting, A., and Briggs, J.D. 1985. Renal transplantation in the United Kingdom and Ireland - the centre effect. Lancet i, 798-802.
3. Taube, D.H., Winder, E.A., Ogg, C.S., Bewick, M., Cameron, J.S., Rudge, C.J., Williams, D.G. 1983. Successful treatment of middle aged and elderly patients with end-stage renal disease. Brit. med. J. 286. 2018-2020.
4. Benjamin B., and Overton, E. 1981. Prospects for mortality decline in England and Wales. Population Trends. 23, 22-28.
5. Challah, S., Wing, A.J., Bauer, R., Morris, R.W., and Schroeder, S.A. 1984. Negative selection of patients for dialysis and transplantation in the United Kingdom. Nriths med. J. 288, 1119-1122.

9. DECLINE OF RENAL FUNCTION WITH AGE: MECHANISMS, RISK FACTORS AND THERAPEUTIC IMPLICATIONS

SHARON ANDERSON, M.D.

The biologic price of aging includes progressive deterioration of renal function and structure. Changes in renal function during normal aging are among the most dramatic of any organ system, so that the glomerular filtration rate of healthy octagenarians is only one-half to two-thirds that measured in young adults (1,2). In the absence of therapeutic intervention, acquired renal disease superimposed on the kidney already compromised by age-related structural and function changes may hasten appreciably progression to end-stage renal disease. This chapter considers the functional and structural changes that occur in the aging kidney, and the factors which modify the progressive course of age- and disease-related progressive renal insufficiency.

AGE-RELATED CHANGES IN RENAL FUNCTION

The glomerular filtration rate (GFR) is low at birth, approaches adult levels by the end of the second year of life, and is maintained at approximately 140 ml/min/1.73 m^2 until the age of 30. Thereafter, GFR declines in a roughly linear manner by about 8 ml/min/1.73m^2/decade (1,2). The reduction in creatinine clearance with aging is accompanied by a reduction in daily urinary creatinine excretion, reflecting decreased muscle mass (2). Therefore, the relationship of serum creatinine to creatinine clearance changes with age; the net effect is near-constancy of serum creatinine concentration while GFR (and creatinine clearance) declines. Thus, a serum creatinine level of 1 mg/dl may represent a creatinine clearance of 120 ml/min at age 20, but only 60 ml/min at age 80. The approximate creatinine clearance in adult males can be derived from the serum creatinine value with the following formula:

Creatinine clearance = (140 - age)(wt in kg)/72 x serum creatinine and, in females, by multiplying the calculated value by 0.85 (3). Parallel changes occur in renal blood flow (RBF), so that RBF is well maintained at about 350 ml/min/1.73m^2 until approximately the fourth decade, and then declines by

about 10% per decade (4,5). The reduction in total RBF is due not solely to loss of renal mass; xenon-washout studies demonstrate a progressive reduction in blood flow per unit kidney mass with advancing age (5). The decrement in renal perfusion associated with aging is most profound in the cortex; redistribution of flow from cortex to medulla may account for the slight increase in filtration fraction seen in the elderly (4,5).

Studies in laboratory rats, whose age-related renal changes resemble an accelerated version of those seen in humans, suggest that another functional change in the aging kidney is an increase in glomerular basement membrane (GBM) permeability, leading to an increase in urinary protein excretion. Young rats excrete very little protein and virtually no albumin. With aging, both the total amount of protein and the percentage of albumin rise sharply. Eventually, the full spectrum of serum proteins appears in the urine (6,7). This progressive proteinuria heralds the development of age-associated glomerular structural injury.

AGE-RELATED CHANGES IN RENAL STRUCTURE

Renal mass increases from about 50 g at birth to over 400 g during the 3rd and 4th decades, and then declines to under 300 g by the 9th decade. The loss of renal mass primarily is cortical, with relative sparing of the renal medulla (8). The number of functioning glomeruli declines roughly in accord with the changes in renal weight, while the size of the remaining glomeruli increases (9,10). With maturation and aging, important changes also occur in glomerular shape (9). The spherical glomerulus in the fetal kidney develops lobular indentations as it matures, which increases the surface area available for filtration. With aging, lobulation tends to diminish and the length of the glomerular-tuft perimeter decreases relative to its area. Studies using microangiopathic and histologic techniques have elucidated the sequence of glomerular structural changes with aging (11-13). Briefly summarized, the GBM undergoes progressive folding and then thickening. This stage is accompanied by glomerular simplification, with the formation of free anastomoses between a reduced number of glomerular capillary loops. Frequently, dilatation of the afferent arteriole near the hilum is seen at this stage. Eventually, the folded and thickened GBM condenses into hyaline material with collapse of the glomerular tuft. Degeneration of glomeruli in the renal cortex results in atrophy of the afferent and efferent arterioles, with eventual global sclerosis. However, a different pattern of change predominates in the juxtamedullary area. In these units, sclerosis of the glomerular tuft is accompanied by the formation of a direct channel between afferent and efferent arterioles, resulting in the *arteriolae rectae verae*, or aglomerular arterioles (12,13). Presumably, the formation of these direct channels contributes to the maintenance of medullary blood flow as cortical perfusion declines. The

Table I: *Factors Which Modify Age-Related Proteinuria and Glomerular Sclerosis*

Accelerating Factors	*Protective Factors*
Overfeeding (19,20)	Food restriction (16, 24, 34-37)
High protein diet (16,21,22)	Protein restriction (16,28,35,40)
High sodium diet (23)	Sodium restriction (18)
Male gender (16,18,22,24)	Female Gender (16,18,22,24)
Androgen therapy (25,26)	Castration (25,26)
Uninephrectomy (19,27-29)	Adrenalectomy (41)
Renal irradiation (29-31)	Hypophysectomy (42)
Thyroid supplements (32)	
Thymectomy (33)	

aglomerular arterioles rarely are found in kidneys from healthy young persons; their frequency increases both in aging kidneys and in kidneys from patients with intrinsic renal disease (13).

The incidence of sclerotic glomeruli increases with advancing age. To the age of 40, sclerotic glomeruli comprise fewer than 5% of the total. With increasing age thereafter, the incidence increases so that sclerosis involves 10 to 30% of the total glomerular population by the eighth decade (14,15). Accordingly, diminished glomerular lobulation and glomerular loss contribute to a reduction of the surface area available for filtration and thus to the observed age-related decline in GFR (9).

DIETARY MODIFICATION OF AGE-RELATED GLOMERULAR SCLEROSIS

Progressive glomerular sclerosis, heralded by proteinuria, takes place in aging animals of many species as well as humans (16-18). Attempts to elucidate the mechanisms responsible for age-related glomerular sclerosis have identified a number of factors which modify the process in experimental animals (Table I). Of these, dietary manipulations have been the most promising and the most extensively studied. McCay and colleagues (43) in 1935 first recognized the importance of nutrition in the aging process when they demonstrated that restriction of food intake increases the lifespan of laboratory rats. During the next 50 years, many investigators have offered evidence that food restriction slows the aging process, as manifested by [1] extension of lifespan, [2] retardation of age-related physiologic processes, and [3] retardation of age-related disease processes in experimental animals (44). In 1941, Saxton and Kimball (16) noted that 'chronic nephrosis' was second in frequency only to chronic pneumonia in pathologic lesions found in aged rats, and that limitation of caloric intake resulted in fewer glomerular lesions. Female animals, which eat less and have smaller kidneys, acquire renal lesions more slowly (16,18,22,24). Subsequent studies have confirmed that renal lesions may be delayed by making food available on alternate

days, or by limiting the amount of food to one-half to two-thirds the amount consumed by animals fed *ad libitum* (24,34-36). In contrast, progression of glomerular sclerosis in rats is hastened when the overeating is conditioned by heredity (20) or induced by hypothalamic injury (19). In these rats, as in normal rats fed *ad libitum*, progression of glomerular injury may be retarded by restricting food intake (20). Reduction of dietary protein content delays the development of age-related proteinuria and glomerular scleroisis, even when total caloric intake is not restricted (16,28,39,40). Although the most complete protection of the kidney is afforded by restricting protein intake to levels low enough to limit body growth, significant protection is also afforded by reducing protein intake to a level that does not impair growth (39,42).

It seems likely that hemodynamic alterations mediate these glomerular structural changes (45). While dietary intake of carbohydrates and fats have little effect on the kidney, renal size, structure and function are markedly influenced by protein intake. Renal blood flow and glomerular filtration rates rise acutely by 40 to 100% in dogs fed a meal of meat (46,47), and significant increases in GFR (48) and RBF (49) follow meat-feeding in normal humans. The postprandial increase in RBF is unrelated to changes in cardiac output (49,50); thus, ingestion of protein, as opposed to other nutrients, appears to result in a preferential increase in renal perfusion and GFR. When animals are maintained continuously on protein-rich diets, the mechanisms which increase RBF and GFR after individual protein meals are presumed to lead, by cumulative effect, to sustained increases in GFR and RBF and to renal hypertrophy (46,51). In humans, baseline GFR values have been found to be markedly higher in subjects eating conventional diets than in vegetarians eating less quantities of protein-rich foods (48).

The mechanism by which protein ingestion increases renal perfusion and filtration remains unclear. The renal hemodynamic changes triggered by a meat meal may be reproduced by gastric instillation or intravenous infusion of amino acids /52-55), but not by consumption of urea, sulfate or acid in amounts equivalent to those produced by catabolism of the meat (56,57). Administration of somatostatin recently has been reported to block the increases in GFR and RBF otherwise seen following amino acid infusions in humans (55) and in rats (54), and GFR fails to rise after a protein load in growth hormone-deficient adults (58). It seems likely, therefore, that amino acids trigger the release of a circulating hormone or other intermediate effector, which in turn is responsible for increasing RBF and GFR.

It has been suggested that the protein-rich diet characteristic of modern Western society itself induces chronic renal hyperfiltration and hyperperfusion, and thereby contributes to the functional and structural deterioration of the aging kidney (45). According to this hypothesis, the excessive glomerular pressures and flows necessary to meet demands of a protein-rich diet may contribute to eventual glomerular sclerosis. The potential mechanisms and consequences of this process are summarized in Fig. 1 (59). The bottom panel depicts the nephron population

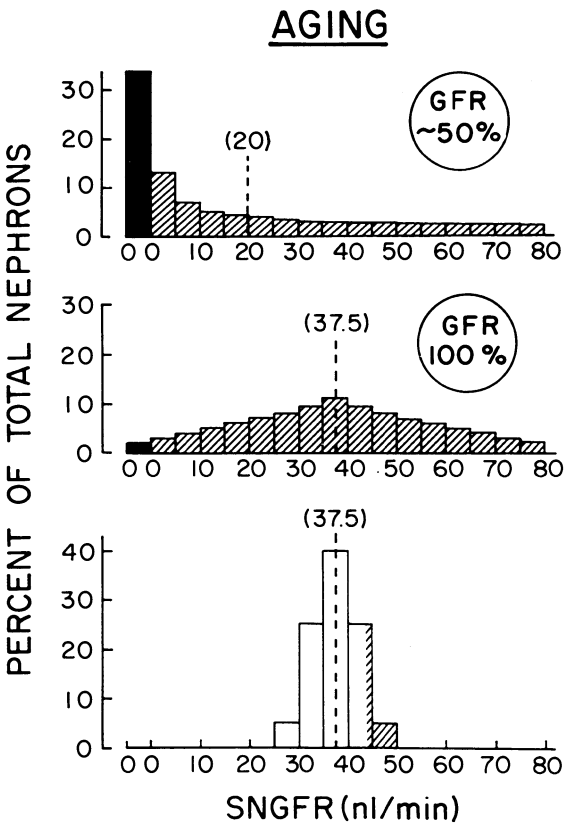


Figure 1. Sequential adaptation of the nephron population to normal aging. SN, single nephron; GFR, glomerular filtration rate. See text for discussion. (Reproduced from reference 59 with permission).

typical of the healthy young rat, and presumably the healthy young human as well. Single nephron GFR (SNGFR) values for the entire glomerular population follow a relatively narrow Gaussian distribution, with the mean value depicted by the dashed line. By eating our modern protein-rich diet, a fraction of the glomeruli at the upper end of the function scale (the shaded area in the bottom panel) is considered to be burdened, due to the adaptive increases in pressures and flows that account for their relative hyperfiltration. Over time, these glomeruli develop progressive sclerosis and eventually fail, giving rise, as shown in the middle panel, to populations of non-functioning and poorly functioning nephrons. In consequence, more normal glomeruli hyperfilter to accommodate the high protein diet in the face of fewer functioning nephrons. Therefore SNGFR values widen considerably in distribution and in doing so, all operate at risk, as depicted by the marked expansion of the shaded area. This risk in low SNGFR nephrons reflects the high hydraulic pressures regularly seen in chronically injured glomeruli whereas in higher SNGFR glomeruli, pressures and flows must both be elevated to

achieve hyperfiltration. Despite the heterogeneity in SNGFR values shown in the middle panel, the population is still largely Gaussian and the average SNGFR value is unchanged from that shown in the bottom panel. Since total nephron number remains constant, total GFR at this stage also remains at 100% of the starting value. Eventually, the stage depicted in the top panel is reached where the previously most burdened glomeruli cease functioning, yielding a large population with SNGFR values essentially equal to zero (black bar, bracketed by zero values) and an increasing fraction of the total nephron population with SNGFR values below normal. Not surprisingly, therefore, total GFR must also decline, but in this example, by only 50%, since that is the magnitude of assumed reduction in average nephron GFR. Certainly, it would seem unsound to withhold therapy for any disorder that had progressed to this stage of nephron injury and adaptation, even though total GFR is reduced by only 50%, i.e. corresponding to a serum creatinine concentration of 2 mg/dl or less.

ACCELERATION OF AGE-RELATED GLOMERULAR SCLEROSIS

By itself, age-related glomerular sclerosis poses little threat to well-being. However, while excessive glomerular pressures and flows may contribute to gradual nephron destruction over a lifetime, the process may be greatly accelerated when functioning nephron number is abruptly reduced by surgical ablation or by acquired renal disease. The incidence of primary renal disease in the elderly may not be significantly greater than in younger adults, but the frequency of acute renal failure and of renal disease associated with such systemic diseases as atherosclerosis, hypertension, cardiac failure, diabetes mellitus, and malignancy most certainly increases with advancing age (60).

Experimentally, this compounded process is illustrated by surgical ablation of renal tissue. Reduction of renal mass leads to structural and functional hypertrophy of the residual nephrons beyond that due to age alone, with marked increases in the perfusion and filtration of remaining nephron units (61). Hyperfiltration in remnant nephrons generally has been regarded as beneficial, because it minimizes the reduction in total GFR which otherwise would ensue. Recent experimental observations, however, suggest that these changes are in fact 'maladaptive', in that sustained glomerular hypertension and hyperperfusion cause progressive glomerular structural damage. More than 50 years ago, Chanutin and Ferris (62) demonstrated a syndrome of progressive azotemia and eventual glomerular sclerosis following removal of 3/4 of the total renal mass in the rat. The progressive morphologic changes subsequently were documented by Shimamura and Morrison (63). Within three months after ablation, remnant glomeruli exhibited hypertrophy, accompanied by ultrastructural alterations including vacuolization of epithelial cells, deposition of osmophilic droplets in these cells, and foot process fusion. After six months, mesangial matrix expansion and denudation of cells from areas of basement membrane were evident. These

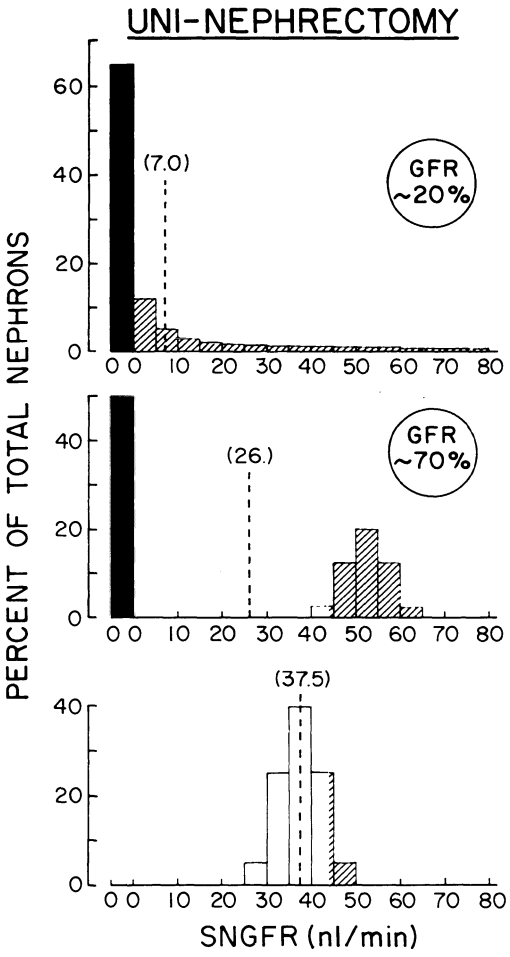


Figure 2.Sequential adaptation of the nephron population to uninephrectomy. SN, single nephron; GFR, glomerular filtration rate. See text for discussion. (Reproduced from reference 59 with permission).

ultrastructural alterations heralded progressive hyalinization and eventual sclerosis of remnant glomeruli. The glomerular morphologic injury, which follows reduction of renal mass, is reflected by progressive proteinuria (28,62). Olsen and coworkers (64), in studies of glomerular processing of tracer macromolecules following extensive renal ablation, demonstrated that the proteinuria is due to defects in both the size- and charge-selective properties of the glomerular capillary wall.

The hypothetical consequences of acute reduction of renal mass, as in uninephrectomy, are depicted in Fig. 2 (59). The initially normal nephron population profile, again seen in the bottom panel, quickly transforms within a

few weeks of uninephrectomy to that shown in the middle panel, in which one-half the glomeruli have SNGFR values equal to zero, and the remainder accommodating our customary protein-rich diet by adaptive hyperfiltration. The price of the latter, namely high glomerular pressures and flows, contributes in turn to eventual destruction of remaining glomeruli, as depicted in the top panel.

The glomerular changes in the rat remnant kidney are morphologically identical to those seen in the aging rat kidney; the only difference is the rapidity of glomerular structural deterioration. In the rat, the pace of glomerular structural injury, like the magnitude of remnant glomerular hemodynamic changes, increases in proportion to the amount of renal tissue removed. The modest increases in glomerular capillary pressures and flows following uninephrectomy are associated with moderate acceleration of the glomerular sclerosis seen in aging rats (27,28). The marked elevations in pressures and flows which occur after more extensive (over 75%) nephrectomy, produce extensive structural alterations of remnant glomeruli within a few weeks (65).

In the remnant kidney, maneuvers which limit these compensatory increases in glomerular capillary pressures and flows retard the progressive sclerosis of the remaining glomeruli. Dietary protein restriction, which slows the pace of glomerular sclerosis in the aging kidney, also has been shown to retard glomerular injury in the remnant kidneys of animals with reduced renal mass. In a study of rats subjected to 90% renal ablation, Hostetter and coworkers (65) found that SNGR in remnant nephrons of animals fed standard (24% protein) chow averaged more than twice normal by one week after ablation. This increment in SNGFR resulted from marked increases in the glomerular plasma flow reate and glomerular capillary hydraulic pressure, In contrast, glomerular capillary pressures and flows, and thus SNGFR, remained at near-normal levels in similarly prepared rats fed a 6% protien diet, despite equivalent ablation of renal tissue. Limitation of glomerular capillary pressures and flows by protein restriction was associated with preservation of glomerular structure; glomerular morphologic abnormalities were much less extensive in remnant kidneys of protein-restricted rats (65). Subsequent longterm studies have confirmed that dietary protein restriction delays the development of proteinuria and pathologic changes in remnant kidneys of rats and dogs subjected to less extensive renal ablation (28, 66-68).

Glomerular capillary pressures and flows increase not only following renal ablation, but also when functioning nephron number has been reduced by intrinsic renal disease. Pathologic studies in diverse forms of human renal disease have revealed hypertrophy (presumably reflecting hyperfiltration) of the nephrons least damaged by the original disease process (69). In rats with mineralocorticoid-induced hypertension, as with renal ablation, lowering of glomerular capillary pressures and flows by dietary protein restriction results in limitation of proteinuria and protection against glomerular injury (70). Reduction of dietary protein intake also retards the progression of nephrotoxic serum nephritis in rats

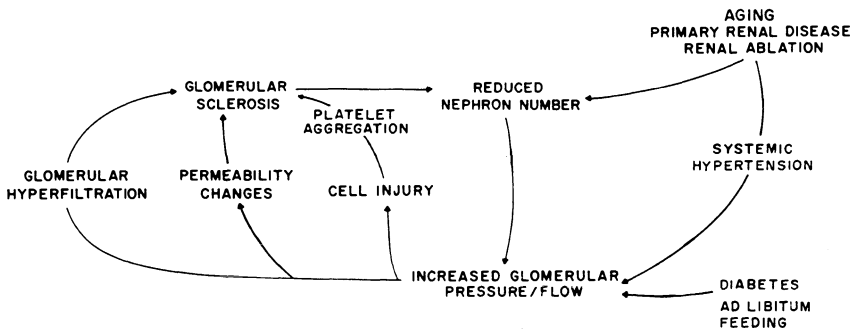


Figure 3. Role of increased glomerular pressures and flows in the development of glomerular sclerosis. See text for discussion.

(71,72) and the lupus-like nephropathy of the NZB/NZW mouse (73), as well as the glomerulopathy of the rat with streptozotocin-induced diabetes (74,75). Dietary protein restriction lowers glomerular pressures and flows, in diabetic rats (75); it is likely that the beneficial effects of protein restriction in these models are likewise to do limitation of hyperfiltration. conversely, maneuvers such as uninephrectomy which increase glomerular pressures and flows accelerate the pace of glomerular injury in such diverse forms of experimental renal disease as nephrotoxic serum nephritis, diabetes mellitus, puromycin aminonucleoside nephrosis, and lupus-like nephropathy (76-79). Presumably, uninephrectomy adds to the hemodynamic burden of glomerular capillaries previously subjected to various injurious influences, thereby accelerating glomerular destruction.

Taken together, the foregoing observations in normal aging, and in patients and animals with various forms of renal parenchymal disease, are consistent with the hypothesis that sustained hyperfiltration, or some hemodynamic determinant(s) thereof, ultimately is detrimental to glomerular structure and function. According to this scheme (Fig. 3), age- or disease-related reduction in functioning renal mass, systemic hypertension, conventionally treated diabetes, and ßad libitumß protein intake all lead to unrelenting renal vasodilatation. The resulting longterm elevations in glomerular pressures and flows promote hyperfiltration, impair the permselective properties of the glomerular wall, and injure the component cells of the glomerulus. The resulting glomerular sclerosis exerts a positive feedback stimulus to compensatory hyperfiltration in less affected glomeruli, contributing in turn to their eventual destruction.

These observations raise an important clinical question: how much renal mass must be lost to induce progressive glomerular disease, or to significantly accelerate age-related glomerular injury? An increased incidence of glomerular sclerosis has been reported in patients with unilateral renal agenesis (80,81); but these solitary kidneys may be congenitally abnormal. Longterm followup of patients undergoing uninephrectomy for unilateral renal disease or kidney transplant

Table II: *Risk Factors for Chronic Renal Failure*

Persistent activity of underlying renal disease
Commonly sought amplifiers
Uncontrolled hypertension
Obstruction/reflux
Infection
Nephrotoxic drugs
Calcium or urate deposits
Maked reduction in nephron number
Other factors promoting sustained elevations in glomerular pressures/flows
High protein diet
Diabetes mellitus
Severe anemia
Chronic renal vasodilator therapy, e.g., steroids
Diastolic blood pressure over 70 mmHg
Persistent nephrotic range proteinuria

donation are required to establish the consequences of reducing nephron number in humans with an initially normal complement of nephrons. Followup of renal transplant donors, who have been screened to rule out pre-existing renal disease, are only now becoming available. From these studies, it appears that renal function is well maintained in the majority of donors for up to three decades post-donation (82-84). However, studies of donors 10-30 years after nephrectomy have revealed significantly higher incidences of hypertension and proteinuria than in age- and sex-matched controls (82,83,85). Clearly, further studies are required to assess the longterm sequelae of kidney donation, particularly in the younger donor who presumably will have longer exposure to glomerular hyperfiltration after uninephrectomy.

THERAPEUTIC IMPLICATIONS

Given the vulnerability of the aging kidney to acceleration of renal insufficiency, it is imperative to pay particular attention to those factors which might hasten the decline in renal function (Table II). Specific therapy of acquired renal disease, and control of known amplifiers such as hypertension, infection, and nephrotoxic drugs, are important therapeutic interventions. In addition, if elevated glomerular capillary pressures and flows contribute to the progression of glomerular sclerosis in patients with age- or disease-induced renal insufficiency, it is reasonable to anticipate that therapies aimed at reducing glomerular hypertension and hyperperfusion will be effective in preserving renal function over the long term. One obvious therapy is restriction of dietary protein intake, implemented early in the course of glomerular adaptation. More than 30 years ago, Thomas Addis (86)

suggested that protein intake be restricted in patients with renal insufficiney. His aim was to decrease the 'workload' of surviving nephrons in diseased kidneys to preserve their function. The subsequent development of dialysis and transplantation distracted attention from the effects of diet on renal disease. Recently, however, interest has been renewed in the possibility that protein restriction may slow the typically progressive course of renal insufficincy (87). Several investigators have demonstrated that reduction of dietary protein intake can slow the rate of decline in renal function, and postpone the necessity for dialysis or transplantation, in patients with chronic renal failure (88-91). In these studies, reduction of dietary protein intake to 0.6 g protein/kg body weight/day, or to even lower levels with supplementation by essential amino acids or their nitrogen-free keto-analogues, appeared to favorably affect renal function, and nitrogen balance was generally well-maintained.

Early and aggressive therapy of systemic hypertension, perhaps to reduce diastolic pressure to levels below those now generally sought by physicians - i.e. to 65-70 mmHg diastolic, also may protect against hemodynamically-mediated glomerular injury when functioning nephron number is reduced. While uncontrolled hypertension hastens the decline in GFR which accompanies both normal aging (92) and chronic renal disease (91,93), longterm studies of the effect of strict blood pressure control on the progression of renal disease remain to be performed. Nevertheless, studies evaluating moderate blood pressure control over periods of up to one year suggest that reduction of systemic blood pressure may slow renal functional deterioration in patients with renal insufficiency due to intrinsic renal disease or to essential hypertension (94-96). In this regard, reduction of systemic and glomerular pressures with the converting enzyme inhibitor-enalapril, lessens glomerular structural injury in rats with renal ablation (97), and limits the development of albuminuria in the hyperfiltering kidneys of rats with streptozotocin-induced diabetes (98).

These encouraging findings notwithstanding, a great deal clearly remains to be learned about the mechanisms responsible for glomerular injury in noral aging as well as in acquired renal disease. It is hoped that further experimental and clinical studies relating both nutritional and pharmacologic maneuvers to glomerular function ultimately will enable us to prevent deterioration of renal function in patients who are at risk for progressive renal injury.

ACKNOWLEDGEMENTS

Studies in the author's laboratory were supported by U.S. Public Health Service Grants AM 19467 and AM 30410. Dr. Anderson is the recipient of an Individual National Service Award of the National Institutes of Health (S F32 AM 07206).

The author is grateful to Michelle Hardiman for expert secretarial assistance.

REFERENCES

1. Davies DF, Shock NW. 1950. Age changes in glomerular filtration rate, effective renal plasma flow, and tubular excretory capacity in adult males. J Clin Invest, 29:496-507.
2. Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW. 1976. The effect of age on creatinine clearance in men: a cross-sectional and longitudinal study. J Gerontol, 31:155-163.
3. Cockcroft DW, Gault MH. 1976. Prediction of creatinine clearance from serum creatinine. Nephron, 16:31-41.
4. Wesson LG. 1969. Renal hemodynamics in physiological states. In: Wesson LG, ed. Physiology of the human kidney. New York: Grune & Stratton, 96-108.
5. Hollenberg NK, Adams DF, Solomon HS, Rashid A, Abrams HL, Merrill JP. 1974. Senescence and the renal vasculature in normal man. Circ Res, 34:309-316.
6. Bolton WK, Benton FR, Maclay JG, Sturgill BC. 1976. Spontaneous glomerular sclerosis in aging Sprague-Dawley rats. I. Lesions associated with mesangial IgM deposits. Am J Pathol, 85:277-302.
7. Neuhas OW, Flory W. 1978. Age-dependent changes in the excretion of urinary proteins by the rat. Nephron, 22:570-576.
8. Tauchi H, Tsuboi K, Okutomi J. 1971. Age changes in the human kidney of the different races. Gerontol, 17:87-97.
9. McLachlan, MSF. 1978. The ageing kidney. Lancet, 2:143-146.
10. Goyal VK. 1982. Changes with age in the human kidney. Exp Gerontol, 17:321-331.
11. McManus JFA, Lupton CH, Jr. 1960. Ischemic obsolescence of renal glomeruli. The natural history of the lesions and their relation to hypertension. Lab Invest, 9:413-434.
12. Ljungqvist A, Lagergren C. 1962. Normal intrarenal arterial pattern in adult and ageing human kidney. A micro-angiographical and histological study. J Anat, 96:285-300.
13. Takazakura E, Sawabu N, Handa A, Takada A, Shinoda A, Takeuchi J. 1972. Intrarenal vascular changes with age and disease. Kidney Int, 2:224-230.
14. Kaplan C, Pasternack B, Shah H, Gallo G. 1975. Age-related incidence of sclerotic glomeruli in human kidneys. Am J Pathol, 80:227-234.
15. Kappel B, Olsen S. 1980. Cortical interstitial tissue and sclerosed glomeruli in the normal human kidney, related to age and sex. A quantitative study. Virch Arch A, 387:271-277.
16. Saxton JA, Jr., Kimball GC. 1941. Relation of nephrosis and other diseases of albino rats to age and to modifications of diet. Arch Pathol, 32:951-965.
17. Guttman PH, Andersen AC. 1968. Progressive intercapillary glomerulosclerosis in aging and irradiated beagles. Radiation Res, 35:45-60.
18. Elema JD, Arends A. 1975. Focal and segmental glomerular hyalinosis and sclerosis in the rat. Lab Invest, 33:554-561.
19. Kennedy GC. 1957. Effects of old age and over-nutrition on the kidney. Brit Med Bull, 13:67-70.
20. Shimamura T. 1982. Relationship of dietary intake to the development of glomerulosclerosis in obese Zukher rats. Exp Mol Path, 36:423-434.
21. Newburgh LH, Curtis AC. 1928. Introduction of renal injury in the white rat by the protein of the diet: dependence of the injury on the duration of feeding, and on the amount and kind of protein. Arch Int Med, 42:801-821.
22. Blatherwick NR, Medlar EM. 1937. Chronic nephritis in rats fed high protein diets. Arch Int Med, 59:572-596.
23. Elema JD, Arends A. 1971. Functional overload as a possible cause for non-immune glomerular damage. Effect of nephrectomy and irradiation of the contralateral kidney. J Path, 103:21-29.
24. Berg BN, Simms HS. 1960. Nutrition and longevity in the rat. II. Longevity and onset of disease with different levels of food intake. J Nutr, 71:255-263.
25. Sellers AL, Goodman HC, Marmorston J, Smith M. 1950. Sex differences in proteinuria in the rat. Am J Physiol, 163:662-667.
26. Linkswiler H, Reynolds MS, Baumann, CA. 1952. Factors affecting proteinuria in the rat. Am J Physiol, 168:504-508.

27. Striker GE, Nagle RB, Kohnen PW, Smuckler EA. 1969. Response to unilateral nephrectomy in old rats. Arch Pathol, 87:439-442.
28. Meyer TW, Hostetter TH, Rennke HG, Noddin JL, Brenner BM. 1983. Preservation of renal structure and function by long term protein restriction in rats with reduced renal mass. Kid Int, 23:218 (abstr).
29. Wachtel LN, Cole LJ, Rosen VJ. 1966. X-ray induced glomerulosclerosis in rats: modification of lesion by food restriction, uninephrectomy, and age. J Gerontol, 21:442-448.
30. Guttman PH, Kohn HI. 1960. Progressive intercapillary glomerulosclerosis in the mouse, rat, and Chinese hamster, associated with aging and X-ray exposure. Am J Pathol, 37:293- 306.
31. Elema JD, Koudstaal J, Lamberts HB, Arends A. 1971. Spontaneous glomerulosclerosis in the rat. Effect of nephrectomy and irradiation of the contralateral kidney. Arch Pathol, 91:418-425.
32. Berg BN. 1966. Effect of thyroxine on spontaneous nephrosis in the rat. Proc Soc Exp Biol Med, 121:198-203.
33. Guttman PH, Bailey DW. 1965. Potentiating effect of neonatal thymectomy on X-ray-induced intercapillary glomerulosclerosis. Nature, 207:539-540.
34. Tucker SM, Mason RL, Beauchene RE. 1976. Influence of diet and feed restriction on kidney function of aging male rats. J Gerontol, 31:264-270.
35. Johnson JE, Barrows CH, Jr. 1980. Effects of age and dietary restrictions on the kidney glomeruli of mice: observations by scanning electron microscopy. Anat Rec, 196:145-151.
36. Everitt AV, Porter BD, Wyndham JR. 1982. Effects of caloric intake and dietary composition on the development of proteinuria, age-associated renal disease and longevity in the male rat. Gerontology, 28:168-175.
37. Yu BP, Masoro EJ, Murata I, Bertrand HA, Lynd FT. 1982. Life span study of SPF Fischer 344 male rats fed ad libitum or restricted diets: longevity, growth, lean body mass and disease. J Gerontol, 37:130-141.
38. Bras G, Ross MH. 1964. Kidney disease and nutrition in the rat. Toxicol Appl Pharmacol, 6:247-262.
39. Feldman DB, McConnel EE, Knapka JJ. 1982. Growth, kidney disease, and longevity of Syrian hamsters (Mesocricetus auratus) fed varying levels of protein. Lab Anim Sci, 32:613-618.
40. Spector D, Hill G, DiCiani N, Teller D. Sacktor B. 1985. Low protein but not low phosphate diet inhibits proteinuria in aging rats. Kidney Int, 27:251 (abstr).
41. Addis T, Marmorston J, Goodman HC, Sellers AL, Smith M. 1950. Effect of adrenalectomy on spontaneous and induced proteinuria in the rat. Proc Soc Exp Biol Med, 74:43-46.
42. Everitt AV, Seedsman NJ, Jones F. 1980. The effects of hypophysectomy and continuous food restriction, begun at ages 70 and 400 days, on collagen aging, proteinuria, incidence of pathology and longevity. Mech Age Develop, 12:161-172.
43. McCay CM, Crowell MF, Maynard LA. 1935. The effect of retarded growth upon the length of life span and upon the ultimate body size. J Nutr, 10:63-79.
44. Masoro EJ, Yu BP, Bertrand HA, Lynd FT. 1980. Nutritional probe of the aging process. Fed Proc, 39:3178-3182.
45. Brenner BM, Meyer TW, Hostetter TH. 1982. Dietary protein intake and the progressive nature of kidney disease. N Engl J Med, 307:652-660.
46. Shannon JA, Jolliffe N, Smith HW. 1932. The excretion of urine in the dog. IV. Effect of maintenance diet, feeding, etc., upon the quantity of glomerular filtrate. Am J Physiol, 101:625-638.
47. O'Connor WJ, Summerill RA. 1976. The effect of a meal of meat on glomerular filtration rate in dogs at normal urine flows. J Physiol, 256:81-91.
48. Bosch JP, Saccaggi A, Lauer A, Ronco C, Belledonne M, Glabman S. 1983. Renal functional reserve in humans: effect of protein intake on glomerular filtration rate. Am J Med, 75:943-950.
49. Avasthi PS, Greene ER, Voyles WF, Fisher DC. 1985. Postprandial renal hemodynamics in humans. Kidney Int, 27:291 (abstr)

50. Fronek K, Stahlgren LH. 1968. Systemic and regional hemodynamic changes during food intake and digestion in nonanesthetized dogs. Circ Res, 23:687-692.
51. Schoolwerth AC, Sandler RS, Hoffman PM, Klahr S. 1975. Effects of nephron reduction and dietary protein content on renal ammoniagenesis in the rat. Kidney Int, 7:397-404.
52. Pitts RF. 1944. The effects of infusing glycin and of varying the dietary protein intake on renal hemodynamics in the dog. Am J Physiol, 142:355-365.
53. Lee KL, Summerill RA. 1982. Glomerular filtration rate following administration of individual amino acids in conscious dogs. Quart J Exper Physiol, 67:459-465.
54. Meyer TW, Ichikawa I, Zatz R, Brenner BM. 1983. The renal hemodynamic response to amino acid infusion in the rat. Trans Assoc Amer Phys, Washington, 96:76-83.
55. Castellino P, Coda B, DeFronzo RA. 1985. The effect of intravenous amino acid infusion on renal hemodynamics in man. Kidney Int, 27:243 (abstr).
56. O'Connor WJ, Summerill RA. 1976. The excretion of urea by dogs following a meal of meat. J Physiol, 256:93-102.
57. O'Connor WJ, Summerill RA. 1976. Sulphate excretion by dogs following ingestion of ammonium sulphate or meat. J Physiol, 260:597-607.
58. Kleinman KS, Glassock RJ. 1985. GFR fails to increase following protein ingestion in growth hormone deficient adults. Kidney Int, 27:296 (abstr).
59. Brenner BM. 1985. Nephron adaptation to renal injury or ablation. Mechanisms, benefits and risks. Am J Physiol, In Press.
60. Samiy AH. 1983. Renal disease in the elderly. Med Clin N Am, 67:463-480.
61. Hayslett JP. 1979. Functional adaptation to reduction in renal mass. Physiol Rev, 59:137-164.
62. Chanutin A, Ferris EB. 1932. Experimental renal insufficiency produced by partial nephrectomy. I. Control diet. Arch Int Med, 49:767-787.
63. Shimamura T, Morrison AB. 1975. A progressive glomerulosclerosis occurring in partial five-sixths nephrectomized rats. Am J Pathol, 79:95-106.
64. Olson JL, Hostetter TH, Rennke HG, Brenner BM, Venkatachalam MA. 1982. Altered glomerular permselectivity and progressive sclerosis following extreme ablation of renal mass. Kidney Int, 22:112-126.
65. Hostetter TH, Olson JL, Rennke HG, Venkatachalam MA, Brenner BM. 1981. Hyperfiltration in remnant nephrons: a potentially adverse response to renal ablation. Am J Physiol, 241:F85-F93.
66. El-Nahas AM, Paraskevakou H, Zoob S, Rees AJ, Evans DJ. 1983. Effect of dietary protein restriction on the development of renal failure after subtotal nephrectomy in rats. Clin Sci, 65:399-406.
67. Madden MA, Zimmerman SW. 1983. Protein restriction and renal function in the uremic rat. Kidney Int, 23:217 (abstr).
68. Polzin DJ, Osborne CA, Hayden DW, Stevens JB. 1984. Influence of reduced protein diets on morbidity, mortality, and renal function in dogs with induced chronic renal failure. Am J Vet Res, 45:506- 517.
69. Gottschalk CW. 1971. Function of the chronically diseased kidney: the adaptive nephron. Circ Res, 28 (suppl 1):1-13.
70. Dworkin LD, Hostetter TH, Rennke HG, Brenner BM. 1984. Hemodynamic basis for glomerular injury in rats with desoxycorti- costerone-salt hypertension. J Clin Invest, 73:1448-1461.
71. Farr LE, Smadel JE. 1939. The effect of dietary protein on the course of nephrotoxic nephritis in rats. J Exp Med, 70:615-627.
72. Neugarten J, Feiner HD, Schacht RG, Baldwin DS. 1983. Amelioration of experimental glomerulonephritis by dietary protein restriction. Kidney Int, 24:595-601.
73. Friend PS, Fernandes G, Good RA, Michael AF, Yunis EJ. 1978. Dietary restrictions early and late: effects on the nephropathy of the NZB x NZW mouse. Lab Invest, 38:629-632.
74. Wen SF, Benell NM, Moorthy AV. 1984. Effects of low protein diet on experimental diabetic nephropathy. IXth Int Cong Nephrol, 363 (abstr).

75. Zatz R, Meyer TW, Rennke HG, Brenner BM. Predominance of hemodynamic rather than metabolic factors in the pathogenesis of diabetic glomerulopathy. Proc Nat Acad Sci (USA), In Press.
76. Teodoru CV, Saifer A, Frankel H. 1959. Conditioning factors influencing evolution of experimental glomerulonephritis in rabbits. Am J Physiol, 196:457-460.
77. Beyer MM, Steinberg AD, Nicastri AD, Friedman EA. 1977. Unilateral nephrectomy: effect on survival in NZB/NZW mice. Science, 198:511-513.
78. Velosa JA, Glasser RJ, Nevins TE, Michael AF. 1977. Experimental model of focal sclerosis. II. Correlation with immunopathologic changes, macromolecular kinetics, and polyanion loss. Lab Invest, 36:527-534.
79. Seyer-Hansen K. 1978. Renal hypertrophy in experimental diabetes: a comparison to compensatory hypertrophy. Diabetologia, 14:325-328.
80. Kiprov DD, Colvin RB, McCluskey RT. 1982. Focal and segmental glomerulosclerosis and proteinuria associated with unilateral renal agensis. Lab Invest, 46:275-281.
81. Thorner PS, Arbus GS, Celermajer DS, Baumal R. 1984. Focal segmental glomerulosclerosis and progressive renal failure associated with a unilateral kidney. Pediatrics, 73:806-810.
82. Hakim RM, Goldszer RC, Brenner BM. 1984. Hypertension and proteinuria: long-term sequelae of uninephrectomy in humans. Kidney Int, 25:930-936.
83. Vincenti F, Amend WJC, Jr., Kaysen G, et al. 1983. Long-term renal function in kidney donors. Sustained compensatory hyper-filtration with no adverse effects. Transplantation, 36:626-629.
84. Weiland D, Sutherland DER, Chavers B, Simmons RL, Ascher NL, Najarian JS. 1984. Information on 628 living-related kidney donors at a single institution, with long-term follow up in 472 cases. Transplant Proc, 16:5-7.
85. Ferran NL, Delano BG, Beyer MM, Uribarri J, Friedman EA. 1985. Hypertension and proteinuria post renal donation. Kidney Int, 27:137.
86. Addis T. 1948. Glomerular nephritis: diagnosis and treatment. New York: Macmillan, 287.
87. Mitch WE. 1984. The influence of diet on the progression of renal insufficiency. Ann Rev Med, 35:249-264.
88. Giordano C. 1982. Protein restriction on chronic renal failure. Kidney Int, 22:401-408.
89. Maschio G, Oldrizzi L, Tessitore N, et al. 1982. Effects of dietary protein and phosphorus restriction on the progression of early renal failure. Kidney Int, 22:371-376.
90. Mitch WE, Walser M, Steinman TI, Hill S, Zeger S, Tungsanga K. 1984. The effect of a keto acid - amino acid diet supplement to a restricted diet on the progression of chronic renal failure. N Engl J Med, 311:623-629.
91. Oldrizzi L, Rigiu C, Valvo E, et al. 1985. Progression of renal failure in patients with renal disease of diverse etiology on protein-restricted diet. Kidney Int, 27:553-557.
92. Lindeman RD, Tobin JD, Shock NW. 1984. Association between blood pressure and the rate of decline in renal function with age. Kidney Int, 26:861-868.
93. Moyer JH, Heider C, Pevey K, Ford RV. 1958. The effect of treatment on the vascular deterioration associated with hypertension, with particular emphasis on renal function. Am J Med, 24:177-192.
94. Bauer JH. 1984. Role of angiotensin converting enzyme inhibitors in essential and renal hypertension. Am J Med, 77(2A):43-51.
95. Branca GF, Satta A, Faedda R, et al. 1984. Effects of blood pressure control on the progression of renal insufficiency in chronic renal failure. Panminerva Med, 25:215-218.
96. Nabel EG, Kugelmass A, Zins G, Phipps E, Dzau VJ. 1984. Does blood pressure control alter renal function in refractroy hypertension? Cir 70(suppl II):213 (abstr).
97. Anderson S, Meyer TW, Rennke HG, Brenner BM. 1985. Control of glomerular hypertension limits glomerular injury in rats with reduced renal mass. J Clin Invest, In Press.
98. Zatz R, Meyer TW, Dunn BR, et al. 1985. Lowering of arterial pressure (MAP) limits glomerular hypertension and albuminuria in experimental diabetes. Kidney Int, 27:252 (abstr).

10. PREVENTABLE CAUSES OF RENAL FAILURE IN THE ELDERLY

GEORGE E. SCHREINER, MD, FACP* #

One of the great mental traps for the physician treating elderly patients is his assumption that a clinical syndrome or an evidence of deterioration always is due to a chronic or degenerating disease. He is lured into this trap by a graying patient who introduces his symptoms with some variant of a famous line attributed to Dorothy Thompson, 'After fifty, it's patch, patch, patch'. The astute and experienced physician recognizes the senior citizen's reference to the 'one horse shay falling apart' as a method for coping rather than a clue to the diagnosis. Sadly, the contrary assumption or the physicians acceptance of degenerative disease as the sole explanation for clinical syndromes becomes a self-fulfilling prophecy. To make it happen the doctor needs only to let it happen. For this reason, it is worthwhile reviewing some of the preventable causes of renal failure in the elderly patients. Table I lists some of the causes we will discuss.

Table I: *Some Preventable Causes of Renal Failure*

Obstruction
Nephrotoxic drugs
Hypertension
Diabetes
Papillary necrosis

* Professor of Medicine, Director, Nephrology Division, Georgetown University School of Medicine, Washington, DC
# From the Division of Nephrology, Department of Medicine, Georgetown University School of Medicine.

Obstructive uropathy always should be in the forefront as one approaches the differential diagnosis of renal failure. Obstructed kidneys may be destroyed silently even in the absence of infection as John Hodson showed in his elegant pig experiments on reflux nephropathy. Table II presents a classification of the causes of obstruction.

Table II: *Classification of Obstructive Nephropathy*

1. *Closing lumen* - Stenosis, structure, atresia
2. *Intrinsic blockade* - Stones, gravel, crystals, clots, exudates
3. *Extrinsic compression* - Prostatic hypertrophy, tumors, cysts, fibrous bands, aberrant blood vessels
4. *Anomalies of form* - Angulation, ptosis, diverticulae
5. *Wall disease* - Periureteral fibrosis, ureteritis
6. *Functional failure* - Drugs, atony, neuropathy, infection, post-surgical

The lumen of any portion of the lower urinary tract may be occluded but obviously the most important sites are the uretero pelvic and uretero vesical junctions; the bladder neck and the urethra. Other favorite sites are areas of trauma or injury, or irritation by catheters or contracture of the bladder neck.

Intrinsic blockade from stones occurs most often at the narrowest portion. Early experience with the newer non-surgical techniques such as lithotrypsy, indicates a significant incidence of obstruction from the gravel derived from the break-up of large stones; here a favorite site is the terminal end of the ureter. One also encounters accumulated insoluble crystals or sand, blood clots and fibrinous or mucous exudates.

Extrinsic compression is best represented by prostatic hypertrophy but may also occur from tumors, cysts, fibrous bands or aberrant blood vessels.

In the elderly, anomalies of form such as angulation, ptosis and diverticulae may not manifest themselves clinically until they are amplified by minor obstructions. Stones, gravel and blood clots obstructing the urinary tract may bring to notice anomalies which heretofore were silent.

Wall disease - specifically periureteral fibrosis may be seen in association with tumors that stimulate a heavy fibrous capsule, retroperitoneal tumors, infection, or may be aggravated by the ergot drugs. It can also follow a ureteritis, which in turn can follow infection, trauma or surgical intervention. Recently a minor epidemic of ureteritis with stricture was seen after the use of a plastic catheter to stint the ureter during surgical procedures. These instances of chemical ureteritis have been attributed to both powder, used as a packing agent, and to the plasticizer in the catheter.

Functional failure may be due to any cause which alters the normal peristaltic emptying and induces flaccid dilatation of the ureter or bladder. Classically this is seen in pregnancy, where the ureters are dilated, and also in infections, and

after operation or trauma. Neurologic disease may produce atony, and many drugs, for example antihistamines, suppress the peristaltic reflex.

Figure 1 shows a stricture of the urethra just proximal to the meatus with dilatation of the contrast-filled urethra.

Figure 2 shows the outline of a bladder full of dye during an Intravenous pyelogram; the pressure-filling defect represents an enlarged prostate gland. The rounded filling defect of lower density on the left represents a bladder diverticulum. The trabeculation of the bladder seen along the edges of the contrast material on X-ray, which often is overlooked, is a sign of muscular hypertrophy. When it is pumping against resistance, the detrussor muscle hypertrophies as does any other muscle. Often it is seen best in the post-voiding film or as indentations in the margin of contrast material when the bladder is full. *Figure 3*, the anatomical correlative of this, shows the diverticulum coming off of the main lumen of the bladder.

Figure 4 shows a ureteral stricture produced by ureteritis, trauma or post catheter stenosis.

Figure 5 shows caliectasis of the renal pelvis and blunting of the minor calyces, which are among the early radiologic findings of obstruction high in the ureter.

Figure 6 shows the anatomical result of more advanced obstruction, and the destruction of the renal parenchyma and the deleterious effects of pressure on the functioning parenchyma.

Figure 7 illustrates all of the sites of obstruction in the urinary tract.

Figure 8 shows the classical rhomboidal crystals of calcium oxalate whose production can be enhanced by heavy ingestion of oxalic acid in vegetables such as spinach or rhubarb. Excretion of oxalate crystals also is common in patients with oxalosis - the primary causes of oxaluria, and in those with idiopathic calcium oxalate stones - the most frequent type of stones seen on the East Coast of the United States.

Figure 9 which shows the sharp facets of the calcium oxalate stone, explains the excruciating pain which may accompany this type of obstruction. The crystalline structure is characteristic of Weddellite, the mineral which forms the typical calcium oxalate stone. Obstruction during the passage of a stone is one of the most agonizing of human painful experiences. The renal colic which is due to the muscle spasm induced by products of arachidonic acid metabolism, tends to get worse as injury and pain accelerate. Thus it is most important to treat as promptly as possible, for examply by the intramuscular administration of prostaglandin-synthetase inhibitors. Intra muscular diclofenate sodium, 50 mg, relieves pain in 70% of the episodes of ureteral colic after a single injection. When pain persists, a second injection relieves pain in 90% of patients with renal colic. Some older methods are also effective: narcotics such as morphine or demerol and smooth-muscle relaxants such as papaverine and scopolamine. Ancillary methods include soaking in a hot sitz bath, application of heat, loading with fluids which also can make the pain worse temporarily and finally a relief

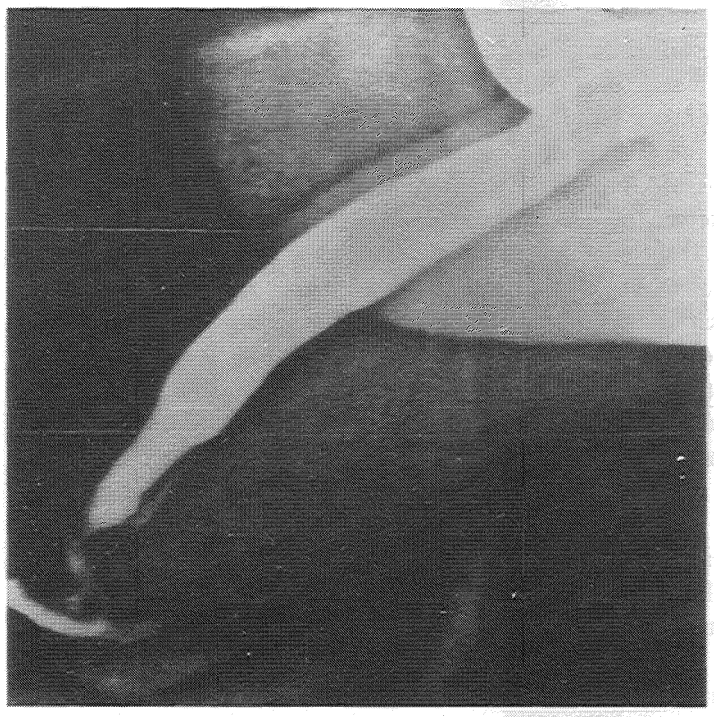


Fig. 1. Stricture of urethra - Note dilatation of contrast filled urethra proximal to the stenosis.

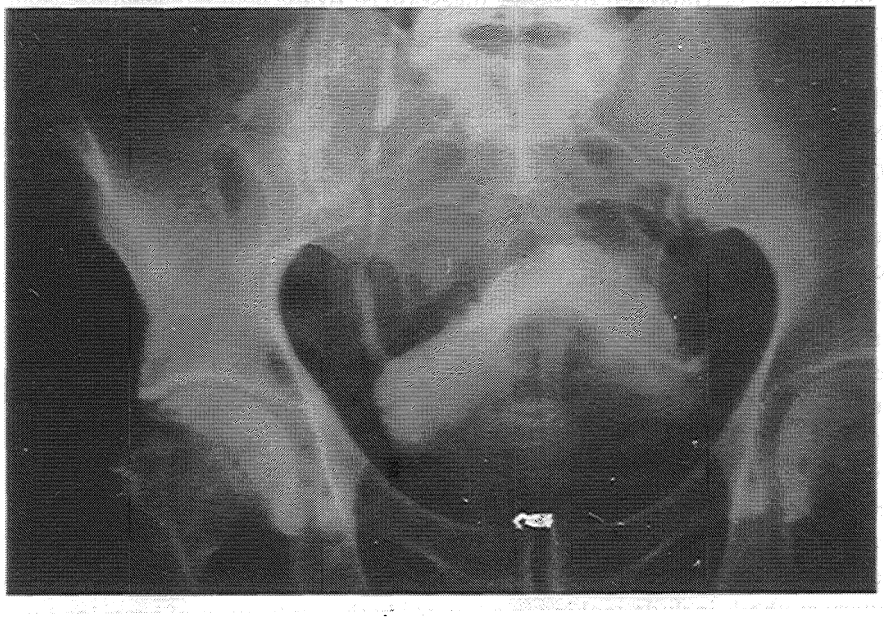


Fig. 2. Prostatic obstruction. Note filling defect in the contrast- filled bladder, diverticulum on left and trabeculation.

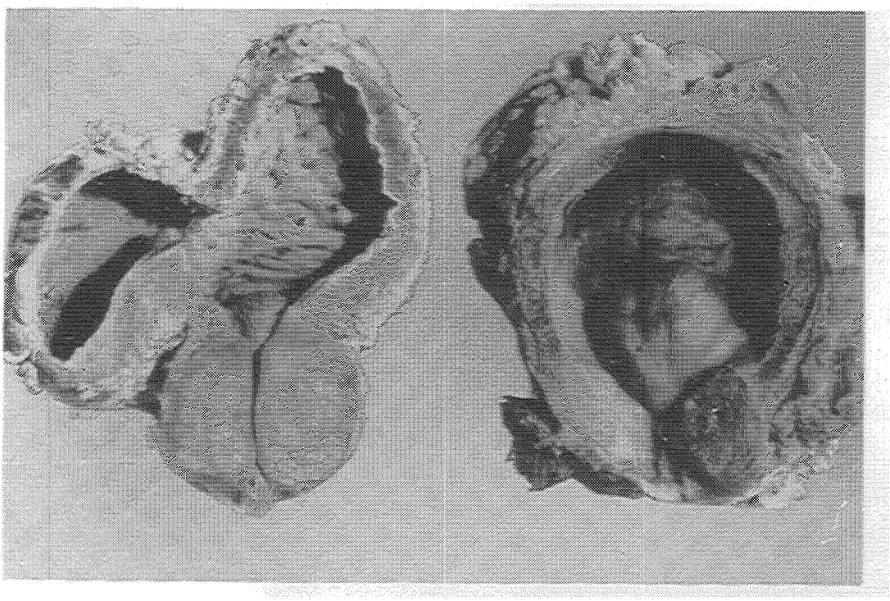


Fig. 3. Anatomical correlate of Fig. 2. Note large prostate, diverticulum and trabeculation.

of the obstruction with a by pass catheter or surgical intervention. *Table III* shows a classification of renal tumors.

Table III: Classification of Renal Tumors

1. Parenchymal	A) Benign	fibroma, adenoma, papillary, cystadenoma, endometriosis
	B) Epithelial	carcinoma, embryoma (WILMS)
	C) Mesothelial	sarcoma, neurogenic
2. Pelvis and calyces		papilloma, papillary ca, squamous ca, hemangioma
3. Renal Capsule		fibroma, fibro lipoma, sarcoma, angiosarcoma, chondroma
4. Perirenal		
5. Metastatic		

When screening for carcinogen-induced tumors, one must take a thorough dietary history, searching for any unusual foods, condiments or nutritional supplements, and a thorough occupational history for environmental exposure to agents such as aniline dyes. Also important is a careful drug history because urothelial tumors are more frequent in those who have a long history of abusing mixed analgesic tablets. It is important to note that tumors may grow and 'become clinical' during immunosuppressive therapy such as that used during kidney transplantation, the treatment of systemic lupus erythematosus, nephrotic syndrome or other immunologic diseases.

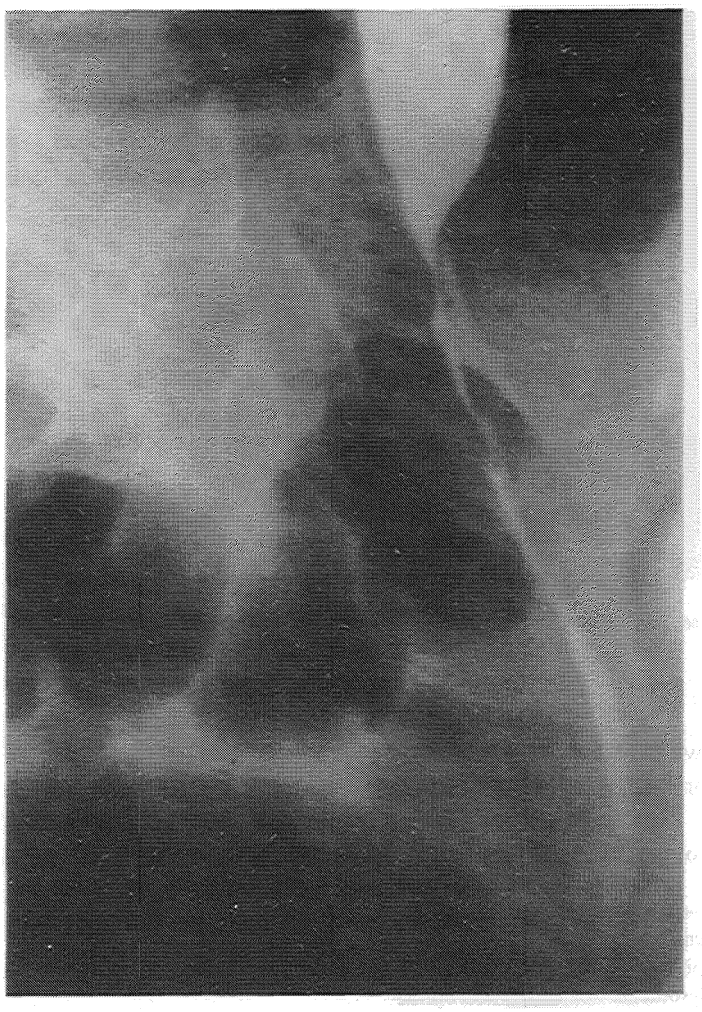


Fig. 4. Urethral stricture.

Renal carcinoma is one of the 'silent killers' of elderly patients. A review from the Mayo Clinic (1), which covered the quarter- century from 1950 to 1974, showed that the mean annual rate per 100,000 at age 60-69 was 58.5/100,000 about 10 times the rate of end-stage renal disease in most Western countries. In the female, there appears to be some slowing of neoplasm development because it is only 6.7/100,000 in the same age group; however, in the later decade from 70-79, the male incidence rises only slightly to 61/100,000 whereas females have a sixfold increase from the previous decade to 42.1/100,000. Beyond age 80, the male rate continues to rise while the female annual rate stays relatively constant. Renal carcinoma is called 'the silent killer' because of the paucity of presenting symptoms (Table IV).

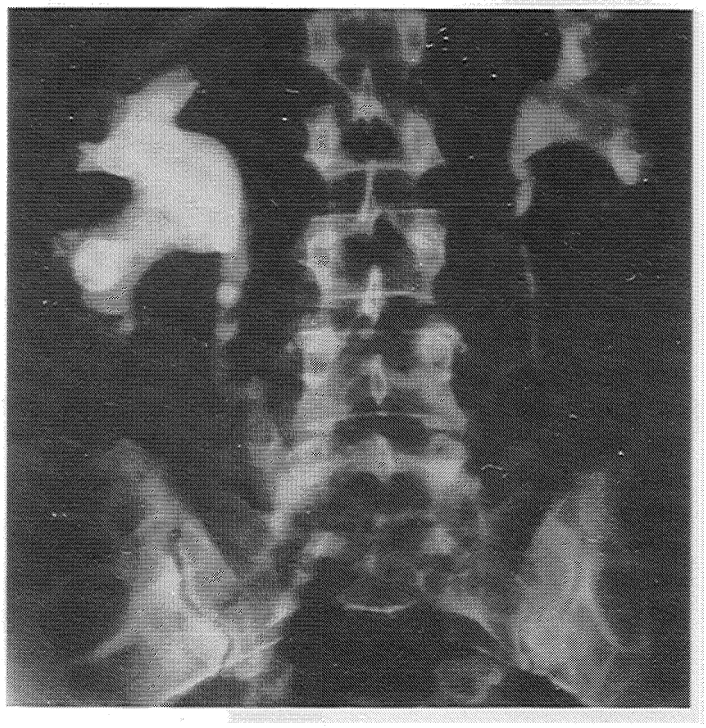


Fig. 5. Caliectasis from ureteral obstruction.

Table IV: Renal Carcinoma: Paucity of Presenting Symptoms

GROSS HEMATURIA	- 22%	INFECTION	- 11%
FLANK PAIN	- 30%	FEVER	- 4%
COLIC	- 11%	WEIGHT LOSS	- 33%
PALPABLE MASS	- 30%	GASTROINTESTINAL	- 39%

Referred pain from stretching of the capsule often is referred to the flank and the pressure pain from an internal mass usually is referred to dermatome of origin of the renal nerves - roughly the area covered by male bathing trunks. In the elderly, this pain most often is interpreted as a gastrointestinal syndrome and often geriatric patients with renal tumors are treated for long periods for a variety of gastrointestinal dialgnoses. As with most forms of carcinoma, the best results from therapy follow early detection. The bitter irony is that, even with all of our modern technology, we still are diagnosing Stage 1 renal carcinoma in less than one-half the cases. *Table V* illustrates the experience at the Mayo Clinic (2).

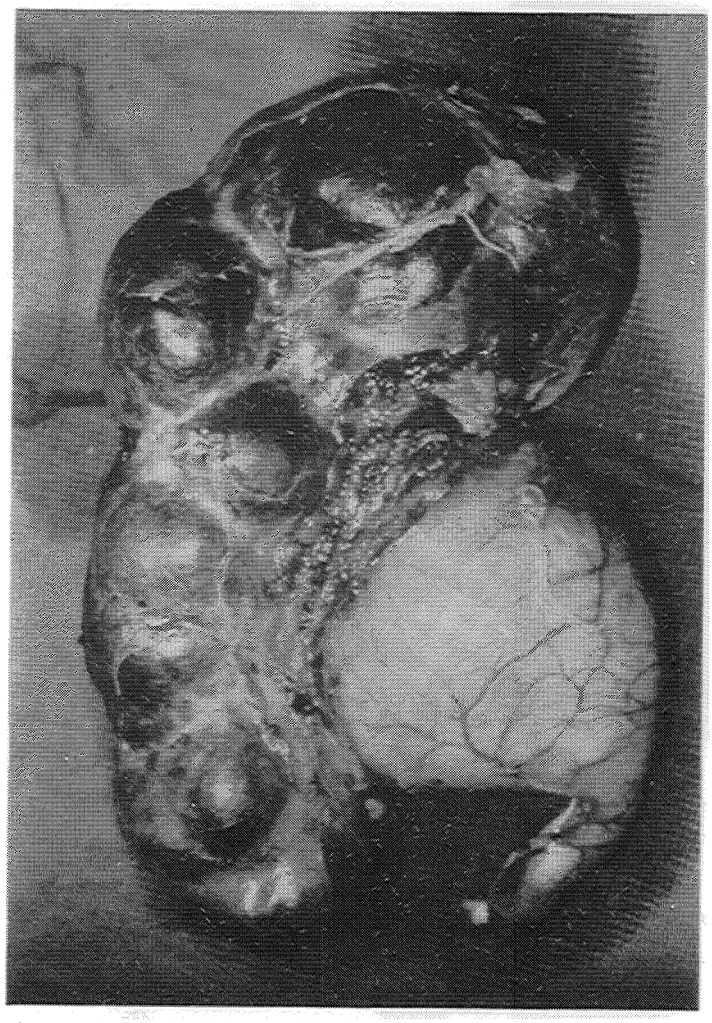


Fig. 6. Casts and parenchymal destruction of the kidney from obstruction.
(Figs. 1-6 used with Permission from slide Atlas of Nephrology. Gower Medical Publishing, Ltd.

Table V: *Renal Carcinoma*: Diagnosis by stage N = 73

Diagnosis -- stage	I	II	III	IV	UNK	%
Made clinically	17	10	6	11	0	63
Made at autopsy	18	2	0	7	0	37

Survival - 87% of Expected 5 and 10 yr. for Stage I
Mayo Clin. Proc. 53-308, 1978.

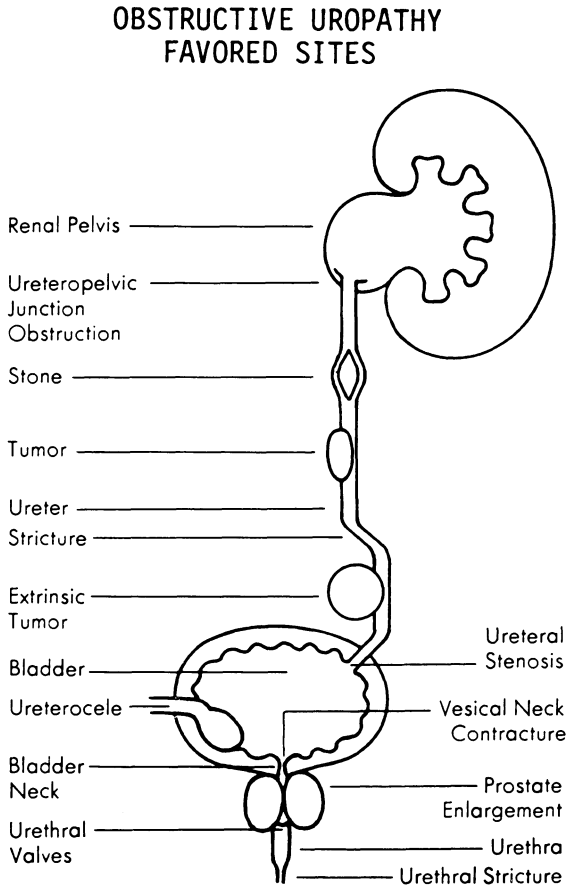


Fig. 7. Favored sites of obstruction.

Overall the diagnosis is made clinically in less than two-thirds of the renal carcinomas of all stages.

Renal carcinomas enjoy oxygen and because usually the difference in oxygen tension between the renal artery and the renal vein is only about one volume per cent, these tumors grow well in renal venous blood. Sometimes they may extend up the laminar stream all the way to the vena cava and to the heart. When one knows or suspects venous involvement, it is extremely important to remove the tumor during venous bypass surgery so as to avoid releasing malignant cells into the lung or systemic circulation.

Table VI shows a classification of drug related nephropathy.

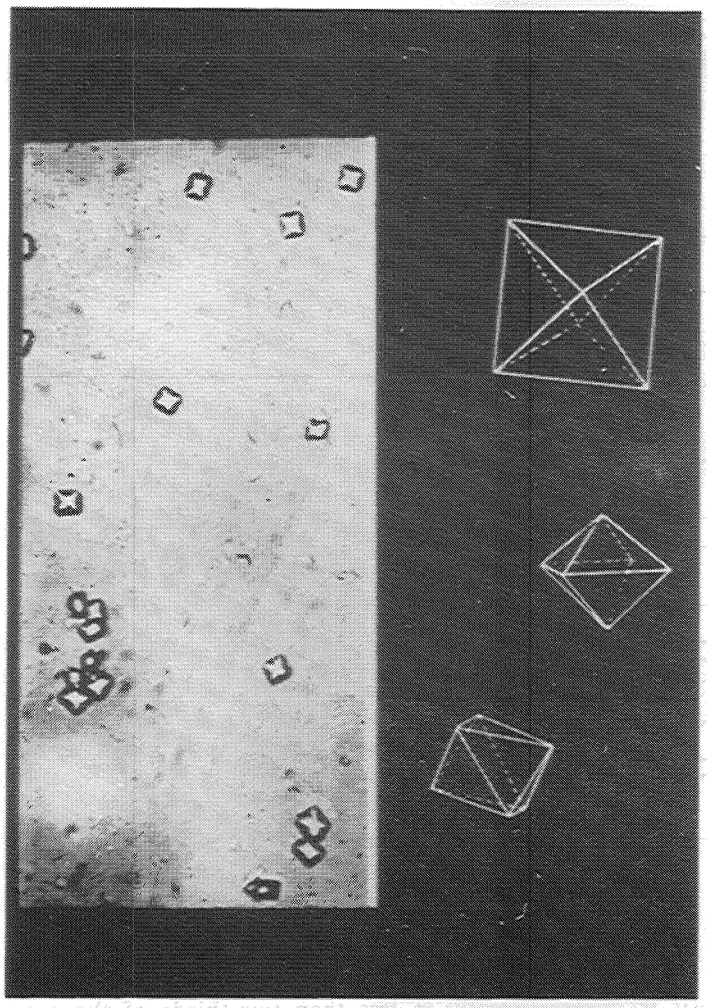


Fig. 8. Rhomboidal crystals of calcium oxalate.

Table VI: *Drug Related Nephropathy: Classification*

A. Direct chemical poisoning - e.g. heavy metals
B. Immunologically induced nephritic or nephrotic syndrome - e.g. methicillin
C. Vasculitides - e.g. sulfonamide, heroin or its contaminants
D. Induced chronic renal disease - e.g. lead, analgesic nephropathy
E. Aggravation of a predisposition to infection or nephrosclerosis - e.g. laxative abuse, hypokalemia, hyperuricemia

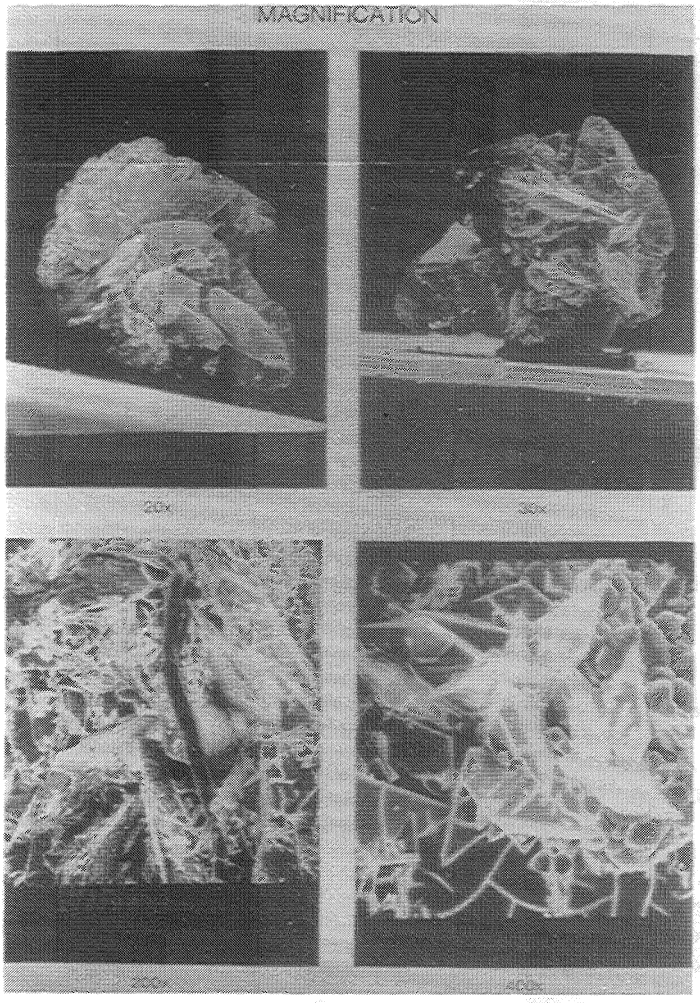


Fig. 9. Calcium oxalate stone magnified 20 X 30 X 200 X and 400 X. Note sharp facets.

The elderly have an even greater predisposition to infection and nephrosclerosis following laxative abuse, hypokalemia from diuretics, and bowel disorders and hyperuricemia from gout diuretics and neoplasm. *Table VII* gives the principle reasons for the vulnerability of the kidney to drug nephropathy.

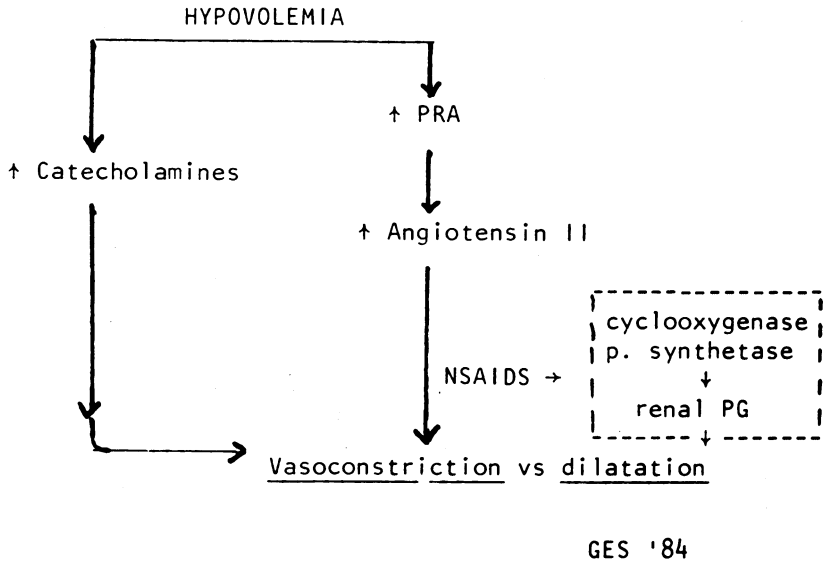


Fig. 10. Schema for mechanism of toxicity of non-steroidal anti-inflammatory drugs in hypovolemia.

Table VII: *Drug Nephropathy: Vulnerability of the Kidney*

1. LARGE BLOOD FLOW (0.4% weight gets 25% of cardiac output)
2. GREAT METABOLIC ACTIVITY (High oxygen consumption and glucose production)
3. LARGEST ENDOTHELIAL SURFACE AREA by weight
4. MANY ENZYME SYSTEMS for blockade
5. COUNTERCURRENT SYSTEM may raise local concentration
6. Mechanisms for PROTEIN UNBINDING
7. TRANSCELLULAR transport provides local exposure

The kidney, because of its large blood flow, receives a dispro-portionate amount of anything that is injected, ingested or rapidly absorbed. The kidneys' metabolism is complex; it has both an aerobic and anaerobic phase and many crucial enzyme systems which are subject to inhibition or blockade. As with the first metabolite of phenacetin, N-acetyl P-aminophenol, it is possible with the countercurrent-flow, multiplier physiology to achieve toxic local concentrations which are considerably higher than blood concentrations. The kidney also has mechanisms for protein unbinding as indicated by its excretion of many organic compounds, for example, the kidney can clear P-aminohippurate (PAH) totally in one circuit despite its protein binding. Transcellular transport processes provide local intracellular exposure of such vital structures as mitochondria and other organelles. *Table VIII* sets out the delayed drug toxicities, which are particularly prevalent in the elderly.

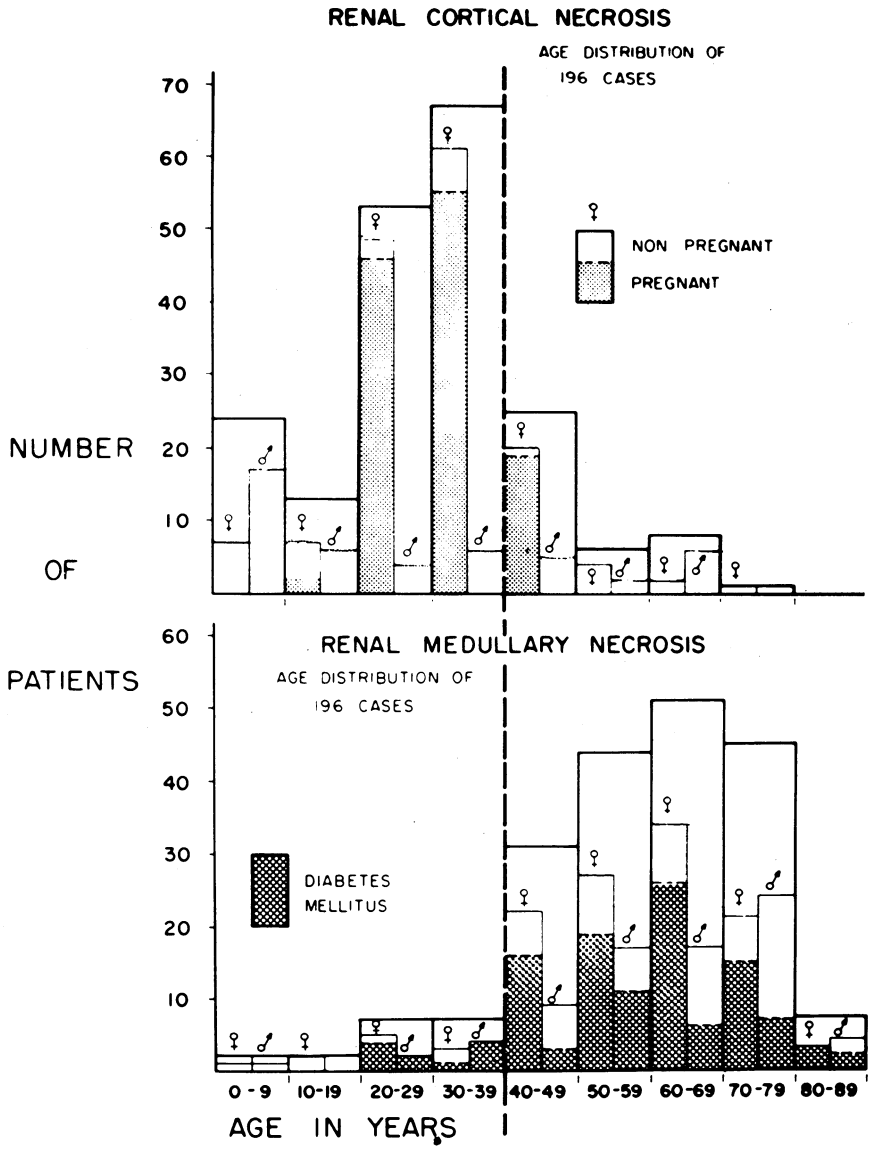


Fig. 11. Composition of renal medullary and cortical necrosis. From: *Am J Med* (Schreiner and Lauler, 1958).

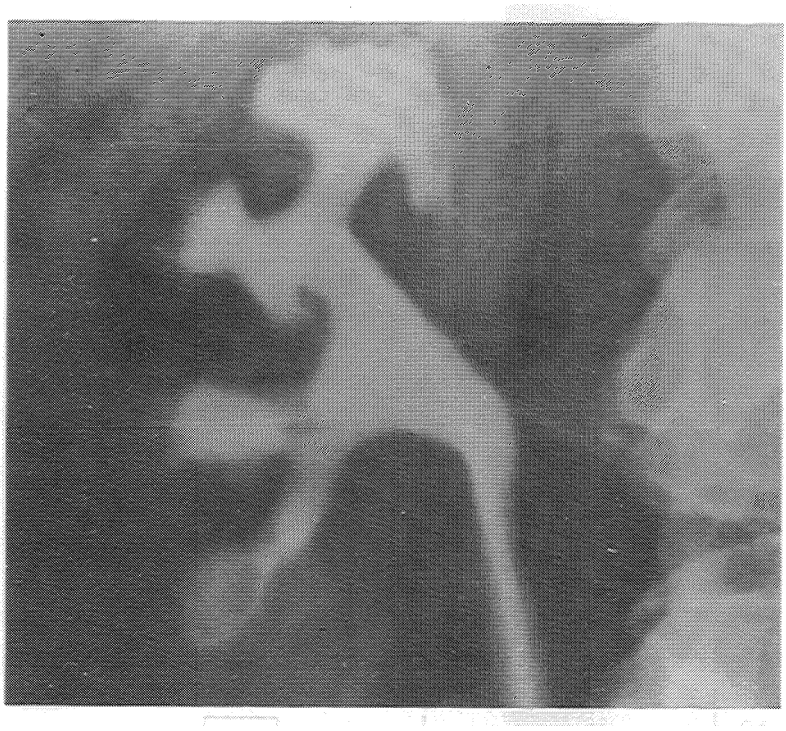


Fig. 12. 'Ring' sign in papillary necrosis.

Table VIII: Preventable Renal Failure Drugs

Delayed Toxicity - Closporine A, cis-platinum, amino glycosides, analgesics
Acute Toxicity - Metals, contrast agents, antibiotics, solvents

The agents often are difficult to anticipate and even more difficult to demonstrate because many years may elapse between exposure and pathology; indeed, many elderly patients have forgotten the very fact of exposure when giving their history, particularly of something that may have occurred many years before. Using a classical example, many decades passed before it was established that lead nephropathy was the cause of the increased incidence of chronic glomerulonephritis in Queensland, Australia. Our experience with cyclosporine A in heart transplantation indicates that initial uses of fairly high initial doses may induce a chronic interstitial fibrosis, which can destroy kidney function some years after the transplant. A significant number of patients with successful heart transplants now are on dialysis as a result. *Table IX* shows some ways that drug toxicity can be prevented or minimized.

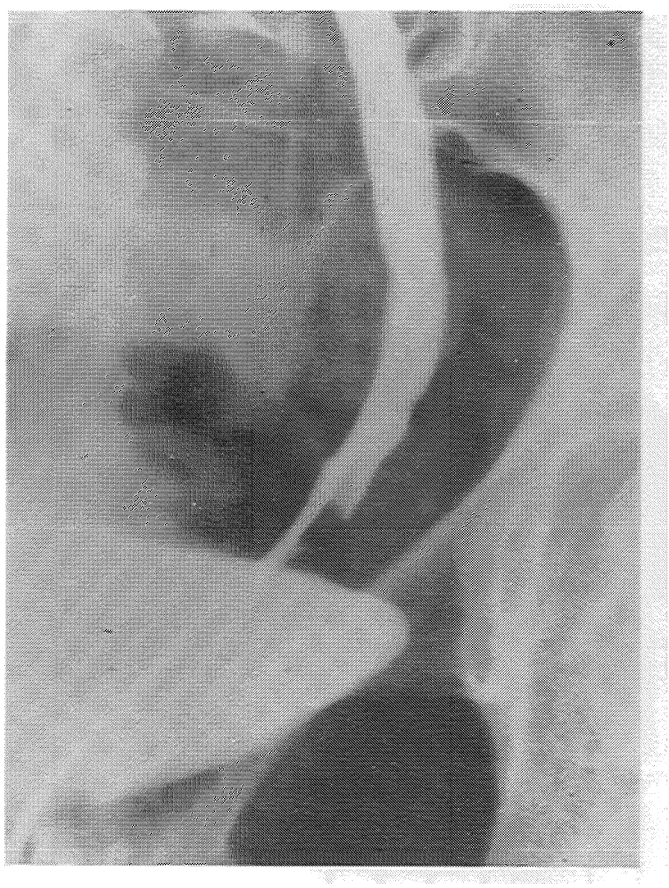


Fig. 13. Filling defect in lower ureter.

Table IX: *Prevention of Renal Failure from Oncologic Drugs*

Cis-Plat	- in 250 ml 3% saline + 250 ml/h N.S. + KCL (20 mEq/l)
Methotrexate	- Alkalinization + Hydration
Streptomycin	- Hydration + Diuretic
Methyl-CCNU	- Limit dose
Mithramycin	- Slow administration

Much of this prevention we learned from oncologists who use these cytotoxins in chemotherapy. A frequent cause of renal failure in the elderly is contrast-medium toxicity especially when the agents are given in the naturally hydrated state and in warm weather. Most elderly patients tend toward chronic hydropenia and hypovolemia, both of which predispose to renal failure following exposure to a contrast medium. As shown in *Table X*, it is important to ensure adequate hydration and to administer an osmolar load in the form of saline or mannitol.

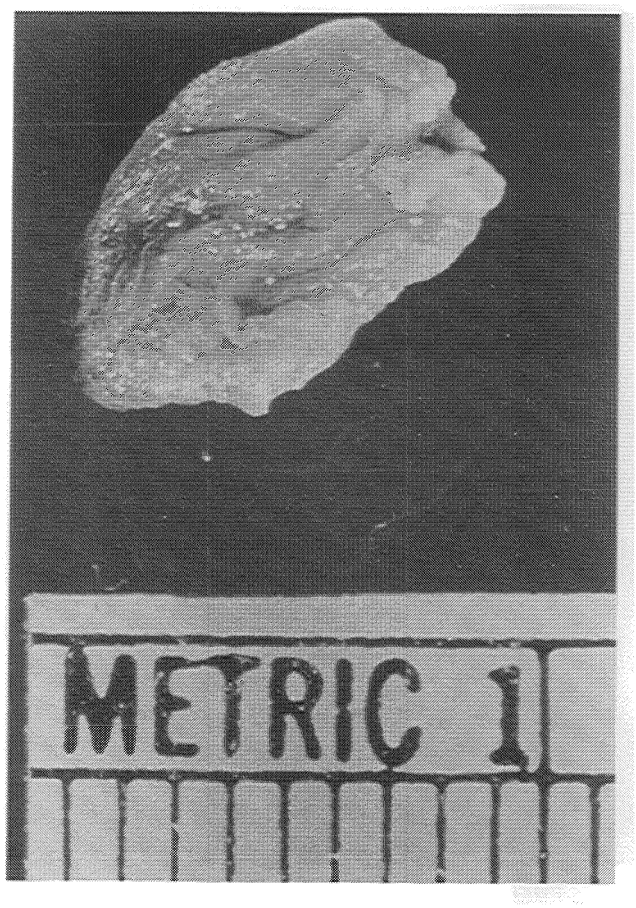


Fig. 14. Papilla removal from ureter shown in Fig. 13.

Table X: *Mannitol and Contrast Toxicity*

Shati and Anto	- (250 ml)	- 61%	- 18%	incidence RF
	Diabetes	- 92%	- 33%	incidence RF
Vosnides	- (100-ml)	13%	13%	incidence FF

Rx suggested 3-500 ml 20% + 120 mg Furosemide 1/h 6h
Replace urine vol with 5% in .5 N saline + 30 mEq KCl/L

Nonsteroidal anti-inflammatory durgs are a frequent causes of functional renal failure In the United States; it is estimated that 600,000 patients ingest one of these drugs each day and two such preparations now are available without a prescription. *Table XI* summarizes the nephropathic syndromes seen with nonsteroidal inflammatory drugs.

Table XI: *Analgesic Nephropathy*: Syndromes associated with NSAIDS

1. Transient RBF, GFR B.P., - syncope
2. Acute renal insufficiency with Acute tubular necrosis
3. Papillary necrosis (Zomepirac)
4. Acute Tubulo-interstitial nephritis - 30% Eosinophiles, T-Cells
5. Nephrotic Syndrome - (Lipoid nephrosis)
6. Lipoid nephrosis + Interstitial nephrosis (T-Cell), - (50% due to Fenoprofen). Notable in those over 60, hypertensives and those on diuretics.

The most frequent clinical picture is functional renal failure produced by an interruption of the normal defenses against hypovolemia and postural hypotension - both common situations in the elderly. Prostaglandins are involved in autoregulation of the kidney, modulation of the renin angiotensin system, macrophage cytolysis, sodium and potassium transport and water excretion. *Figure 10* illustrates the pathophysiology of functional renal failure.

HYPERTENSION

Hypertension, becuae it is an important cause of renal failure in the elderly, should be carefully monitored. *Table XII* presents several important considerations.

Table XII: *Hypertension in the Elderly*: Blood Pressure Readings

1. 'Reality' - problems of compression of rigid vessels
2. Response to upright posture - baroreceptor and drug effects
3. Systolic Proportionality Systolic should equal twice the diastolic blood pressure minus 15 mmHg. aortic complicance aortic insufficiency, arterio-venous aneurysm, Thipotoxicosis hyperkinesis
4. Sleep, alcohol - diurnal Variations - may require a 24 hour study

Stiffening and arterosclerosis of the brachial arteries may interfere with proper monitoring of blood pressure by the standard monometer. The Karotkoff sounds can be affected by stiffening of the vascular wall. Similarily, elderly patients

often will have marked postural hypotension with a potential for renal ischemia and infarction. This hypotension may be due either to vascular or drug effects on the baroreceptors. One should also keep in mind 'systolic proportionality'. If the systolic is greater than two times the diastolic blood pressure *minus* 15, it usually means that there is some form of decreased aortic compliance, for example, aortic isufficiency, arterio-venous aneurysms, thyrotoxicosis, or any cause of a hyperkinetic circulatory system. All hypertensive individuals, but especially the elderly, may show marked effects during sleep when sleep apnea, certain sleeping positions, or dream-sequences may induce hypertension. Alcohol in excess of three drinks a day can activate hypertension. To detect sleep or dream effects, one must monitor the 24-hour diurnal blood pressure cycle, by self-inflating monitors used in the same way as during Holter monitoring.

Table XIII lists the cardiovascular changes seen regularly in geriatric patients.

Table XIII: *Geriatric Changes in Cardiovascular Function*

Peripheral vascular resistance
Cardiac output
Cardiac and stroke index
Heart rate
Baroreceptor sensitivity
Beta-adrenoreceptor sensitivity
Arterial rigidity

There is an increase in peripheral vascular resistance, a decrease in cardiac output, a decrease in cardiac and stroke index, usually no change in the heart rate, a decrease in baroreceptor sensitivity, a decrease in beta-adrenoreceptor sensitivity and an increase in arterial rigidity. *Table XIV* lists some pathophysologic changes in geriatric patients.

Table XIV: Geriatric Changes in Renal Pathophysology

Renal mass
Glomerular filtration rate
Renal blood flow
Ability to conserve sodium
Plasma renin activity
Serum catecholamines
Plasma volume

Table XV lists the keys to treating hypertension in the elderly.

Table XV: *Hypertension in the Elderly*: Keys to Treatment

1. Proper reading of blood pressure
2. Rule out secondary causes of hypertension
3. Discontinue drugs that effect baroreceptors
4. When using an anti-hypertensive drug start with a very small dose
5. Remember the increased sensitivity to Sympatholytics and alpha blockers
6. Calcium blockers and Converting enzyme inhibitors are useful
7. Drugless methods are valuable - diet, decrease in obesity, elimination of stress and consistent exercise.

One should be aware of pitfalls in reading and analyzing the blood pressure in sclerotic subjects. Secondary hypertension should always be ruled out particularly when the onset is after age 50. One should consider renal artery stenosis, aortic stenosis, plaque embolization, renal infarction and other causes of secondary hypertension. One should avoid drugs that affect baroreceptors preferentially, such as the gangllonic blockers and prefer other drugs, which are effective. If it is necessary to use potent antihypertensive agents, start with very small doses remembering that these patients have an increased sensitivity to sympatholytic drugs and to alpha blockers. Converting enzyme inhibitors (especially in the presence of congestive heart failure) and the newer calcium blocking agents are very useful. Whenever possible, try to get along with ancillary or non-drug treatment such as decrease in weight, decrease in alcohol (when that has been demonstrated to be an inducer of hypertension) and elimination of stress. Regular exercise often is excellent treatment for mild hypertension. In elderly patients, the overall therapeutic strategy is to reduce the usual adult dose of any drug by one-half and gradually increase it again over a period of weeks. The patient should be seen every two to four weeks until the blood pressure stabilizes and then followed every three to four months to avoid significant orthostatic hypotension. Physical findings, which suggest secondary hypertension, include abdominal or flank aneurysms and, in renal vascular disease, abdominal bruits with diastolic components. However, in the elderly, sclerotic vessels may produce bruits, which do not necessarily connote renal vascular hypertension. Flank masses are present in polycystic disease. Absent or delayed femoral pulses are present in coarctation of the aorta; truncal obesity with pigmented striae in Cushing's syndrome and tachycardia, sweating and pallor may be a clue to pheochromacytoma or other causes of catecholamine release.

DIABETES

A detailed discussion of diabetic nephropathy is beyond the scope of this overview. However, Type I diabetics usually develop nephropathy before they become elderly. However, Type II diabetics show a significant incidence of diabetic nephropathy. As has been demonstrated recently, close attention to euglycemia can delay the onset and severity of diabetic nephropathy, which clearly is due to the abnormal *milieu* of the diabetic circulation. Normal kidneys transplanted into diabetic subjects undergo glomerular changes typical of diabetic nephropathy. The glomerular changes seen in early diabetic nephropathy can reverse when these kidneys are transplated into euglycemic subjects. But, of course, the scars or obsolescent glomeruli of nephosclerosis do not change. Hypertension appears to aggravate diabetic nephropathy, especially in certain ethnic groups. Black, urban patients, in particular, seem subject to a more malignant form of diabetic nephropathy when they combine the dual vascular threats of diabetes and significant diastolic hypertension. Non-hypertensive diabetics, common among Polynesians and certain Oriental races, tend to develop end-stage kidney disease a decade or more later than urban blacks. In the future it is hoped that, of itself, transplantation of islet beta cells will keep diabetics euglycemic and significantly delay the onset of diabetic nephropathy.

INFECTION

Infection in the elderly is not significantly different than in younger patient. Venereal infection is less frequent but infection related to obstruction is more frequent in geriatric patients. Infections are more common after instrumentation, trauma, operations, indwelling catheterization, and a reduction in the efficiency of the immune system - in the very elderly or after immunosuppressent drugs, x-irradiation and chemotherapy.

PAPILLARY NECROSIS

In the elderly, papillary necrosis is a form of preventable renal failure that is frequently overlooked. *Figure 11* contrasts papillary with cortical necrosis - the latter largely is a disease of the young and is accentuated in pregnancy. Papillary necrosis is a disease of the elderly and is accentuated by obstruction, diabetes and analgesic nephropathy.

Figure 12 shows the 'ring sign' of papillary necrosis with a deformity in the calyx of the lower pole. *Figure 13* shows a patient with one kidney who has a filling defect on the retrograde pyelogram; he had had a unilateral nephrectomy

earlier for severe infection and a poorly functioning contralateral kidney. At the time of nephrectomy, it was not appreciated that this patient had a longstanding habit of abusing mixed analgesic tablets. *Figure 14* shows the papilla, which had caused the filling defect shown in *Figure 13*; it was removed by a ureteral basket catheter.

SUMMARY

This paper has reviewed some of the most frequently encountered causes of preventable renal failure in the elderly. Diagnosing and treating these causes correctly can save huge human costs in terms of mortality, morbidity and money. Following obstruction due to the 'silent killer' carcinoma, prompt diagnosis and treatment can mean a radically different life expectancy and avoid a great deal of suffering from metastatic disease. In the mistaken assumption that deterioration in function always means chronic disease, a proper diagnosis can save the patient from being considered for dialysis. We should remember that one way a doctor can *make* it (premature renal failure) happen, is to *let* it happen. Our grandmothers were right when they said, 'An ounce of prevention is worth a pound of cure'. The only thing that has changed is the unit of measurement. Today, a gram of prevention is worth a kilogram of cure.

ACKNOWLEDGEMENT

The author wishes to thank Mrs. Betty Mendelson and Mrs. Marilyn Davis for the editorial and secretarial assistance during the preparation of this manuscript.

11. BACTERIURIA IN THE ELDERLY SUBJECT; ITS RELATIONSHIP TO SURVIVAL

ANASTASIOS S. DONTAS, M.D.

The prevalence of bacteriuria - usually defined as bladder urine containing bacteria in excess of 10^5 colony-forming units/ml increases with advancing age. Beyond age 60 this trend sharply accelerates, and is closely correlated with progressive musculoskeletal impairment. The 'spot' prevalence (i.e., the prevalence at any particular moment) and yearly incidence of bacteriuria appear to depend much more on the clinical status of the examined subjects than on their absolute age (1-4). Thus, the frequency of bacteriuria ranges from 6 to 50% in various groups of elderly subjects, and the higher rates are seen in institutions where the residents are kept at markedly reduced mobility (5,6).

In addition to its association with mobility impairment, bacteriuria has been correlated with brain failure: mentally impaired patients residing in institutions and requiring a high level of nursing care as a rule have positive urine cultures (4,7,8). Bacteriuria in the elderly produces few or no symptoms; voluntarily, most subjects do not declare any symptoms, so that this low grade infection generally is termed covert or asymptomatic.

IMPACT ON RENAL FUNCTION AND OTHER CLINICAL CORRELATES

Whether the initial source of this common infection is in the upper or the lower urinary tract, constant bacteriuria in old age is associated with measurable deficits of tubular and renovascular functions (9,10); thus, a predictable consequence in old age is damage of renal tissue. It is not clear, however, whether this damage is an effect of the infection or the background for its development. After a two-year follow-up of elderly subjects with covert bacteriuria, Marketos *et al* (11), showed that infected subjects had a yearly decline in glomerular filtration rate and renal plasma flow four to six times greater than did non-infected controls of the same age. Thus it appears that the unavoidable nephrosclerotic changes of old age are accelereated markedly by a longstanding urinary tract infection, even in the abscence of symptoms.

A urinary-tract infection imposes several other long-term effects on health. For example, approximately one-half of hospitalized patients with either urinary or fecal incontinence have bacteriuria and commonly indwelling bladder catheters are inserted in such patients (7). Each year, approximately 500,000 acute urinary tract infections are seen in acute-care hospitals in the United States, and almost all are associated with indwelling bladder catheters (12) and many of these patients develop such alarming signs as rigors, fever, and septic shock. Such nosocomial infections result in nearly a threefold increase in inpatient mortality and delayed discharge from any medical service (13). In addition, in ambulatory older persons with acute urinary tract infections, the presence of pus cells and bacteria in the urine induces bladder sensitivity with associated sensory urgency and incontinence. These abnormalities may not disappear when the urine reverts to normal after treatment, so that long-term bladder catheterization may become necessary (7).

These clinical correlates of bacteriuria increase the rate of hospitalization and length of the hospital stay of older patients. They also result in excessive demands on paramedical services following hospital discharge, and thus contribute to the high cost of health care in the elderly of any population.

BACTERIURIA AND MORTALITY

Because the overall death rate increases rapidly with advancing age, the contribution of the major causes of death gradually changes. 'Heart diseases', mostly related to atherosclerosis remain the major 'immediate' cause of death in individuals older than 55 years, but the individual case may not record important factors contributing to mortality.

Furthermore, the contribution of the major risk factors to mortality from a given group of diseases appears to be different after age 65. Cholesterol levels and body mass index in men remain significant and independent predictors of death from ischemic heart disease, in contrast to blood pressure and cigarette smoking, which remain such predictors only of 'all-causes' mortality in older men and women (14).

The influence of bacteriuria on subsequent survival has been studied in men, in women, in both sexes, and in groups of various age composition. These studies may be divided into: those investigating patients who acquired bacteriuria in hospital as a result of catheterization (13,15,16); those on non-catheterized geriatric patients, who had multiple medical problems (4); and finally, those on groups of ostensibly healthy individuals living in residential homes for the elderly or at home (17,18,19).

A detailed study on 1458 acutely catheterized hospital patients (median age 60 years) indicates that nosocomial urinary-tract infection during indwelling bladder catheterization produces a nearly threefold increase in mortality even in the

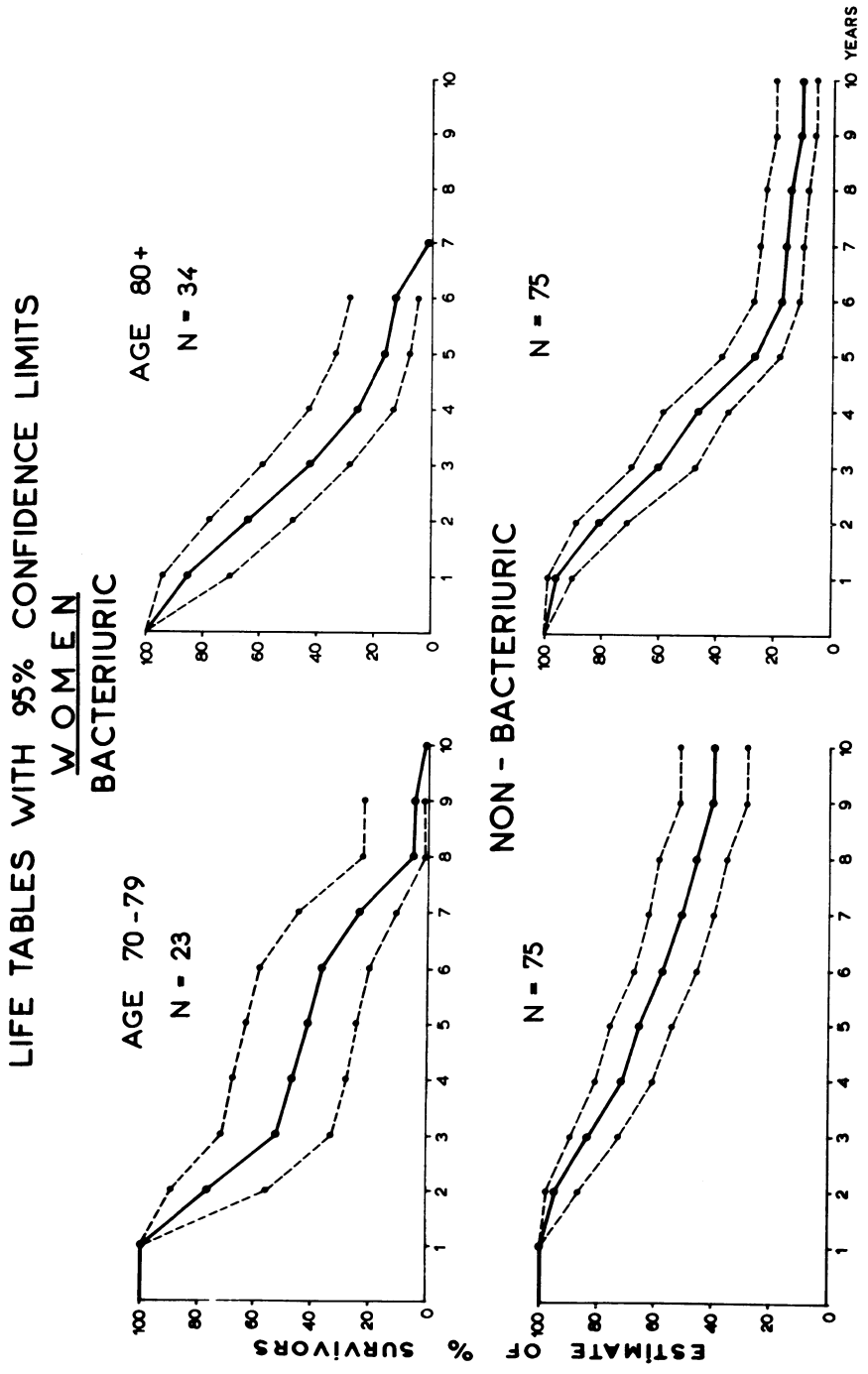


Figure 1. Life tables and 95% confidence limits (dashed lines) during a 10-year follow-up in elderly women, bacteriuric (above) and non-bacteriuric (below).

absence of documented bacteremia (13). A specific catheter-care program can reduce the rates of infection and of mortality on a short-term basis (15). However, the evidence on non-catheterized subjects and in old age is not as clear-cut.

Our own 10-year follow-up of 342 ambulant residents of a home for the aged showed that bacteriuric men and women aged 70-79 years at entry had median survivals of 33 and 34 months respectively, compared with 53 and 75 months for non-infected controls. In bacteriuric subjects over age 80, median survivals were 31 and 30 months, compared to 45 for all non-bacteriuric subjects (Fig 1). Because there were no differences at entry in most factors commonly associated with accelerated death from cardiovascular causes, the differences in survival have been attributed to the presence of bacteriuria (17). The differences between infected and non-infected subjects tended to be more significant in age groups below 80. Unfortunately, no accurate data concerning the causes of death were available for large numbers of subjects in the two groups.

At entry, the subjects in this study had had two consonant (positive or negative) cultures over two months. A major drawback of studies involving subjects who have an 'on-off' characteristic at a certain period is the possibility that the particular characteristic may be present only transiently; thus, a number of subjects who were not bacteriuric at entry may have become bacteriuric subsequently and *vice-versa*. Lacking this knowledge, it is difficult to undertake a prospective study of survival on the basis of entry data because we are uncertain of each subject's status during the rest of the study.

Evans and associates (20) who studied women in general population surveys in Wales and Jamaica have taken an important step in overcoming this obstacle. In this study 1538 women aged 15 to 84; were checked for bacteriuria three times - at entry, after six, and after 12 years, over a 12-year period. Mortality was determined at the second and third survey. After adjustment for the effects of age and body weight, which are significant predictors of bacteriuria, the ratio of the risk of death of bacteriuric women compared to that of non-bacteriuric ones, (relative risk of death) between the second and third surveys was highest (2.0; 95% confidence limits 1.05 to 3.92) in women bacteriuric at both the first and the second survey. Compared with those non-bacteriuric at both surveys, for women bacteriuric at only one of the first two surveys, the adjusted risk ratio for death was 1.6 (95% confidence limits - 0.99 to 2.57). Data similar to those in this study and those of our own mentioned above have been reported several years ago by Sourander *et al* (18) on 405 subjects of both sexes aged 65 and over.

Nordenstam *et al* (19) reported a long-term study of bacteriuria and mortality in 1996 men and women aged 70 years living in Goteborg, Sweden. Their data may be summarized as follows: Compared to non-bacteriuric controls, bacteriuric women had a relative risk of death of 1.4 after a follow-up of five years, but there was no difference at nine years. Compared to the nonbacteriuric, bacteriuric men had a two-to-three times greater relative risk of death at 5 years. The authors concluded that the number of bacteriuric subjects was too small to permit a reliable analysis,

but on the basis of their data, which were based on 5- and 9-year mortality rates, rather than lifetable analysis, they could not exclude an association between bacteriuria and mortality.

Given the differences in age and in clinical status of the elderly subjects in these studies, it is not surprising that the survival rates were different both in crude data and after adjustment for the major confounding variables. Indeed, in these studies, differences in survival persist even between subgroups of noninfected, as well as infected subjects. For example, in the study of Nordenstam et al (19), the five-year survival of nonbacteriuric women aged 70 at entry was 90.6%; in our study of non-bacteriuric women with median age of 75 at entry, survival at five years was 65% (17). In these two studies, non-bacteriuric women comprised 91 and 76.5% respectively of the samples followed up, one evidence of the better health status of the Swedish sample.

Similar differences in survival related to differences in clinical status also were found between bacteriuric groups: thus, in males with median age of 80 years studied by Nicolle et al., (4), the survival rate of treated and non-treated subjects was 50% at 19 and 21 months of follow-up respectively, whereas in our own study of untreated bacteriuric men aged 80-89, a 50% survival was reached at 25 months (median age at entry 85). These differences again highlight the dissimilar composition of the two groups, which overrides the factor of age: the men in our study were older but did not have multiple medical-psychological-social problems, so characteristic of the relatively younger but bed-ridden or confused men studied by Nicolle *et al* (4).

TRUE 'BURDEN' OF BACTERIURIA

The substantial 'turn-over' rate is a particular property of bacteriuria in the elderly, which usually is not taken into account in studies of its long-term impact on life events. Kass et al (21) concluded that Jamaican and Welsh women aged 15-64 years and residing at home acquired new bacteriuria at about 1 per cent per year. In groups of ambulant residents of a home for the aged, 70-89 years of age, we have found higher levels, i.e. 11% for men and 23% for women (22). Finally, in hospital patients with restricted mobility, positive conversion may reach levels of about 50% per year (4,7). Thus, the incidence of bacteriuria increases both with age and immobility.

The opposite trend, i.e. spontaneous negative conversion varies over a narrower range: it happens in 20 to 25% of bacteriuric Jamaican and Welsh women aged 15 to 65 (21) and in 22 and 27% of 352 men and women respectively - residents of an old peoples' home aged 70 to 90 (22). In a group of severely impaired men, however, spontaneous clearing of bacteriuria is extremely low (4); also, such groups have high levels of 'spot' prevalence. Subjects found negative at one survey but who were known to have been positive before are prone to become positive

again: 77% of men and 44% of women with such a history will be infected again within six months (22).

Considering that many bacteriuric subjects cycle between exposure, non-exposure and re-exposure modalities, and knowing that each period of exposure carries its own mortality rate, one can compare survival of infected vs. non-infected subjects only if he knows the total long-term exposure to bacteriuria. Probably published studies have underestimated the size and the length of exposure of the bacteriuric population to the advantage of the non-bacteriuric one, because data on urine (and blood) cultures usually provide an incomplete record of the true clinical situation. In studies with sufficiently long periods of follow-up, new cases of bacteriuria will emerge out of the original non-bacteriuric population and yet these cases will not be recorded as such, unless the protocol provides for repeat surveys and adjustments for misclassification. Otherwise, an unknown number of bacteriurics will be misclassified as non-bacteriurics, along with an unknown but much smaller number of (originally) bacteriurics whose infections cleared-up spontaneously or after therapy.

A different bias enters because of the impossibility of taking into account the period of exposure to bacteriuria before the subject is admitted to any of these studies. This is an inherent weakness of all surveys, which rely on infrequent spot sampling; the period includes the unknown duration of bladder colonisation before invasion of the upper urinary tract, as well as of true renal bacteriuria.

MECHANISMS OF FATAL EVENTS IN BACTERIURIA

Given the positive association between bacteriuria and increased mortality in adult life and old age, by what mechanisms does a urinary tract infection lead to accelerated death?

There are two possibilities: First, bacteriuria may be more common in patients with debilitating illnesses or in brain failure than in the general population (8,21). Generally, subjects with brain failure have reduced life expectancy but there is no agreement about the mode of death in such cases - accidents or infections (23). The lower level of personal hygiene, common even in early dementia and the frequency of fecal and urinary incontinence in advanced dementia may be the common links between mental impairment and bacteriuria (7,24). If correct, these assumptions might account for a positive but non-causal relation of bacteriuria to mortality. However, they do not apply in studies carried out in younger subjects, where brain failure must be uncommon (20), or studies of subjects in whom neurologic lesions, psychomotor disturbances, functional or organic psychoses have been excluded beforehand (17).

Alternatively, bacteriuria may lead to death *via* bacteremia and shock, elevation of blood pressure, or development of renal failure. Of these possibilities, bacteremia originating from the urinary tract accounts for less than 20% of all

such nosocomial episodes; further, only a small proportion of all deaths in hospitals can be attributed to bacteremia (16,25), and, of these, less than one-half originate from the urinary tract; finally, most patients dying from hospital-acquired, bacteremic, urinary-tract infections have very serious underlying diseases. In the community studies reported above, an association between unrecognized bacteriuria and death from bacteremia could have been established if bacteriuric subjects succumbed to fatal bacteremia; alternatively, a small per cent of patients discharged from hospitals may have remained infected and at risk of death from subsequent bacteremia. The clinical evidence in the studies reviewed here do not support these hypothetical possibilities.

Because elevated blood pressure is a strong predictor of mortality in all age groups, a positive association between bacteriuria and blood pressure might account, in part, for the association between bacteriuria and mortality. When the analysis of Welsh and Jamaican data included blood pressure as a stratifying variable, bacteriuria still retained a significant association with increased mortality, but the association was not as strong as when bacteriuria was the only stratifying variable. These findings imply that part of the association between bacteriuria and mortality is related to an association between blood pressure and mortality.

Finally, renal failure from all causes, both infectious and non-infectious, was not a frequent cause of death in any of the studies reported, in spite of a more severe impairment of renal function and its more rapid decline in elderly bacteriuric subjects.

An alternative possiblity is that, although frank renal failure is not the obvious chief cause of death, moderate renal insufficiency may contribute significantly to mortality during respiratory infections, diabetic acidosis and other acute states by reducing the kidney's capacity to retain tonicity or correct sudden disturbances of homeostasis. Thus, the immediate cause of death may be classified as 'non-renal', but the decisive factor for the patients death may be the kidney's incapacity to maintain a stable internal environment.

A final point to be considered in studies on subjects of 70-90 years of age is the high baseline mortality at this period of life. With a death rate of 7.5% per year at ages 75-84 in the U.S.A. (26), the effect of a low virulence factor, particularly if it also requires a long application to become effective, might be obscured by the high background mortality; thus intercurrent acute states, such as dehydration, which are not necessarily fatal under more stable conditions, might get the credit for death in the bacteriuric subject of advanced age.

REFERENCES

1. Brocklehurst JC, Dillane JB, Griffiths L, Fry J: 1968. The prevalence and symptomatology or urinary infection in an aged population. Gerontologia Clinica, 10:242-253.

2. Marketos SG, Dontas AS, Papanayiotou P, Economou P: 1970. Bacteriuria and arterial hypertension in old age. Geriatrics, 25:136-146.
3. Akhtar AJ, Andrews SR, Caird FI, Fallow RJ: 1972. Urinary tract infection in the elderly: a population study. Age and Ageing, 1:48-54.
4. Nicolle LE, Bjornson J, Harding GKM, MacDonell JA: 1983. Bacteriuria in elderly institutionalized men. New England Journal of Medicine, 309:1420-1425.
5. Kaye D: 1980. Urinary tract infections in the elderly. Bulletin of the New York Academy of Medicine, 56:209-220.
6. Dontas AS: 1984. Urinary tract infections and their implications. Pp. 162-192 in Brocklehurst JC ed. Urology in the Elderly, Churchill Livingstone, Edinburgh.
7. Brocklehurst JC, Bee P, Jones D, Palmer MK: 1977. Bacteriuria in geriatric patients: its correlates and management. Age and Ageing, 6:240-245.
8. Kirkland JL, Robinson JM: 1982. Bacteriuria and survival in old age. New England Journal of Medicine, 305:586.
9. Dontas AS, Papanayiotou P, Marketos S, Papanicolaou N, Economou P: 1966. Bacteriuria in old age. Lancet II:305-306.
10. Dontas AS, Marketos SG, Papanayiotou P: 1972. Mechanisms of renal tubular defects in old age. Postgraduate Medical Journal, 48:295-303.
11. Marketos S, Papanayiotou P, Dontas AS: 1969. Bacteriuria and non-obstructive renovascular disease in old age. Journal of Gerontology, 24:33-36.
12. Centers for Disease Control. National nosocomial infections Study report; Annual summary 1979. Atlanta, Georgia: Centers for Disease Control. March 1982.
13. Platt R, Polk BF, Murdock B, Rosner B: 1982. Mortality associated with nosocomial urinary-tract infection. New England Journal of Medicine, 307:637-642.
14. Barrett-Connor E, Suarez L, Khaw KT, Criqui MH, Wingard DL: 1984. Ischemic heart disease risk factors after age 50. Journal of Chronic Diseases, 37:903-908.
15. Platt R, Polk BF, Murdock B, Rosner B: 1983. Reduction of mortality associated with nosocomial urinary tract infection. Lancet, I: 893-897.
16. Bryan CS, Reynolds KL: 1984a. Community-acquired bacteremic urinary tract infection: epidemiology and outcome. The Journal of Urology, 132: 490-493.
17. Dontas AS, Kasviki-Charvati P, Papanayiotou PC, Marketos SG: 1981. Bacteriuria and survival in old age. New England Journal of Medicine, 304:939-943.
18. Sourander LB, Kasanen A: 1972. A 5-year follow-up of bacteriuria in the aged. Gerontologia Clinica, 14:274-281.
19. Nordenstam GR, Brandberg A, Eden S, Svanborg Eden CM, Svanborg A: Bacteriuria and mortality in a 70-year old population (personal communication).
20. Evans DA, Kass EH, Hennekens CH, Rosner B, Miao L, Kendrick MI, Miall WE, Stuart KL: 1982. Bacteriuria and subsequent mortality in women. Lancet I:156-158.
21. Kass EH, Miall WE, Stuart KL, Rosner B: 1978. Epidemiologic aspects of infections of the urinary tract. Pp 1-7 in Kass EH, Brumfitt W, eds. Infections of the Urinary Tract, University of Chicago Press, Chicago.
22. Kasviki-Charvati P, Drolette-Kefakis B, Papanayiotou PC, Dontas AS: 1982. Turn-over of bacteriuria in old age. Age and Ageing, 11:169-174.
23. Thompson EG, Eastwood MR: 1981. Survivorship and senile dementia. Age and Ageing, 10:29-32.
24. James MH: 1979. Disorders of micturition in the elderly. Age and Ageing, 8:285-288.
25. Bryan CS. Reynolds KL: 1984b. Hospital-acquired bacteremic urinary tract infection. epidemiology and outcome. The Journal of Urology, 132:494-498.
26. Madden TH, Turner IR, Eckenfels EJ: 1982. The Health Almanac. Raven Press, New York.

12. ACUTE RENAL FAILURE IN THE ELDERLY

N. LAMEIRE, K. DE KEYZER, W. PAUWELS, E. MATTHYS, R. VANHOLDER AND S. RINGOIR

INTRODUCTION

The prognosis of acute renal failure (ARF), as judged by mortality rates, has not improved over the last few decades. This is remarkable in view of the improvement in dialysis techniques, better blood access, the use of hyperalimentation and more efficient antibiotics. This lack of continued improvement has been attributed to two major factors: An increase in the age of patients who develop ARF, and an increase in the proportion of patients who present with other significant illnesses, complicated by ARF.

Elderly patients, in particular, are likely to suffer from these types of diseases and therefore are at greater risk of developing ARF in response to ischemic or nephrotoxic insultsAs the mean age of the general population advances, this category of ARF patient will continue to grow. It is not easy to estimate the incidence of ARF in an elderly population. In a recent analysis of renal disease in the elderly, Moothy and Zimmerman (1) found 32 patients with ARF among 97 elderly persons with renal disease who were selected for study because renal biopsies were available. Most of those with ARF suffered from crescentic glomerulonephritis. Acute tubular necrosis (ATN) and atheromatous renal embolic disease were exceptional as the causes of ARF. Due to their selection criteria (renal biopsies) these numbers do not reflect the true incidence of ARF in the elderly people.

Many data suggest that prognosis in ARF worsens with age and both earlier (2-8) and recent papers (9-12) report a higher mortality rate in older than in younger patients. However, this view is not shared by others (13-17). Kumar *et al* (14) described a series of patients with ARF over 70 years of age; in them, the mortality was 57.3%, a figure comparable with the overall mortality in ARF, irrespective of age, as reported at that time. Since this paper deals specifically with ARF in the elderly, it is worth analysing it in more detail. These authors described a relatively early experience - data collected between 1961 and 1972; this explains in part the low incidence of dialysis in their patients (only 24.6%)

which was almost entirely peritoneal dialysis. This early experience also explains the spectrum of diseases causing ARF at that time, which is different from the present experience of most renal units. For example, Kumar *et al* do not mention acute interstitial nephritis (AIN) and the incidence of thromboembolic disease is very low. This different spectrum makes it difficult to compare their outcome with that of more recent experience. Inclusion in their series required the presence of oliguria and thus they did not study the recently recognised and more favorable forms of non-oliguric ARF.

The present paper describes a retrospective analysis of ARF encountered in one university renal unit in the years between 1980-1984. Although the study was retrospective, the policy of this unit during the last five years was uniform: It accepted for treatment all ARF patients, irrespective of age; it treated underlying diseases as aggressively as possible in a modern intensive care unit when necessary, and it practised prophylactic dialysis, parenteral nutrition and close supervision by the renal staff. This paper will attempt to answer four questions:

Is the spectrum of diseases which causes ARF different in older than in younger patients?

Is ARF in the elderly characterised by different diagnostic and biochemical abnormalities?

Is there an aged-related difference in overall prognosis? and finally,

Do significantly different prognostic variables exist which make it possible to predict the outcome?

PATIENTS AND METHODS

From Jan. 1980 to Dec. 1984, 280 patients with the presumed diagnosis of ARF were referred to the Renal Unit. From these we excluded patients with post-transplantation and obstetrical ARF. In addition, every patient who suffered from prerenal ARF and a serum creatinine continuously lower than 3 mg % was excluded because we believed that the inclusion of these mild forms, which often may go undetected in hospitalized patients, would distort the prognosis in this series.

Applying these considerations, we chose for analysis 259 patients with ARF. They were divided into two categories depending on age: Group I - 89 patients were 65 years or older, and group II - 170 patients ranged in age from 16-64 years. Table I summarizes the numbers, age and sex distribution of these patients and their source of referral.

In both groups, males predominate, but both sexes had approximately the same referral pattern. Almost one-half of the patients were referred from other peripheral hospitals (PH), while a minority were admitted from other divisions in the University Hospital (UH).

Depending on the seriousness of the clinical condition, each patient was

Table I: Acute renal failure 1980-1984 Gent

	Group I >65 yrs.	Group II <65 yrs.
Total number	89	170
men	53 (72.5 ± 0.8 yrs)	102 (46.3 ± 1.52 yrs)
women	36 (71.0 ± 0.8 yrs)	68 (47.4 ± 2.20 yrs)
Referral UH	19 (21%)	40 (22%)
PH	45 (51%)	72 (43%)
Home	25 (28%)	58 (35%)
Previous renal disease	15 (17%)	24 (14%)

treated in the medical intensive care unit or was admitted directly into the renal ward of the Division. The cardiorespiratory status was monitored by measuring central venous or pulmonary capillary wedge pressure, when necessary. The patients were transfused with whole blood or packed red cells when indicated.

All patients were treated with hypercaloric intravenous solutions, consisting of hypertonic glucose, which assured an intake of at least 2,000 calories daily. Approximately one half of the patients in each group received amino-acid solutions. Infusions were given through a central venous catheter. Blood and urine cultures were collected routinely.

Infections were treated with antibiotics in doses monitored by frequent determinations of serum concentrations. In abdominal infections, we used combinations of an aminoglycoside, mostly tobramycin, a cephalosporin of either second or third generation and metronidazole (Flagyl). The patients were treated with early dialysis, when possible, not allowing the blood urea to rise above 2 g/l. Hemodialysis in ARF was performed by the dialysis staff with a single needle device, as described previously (18). Access was obtained by either a subclavian vein or, in the last two years, by deep jugular-vein dialysis catheters. Peritoneal dialysis in ARF was performed when there were no specific contraindications and the patient was not excessively hypercatabolic. On the other hand, we preferred peritoneal dialysis when the patient had a bleeding disorder or labile hemodynamics.

In Group I, 66 of the 89 patients (74%) and in Group II, 112 of the 170 patients (66%) required dialysis. In the younger group, 54% received hemodialysis alone compared to 45% in the older group. In contrast, 29% of the older patients were treated with peritoneal dialysis alone compared to only 18% of the younger group. In Groups I and II, respectively, 26% and 28% had both peritoneal and hemodialysis.

In the surviving patients, the mean duration of dialysis was 10.7 ± 3.2 days in the elderly *versus* 16.2 ± 1.5 days in the younger ($P < 0.05$).

In Group I, only 12 of 89 patients (13.5%) had non-oliguric ARF, defined as a urinary output never less than 400 ml per day; this was significantly less than

in Group II where 63 of 170 patients (37%) maintained this output. Of the 12 non-oliguric patients in Group I, eight (67%) required dialysis against only 23 of the 63 non-oliguric patients (36%) in Group II.

The overall incidence of pre-existing chronic renal disease in this series was 15%; this was evenly distributed between both groups - 17% in Group I, *versus* 14% in Group II.

CAUSES OF ARF

Although often multifactorial, the renal staff defined the cause of ARF in both groups as the most likely factor directly responsible for the deterioration of renal function. We applied a 'classic' classification in prerenal, renal and postrenal ARF. Figure 1 depicts the causes of ARF as per cent of all etiologies in both age categories.

Prerenal ARF was seen in six patients (6.7%) of Group I and in 13 (7.7%) of Group II. This is an underestimate of the true incidence of prerenal failure because of our strict criteria for inclusion - a rise in serum creatinine of more than 3.0 mg % from normal and because among many of the patients hospitalised in other departments of the University Hospital, mild prerenal ARF is undetected or is treated by the patient's own physician.

Postrenal ARF was seen in nine patients (10%) of Group I and seven (4.1%) of Group II. This difference was significant.

In the renal group of ARF, we made a distinction between the primary vascular renal diseases, including glomerular diseases, renal emboli or vascular thromboses, and acute renal deterioration following converting enzyme inhibitors (CEI), the drug- or infection-induced acute interstitial diseases and the ischemic, nephrotoxic and pigment-induced acute tubular necrosis.

ARF could be attributed to acute glomerulonephritis in four patients of Group I (4.5%) and in 20 patients (12%) of Group II ($p<0.05$). In contrast, eight patients (9%) in Group I and only two (1.2%) in Group II suffered from renal emboli or renal vascular thrombosis. CEI-induced ARF noted in only one patient of Group I and 5 (3%) of Group II.

Drug or infectious-induced acute interstitial diseases were relatively uncommon in Group I (six patients, 6.7%); this contrasts with (18 patients, 11%) in the younger age group.

In both categories of patients, the most common cause of ARF was postischemic acute tubular necrosis. Postischemic ARF developed during infectious shock - Group I: 11 patients (12.3%) *vs.* Group II: 28 patients, 16.6%; after hepatobiliary surgery or pancreatitis - Group I: eight patients (12.3%) *vs.* Group II: 10 patients (6%); cardiovascular catastophes or operation - Group I: seven patients (7.8%) *vs.* Group II: 10 patients (6%); or during or after hypovolemia - Group I: 18 patients (20.2%) *vs* Group II: 17 patients (10%). The

incidence of posthypovolemic ATN between Group I and Group II is significantly different ($P<0.01$). Nephrotixic ARF was relatively rare in Group I - five patients (5.6%) and Group II - 14 patients (8.3%) ($P<0.05$).

Pigment-induced ARF (hemolysis, traumatic and non-traumatic rhabdomyolysis) was rare in Group I - 3 patients (3.4%) but quite common in the younger group - 24 patients (14.2%). This difference was also significant. A separate analysis of postsurgical ARF revealed this condition in eight patients (9%) after vascular operations in Group I *vs* 22 (13%) in Group II.

This analysis makes it clear that elderly patients show the same spectrum of causes of ARF as younger persons, but within that spectrum, have a higher incidence of postrenal ARF, renal emboli and ATN from hypovolemia. On the other hand, younger ARF patients suffer more from acute glomerular diseases, and nephrotoxic and pigment - mostly myoglobin - induced ATN. The incidence of postsurgical ARF is similar in both age groups.

BIOCHEMICAL DATA

SERUM VALUES

We detected no major differences in the severity of the acute renal functional impairment, as judged by the peak serum creatinine values between the two groups in every category of ARF (Table II).

However, compared to the other forms, prerenal ARF was characterized by a lower peak serum creatinine in both groups (creatinine of $425+97$ μmol/l in

Table II: Peak serum creatinine values (μmol/l)

	Group I >65 yrs	Group II <65 yrs
Prerenal	n = 6 425 ± 97	n = 11 350 ± 33
Postrenal	n = 9 1124 + 124	n = 7 995 ± 212
Renal		
Vascular		
GN + emboli + CEI	n = 13 929 ± 67	n = 25 844 ± 84
AIN	n = 6 870 ± 142	n = 26 841 ± 106
ATN		
Toxic	n = 6 736 ± 54	n = 14 815 ± 82
Pigment	n = 3 770 ± 89	n = 24 788 ± 142
Ischemic		
Postinfection	n = 12 802 ± 86	n = 27 658 ± 42
Hepato-biliary	n = 8 627 ± 92	n = 10 727 ± 67
Cardiovascular	n = 8 687 ± 138	n = 10 651 ± 79
Hypovolemia	n = 18 805 ± 57	n = 14 708 ± 67
Non-oliguric	n = 12 708 ± 176	n = 63 610 ± 40

Table III: Serum electrolyes on admission in per cent distribution

		Group I >65 yrs	Group II <65 yrs
Serum Na+	(135-145)	49	55
(μmol/l)	>145	10	8
	<135	41	37
Serum K+	(3.5-4.9)	35*	57
(μmol/l)	> 5	48*	34
	< 3.5	17*	11
Serum HCO_3-	> 30	8*	4
(μmol/l)	26-29	6*	12
(n=87)	22-25	16*	28
	18-21	26	22
	14-17	24	22
	< 14	20*	12

*P<0.01

Group I and 350±33 umol/l in Group II).

Table III summarizes the percent distribution of the serum values for sodium (Na), potassium (K) and bicarbonate (HCO_3) on admission. While the incidence of severe hyper- or hyponatremia was similar in both categories of patients, the elderly patients showed a higher incidence of severe hypo-and hyperkalemia.

Only 30 patients in Group I (35%) had initial plasma K-values in the normal range, versus 57% in the second group of younger patients.

From the spectrum of the initial plasma bicarbonate levels can be derived that elderly patients were more frequently severely alkalotic or acidotic than the younger ones.

URINARY PARAMETERS

The great challenge in patients with acute renal functional deterioration is to distinguish between renal ARF and functional (acute) prerenal failure. Differences in such urinary indices as renal failure index (RFI – UNa/(U/P) Creat × 100) or fractional urinary sodium exretion (FE_{Na}) help in this differential diagnosis (19,20). However, Oken (21), pointed out these urinary features become blurred in elderly patients. Those who may have serious volume depletion do not always respond promptly to the administration of fluid, the clinical criterion usually relied upon to differentiate prerenal from renal ('true') ARF.

Therefore, we analysed the changes in urinary composition in our several groups of patients to determine whether the discriminating power of these parameters

Table IV: Urinary parameters (n = determinations)

	n	U/P creat	RFI	FE_{Na}
Prerenal				
>65 yrs	5	29.1 ± 12.3*	2.00 ± 1.43*	1.47 ± 1.00*
<65 yrs	10	55.0 ± 14.2*	1.17 ± 0.20*	0.60 ± 0.19*
Postrenal				
>65 yrs	5	5.34 ± 2.37	18.50 ± 5.90	11.80 ± 3.90
<65 yrs	5	9.50 ± 6.85	19.20 ± 8.20	15.40 ± 6.50
Renal				
1. Vascular (GN + emboli + CEI)				
>65 yrs	11	10.70 ± 2.02	8.55 ± 2.33	6.70 ± 1.70
<65 yrs	21	12.50 ± 3.50	6.10 ± 2.40	4.50 ± 2.15
2. AIN				
>65 yrs	6	36.30 ± 22.6*	4.14 ± 2.20*	3.17 ± 1.70*
<65 yrs	15	8.90 ± 2.3	10.20 ± 1.90	7.80 ± 1.50
3. ATN				
>65 yrs	45	8.01 ± 1.03	11.90 ± 1.60	9.00 ± 1.20
<65 yrs	91	10.39 ± 1.53	9.80 ± 2.42	6.95 ± 1.90

* $P < 0.01$ versus all other values.

was different in elderly and younger patients.

Generally, prerenal acute failure is characterized by a RFI and FE_{Na} less than one, and by a relatively high urinary creatinine to plasma-creatinine ratio. Table IV summarizes these data in the three major classes of ARF in both age groups. As expected, prerenal ARF patients had significantly higher U/P creatinine ratios and lower RFI and FE_{Na} values than the two other classes, in both groups.

We could establish no major differences between the two groups in the patterns of urinary indices in the different renal forms of ARF, except that in those with acute interstitial diseases, the U/P creatinine was significantly higher, and FE_{Na} and RFI were significantly lower in the elderly.

We were struck by the fact that the eight elderly and 22 younger patients, who did not merit the diagnosis of prerenal ARF on clinical grounds had 'prerenal' urinary indices.

Five of the older patients had either postischemic or toxic acute tubular necrosis, three of these had biopsy proven drug-induced acute interstitial nephritis.

In Group II, 14 patients had ATN, two had acute interstitial nephritis, four suffered from acute glomerulonephritis and one from either vascular or postrenal ARF.

Recently, Pru and Kjellstrand (22) have cast doubt on the validity of the urinary

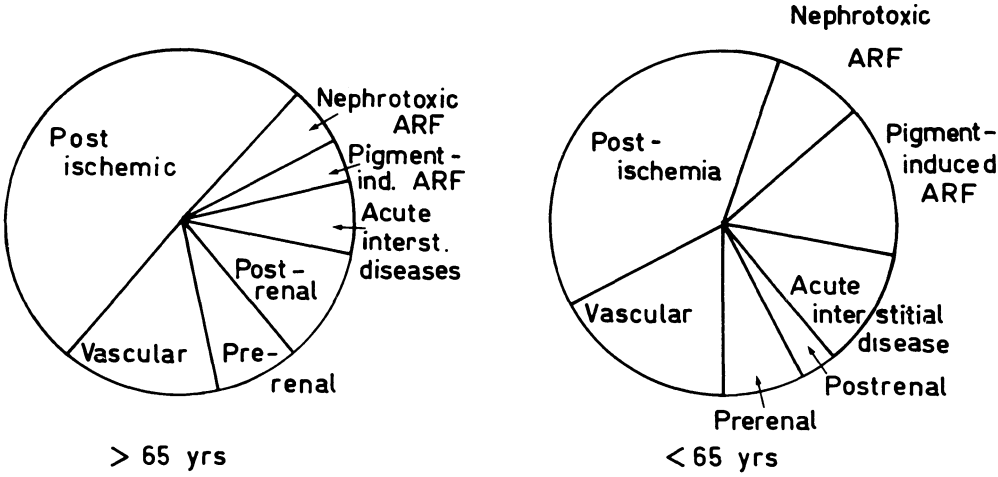


Fig. 1 - Percent distribution of causes of ARF in both groups.

parameters based on urinary sodium concentration (RFI and FE_{Na}) and several workers have reported low FE_{Na} in some forms of ATN (23-25). On the other hand, Anderson *et al*, (26) showed that in differentiating patients with ARF, urinary chloride concentrations exhibited greater sensitivity and the same specificity as urinary sodium concentrations. Particularly in patients with metabolic alkalosis, urinary chloride provides a better index of prerenal failure. Since our patients did not have routine measurements of urinary chloride, the present study does not permit us to confirm these assertions.

PROGNOSIS

Surprisingly the total mortality in both groups was similar.

With respect to sex, 16 women (mean age 41.2 ± 1.3 years) died of a total of 36 (44%) in Group I *versus* 35 women (mean age of 48.1 ± 2.4 years) of a total of 68 (51%) in group II.

In Group I, 27 men died of a total of 53 (52%) - mean age 72.2 ± 1.2 years *versus* 39 men (38%) - mean age 50.1 ± 2.23 years of a total of 120 in Group II.

The total mortality was 48.1% in the older group *versus* 43.5% in the younger (not significantly different).

Both groups showed a striking relationship between survival and the number of complications during hospitalisation (Fig. 2). The major complications were: sepsis or other serious infections as pneumonia, peritonitis and urinary tract infections, myocardial infarction, various serious cardiac arrhytmias, pulmonary emboli, gastrointestinal bleeding, acute respiratory failure, bleeding dyscrasias and thrombophlebitis.

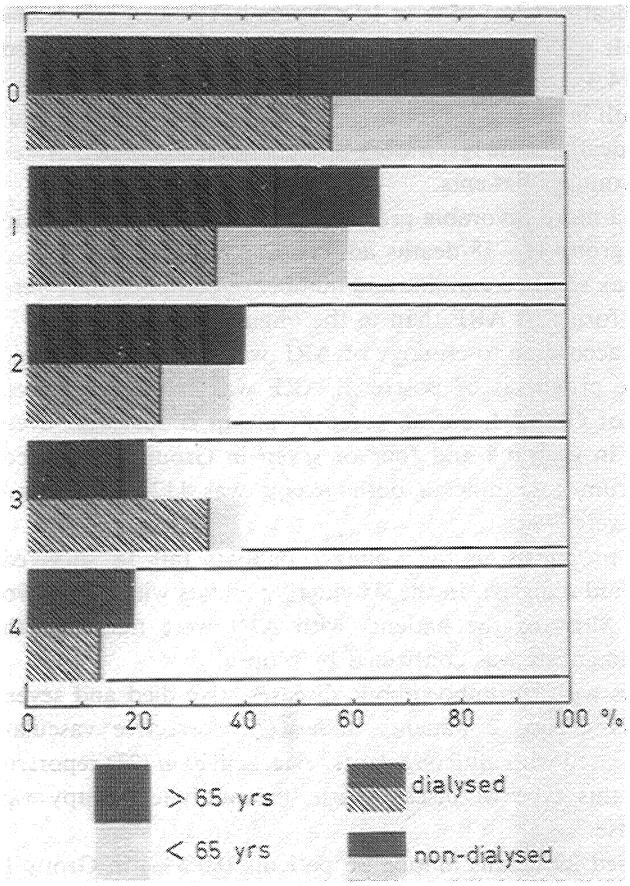


Fig. 2 - Percent survival in relation to number of complications in both groups.

Table V: Cause of death

	Group I	Group II
Infections		
Sepsis	14 (29%)	27 (37%)
Peritonitis	1	0
Pulmonary	2	0
Cardiovasuclar	13 (30%)	24 (33%)
Pulmonary		
Embolism	0	1
ARDS	2 (4.6%)	8 (12.4%)
G.I.-bleeding	2	0
Others	9	14

Survival without complications was 95% in 19 patients in Group I and 100% of 50 patients in Group II; with four or more complications, survival dropped to 20% in Group I and 14.3% in group II.

The main causes of death in both groups (Table V) were septicemia and fatal arrhytmias. As a cause of death, acute respiratory distress syndrome (ARDS) was twice as frequent in the younger patients.

Non-oliguric ARF had a more favorable prognosis in Group I - one death in 11 patients (9%) than in group II - 18 deaths among 63 patients (28.5%).

In both groups, both peak serum creatinine and number of complications were lower in the non-oliguric forms of ARF than in the oliguric forms.

The prognosis assessed according to etiology of ARF was similar in both age groups. For example, the prognosis of postrenal ARF was excellent in both groups; all nine patients of Group I and all seven of group II survived, even though three of the nine in Group I and four of seven in Group II required dialysis and the peak serum creatinine in both groups was 1124 ± 124 and 995 ± 212 μmol/l, respectively.

AIN has an excellent prognosis in the younger patients (all 18 survived although 10 of them required dialysis). In the six elderly patients with AIN, two died and four survived. Most of the patients with AIN were treated with corticosteroids after the diagnosis was confirmed by biopsy.

Of eight elderly patients with thromboembolic diseases, five died and seven required dialysis. Of this group, 2 patients underwent corrective vascular surgery; the others were treated with anticoagulants. Zucchelli *et al* (27) reported a favorable outcome in this type of disease with thrombolytic therapy *viz* streptokinase and urokinase.

Postischemic ATN caused 29 deaths among 36 patients (80.5%) in Group I and 44 deaths among 65 patients (68%) in Group II. In both groups the prognosis of postoperative ARF was equally dramatic. Of 19 patients with postoperative ARF, 13 (68.4%) died in Group I and of 36 in Group II, 27 died (75%). However, of the vascular-surgery-associated ARF in Group I all eight died, *versus* nine of 14 in Group II. On the other hand, the younger patients fared much worse after non-vascular surgery ARF - 18 died of 22 (82%) compared to five of 11 (45%) older patients (group I).

Most of the postvascular surgery ARF was associated with aortic aneurysm repairs. Recently Gornick and Kjellstrand (28), describing their experience with ARF, which complicated this type of operation, reported that only 10 survived of 47 submitted to operation over a 10-year period. Their mortality rate, 79%, is similar to our overall mortality - 77% of 22 patients observed over the past five years.

Whereas we could establish no relationship between the initial serum sodium values and mortality in either group, it is worth noting that in elderly patients, severe hypokalemia (<3.5 μmol/l) was associated with a mortality of 73% *vs* 53% in the younger patients. The latter incidence is similar to the overall survival

in this group. Again, of the seven elderly patients who were admitted with a severe metabolic alkalosis (plasma bicarbonate higher than 30 μmol/l), six ultimately died.

Although a causal relationship could not be established between these electrolyte abnormalities and mortality, these observations suggest that in elderly patients with ARF, the presence of severe hypokalemia and metabolic alkalosis bears a grave prognosis.

In the dialysed group, 31 died of a total of 66 (47%) in Group I *versus* 56 of a total of 113 (49%) in Group II.

Some differences were observed in mortality between the various dialysis strategies. In hemodialysis patients, 48% of 29 patients in Group I and 58% of 60 in Group II died. Of those on peritoneal dialysis, 65% of 20 patients in Group I and 50% of 20 patients in Group II died. Seventeen patients of Group I were treated with both hemo- and peritoneal dialysis, 10 of them (59%) died; In Group II, 40% of 32 patients died.

Therefore, we can conclude that in the elderly patients, peritoneal dialysis alone or in combination with hemodialysis carries worse prognosis. However, the peritoneal route was often selected in hemodynamically unstable patients, a fact which can by itself explain the higher mortality.

Approximately one-half of the patients in each age category received amino-acid solutions in addition to hypertonic glucose during their treatment period. As

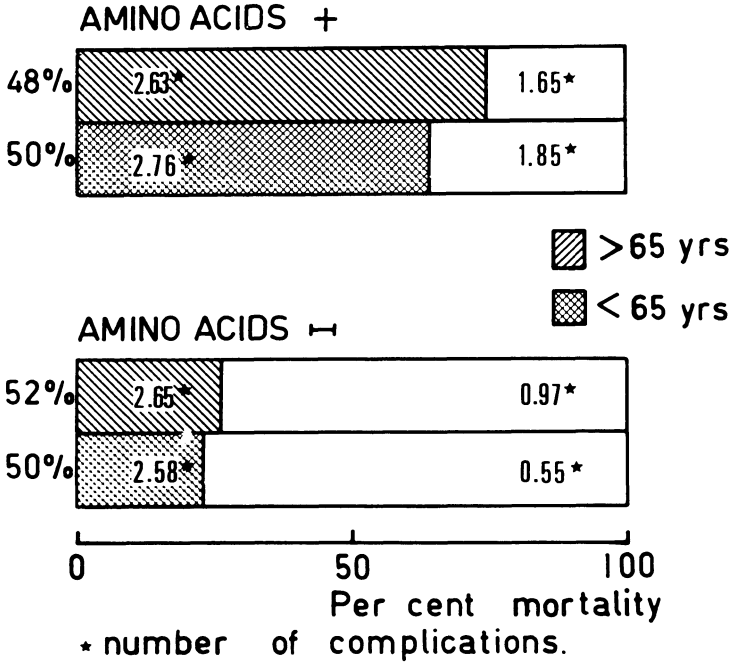


Fig. 3 - Effect of amino-acid administration on mortality in both groups.

can be noted from Fig. 3, amino-acid administration did not confer any benefit and actually the treatment groups showed a lower survival. However, this greater mortality could be attributed principally to the higher incidence of major complications in the patients treated with amino-acids.

RECOVERY

In the surviving patients of Group I, 34 (74%) had complete recovery of renal function, 9 (19.5%) partially recovered, and three were maintained on chronic dialysis. In the 97 survivors in Group II, 73 (76%) had complete recovery, 17 (18%) had partial recovery and six patients were maintained on chronic dialysis. Recent studies (17,29) suggest that, in older patients and in those with ARF due to glomerular and vascular diseases, recovery will be slower and less complete.

Of the 11 survivors in Group I with previous chronic renal disease, seven showed complete and three partial recovery. One patient needed chronic hemodialysis.

In the 24 survivors in Group II with previous chronic renal disease, 13 returned to their initial serum creatinine, seven stabilized on a higher creatinine level but were independent of chronic dialysis and three required chronic assistance.

SUMMARY AND CONCLUSIONS

This retrospective analysis of 259 patients with ARF observed over a 5 year period (1980-1984) demonstrates that by itself, age was not a prognostic factor. Overall survival was simlar in both younger and elderly patients. The prognosis in both groups was related more to the number of complications arising during the treatment period. Hypokalemia and alkalosis was more frequent in the elderly and was associated with a grave prognosis.

In addition, it appears that the spectrum of diseases associated with ARF in the elderly is not basically different, although they show a higher frequency of thrombo-embolic diseases and obstructive nephropathy.

Younger patients suffer relatively more from acute glomerular diseases and traumatic and non-traumatic rhabdomyolysis than older people.

Non-oliguric ARF is rare in older persons compared to the relatively high incidence of this type of ARF in younger people. In both groups, the survival in this category is better than in the oliguric group, partly because of the much lower incidence of additional complications.

In conclusion, our experience suggests that the prognosis of ARF does not depend on the patient's age and, in view of the good prognosis in the surviving patients, treatment of ARF in the elderly should be as aggressive as possible. Finally, we do not believe that age alone should be used as discriminating factor in therapeutic decisions concerning ARF in the elderly.

ACKNOWLEDGEMENTS

We want to express our gratitude to Dr. F. Collardyn, head of the intensive care unit for his excellent co-operation and to our dialysis and nursing staff. The secretarial expertise of Miss C. Van den Berghe is greatly appreciated.

REFERENCES

1. Moorthy, A.V., Zimmerman, S.W. (1980): Renal disease in the elderly clinico-pathologic analysis of renal disease in 115 elderly patients. Clin. Nephrol., 14, 223-229.
2. Swann, R.C., Merill, J.P. (1953): The clinical course of acute renal failure. Medicine, 32, 215-292.
3. Kiley, J.E., Powers, S.R., Beebe, R.T. (1960): Acute renal failure. Eighty cases of renal tubular necrosis. N. Engl. J. Med., 262, 481-486.
4. Alwall, N. (1963): Therapeutic and diagnostic problems in severe renal failure. Scandinavian University Books, Copenhagen.
5. Balslov, J.T., Jorgensen, H.E. (1963): A survey of 499 patients with acute anuric renal insufficiency. Causes, treatment, complications and mortality. Am. J. Med. 34, 753-764.
6. Stott, R.B., Cameron, J.S., Ogg, C.S., Bewick, M. (1972): Why the persistently high mortality in acute renal failure? Lancet, 2, 75-78.
7. Kennedy, A.C., Burton, J.A., Luke, R.G., Brigga, J.D., Lindsay, R.M., Allison, M.E.M., Edward, N., Dargie, H.J. (1973): Factors affecting the prognosis in acute renal failure. Quart. J. Med., 42, 73-86.
8. Kleinknecht, D., Ganeval, D. (1973): Preventive hemodialysis in acute renal failure: its effects on mortality and morbidity. In: Proc. of the Conference on ARF, Eds. Friedman, E.A., Eliahou, H.E., Dhew Pub (NIH), 74-608, Washington, DC, 165.
9. McMurray, S.D., Luft, F.C., Maxwell, D.R., Hamburger, R.J., Futty, D., Szwed, J.J., Lavelle, K.J., Kleit, S.A. (1978): Prevailing patterns and predictor variables in patients with acute tubular necrosis, Arch. Int. Med., 138, 950-955.
10. Werb, R., Linton, A.L. (1979): Etiology, diagnosis, treatment and prognosis of acute renal failure in an intensive care unit; cited in 'Acute Renal Failure', Ed. A. Chapman, Churchill Livingstone, Edinburgh, 1980, p.34.
11. Manis, T., Heneghan, W., Charles, G., Friedman, E.A. (1982): Acute renal failure in a municipal hospital. In Acute Renal Failure. Ed. Eliahou, H.E., John Libbey, London, 129-131.
12. Bullock, M.L., Umen, A.J., Finkelstein, M., Keane, W.F. (1985): The assessment of risk factors in 462 patients with acute renal failure. Am. J. Kid. Dis., 5, 97-103.
13. Bluemle, L.W., Webster, G.D., Elkinton, J.R. (1959): Acute tubular necrosis. Analysis of one hundred cases with respect to mortality, complications and treatment with and without dialysis. Arch. Int. Med., 104, 180-197.
14. Kumar, R., Hill, C.M., McGeown, M.G. (1973): Acute renal failure in the elderly. Lancet, 1, 90-91.
15. Baek, S.M., Makabali, G.G., Shoemaker, W.C. (1975): Clinical determinants of survial from postoperative renal failure. Surgery, 140, 685-689.
16. Minuth, A.N., Terrell, J.B., Suki, W.N. (1976): Acute renal failure: a study of the course and prognosis of 104 patients and the role of furosemide. Am. J. Med. Sci., 271, 317-324.
17. Kjellstrand, C.M., Gornick, C., Davin, T. (1981): Recovery from acute renal failure. Clin. Exp. Dial. & Apheresis, 5, 143-162.
18. Hoenich, N.AN, Ringoir, S. (1984): Dialysis, ultrafiltration and hemofiltration. In: Suki, W.N., Massry, S.G. (Eds.), Therapy of renal and related disorders, Martinus Nijhoff, Boston, 555-565.

19. Espinel, C.H. (1976): The FENa test. JAMA, 236, 579-581.
20. Miller, T.R., Andersson, R.J., Linas, S.L., Henrich, W.L., Berns, A.S., Gabow, P.A., Schrier, R.W. (1978): Urinary diagnostic indices in acute renal failure: a prospective study. Ann. Int. Med., 89, 47-50.
21. Oken, D.E. (1981): On the differential diagnosis of acute renal failure. Am. J. Med., 71, 916-920.
22. Pru, CL, Kjellstrand, C.M. (1984): The FENa test is of no prognostic value in acute renal failure. Nephron, 36, 20-23.
23. Fang, L.S.T., Sirota, R.A., Ebert, T.H. et al (1980): Low fractional excretion of sodium with contrast media-induced acute renal failure.
24. Steiner, R.W. (1982): Low fractional excretion of sodium in myoglobinuric renal failure. Arch. Int. Med., 142, 1216-1217.
25. Diamond, J.R., Yoburn, D.C. (1983): Non-ogliguric acute renal failure associated with a low fractional excretion of sodium. Ann. Int. Med., 96, 597-600.
26. Anderson, R.J., Gabow, P.A., Gross, P.A. (1984): Urinary chloride concentration in acute renal failure. Mineral Electr. Metab., 10, 92-97.
27. Zucchelli, P., Fabbri, L., Cagnoli, L., Grimaldi, C., Pavlica, P., Losinno, F. (1982): Acute renal failure due to renal artery occlusion. In: Acute renal failure. Ed. Eliahou, H.E., John Libbey, London, 152-155.
28. Gornick, C.C., Kjellstrand, C.M. (1983): Acute renal failure complicating aortic aneurysm surgery. Nephron 35, 145-157.
29. Bonomini, V., Stefoni, S., Vangelista A. (1984): Long-term patient and renal prognosis in acute renal failure. Nephron, 36, 169-172.

13. CHRONIC RENAL FAILURE IN THE ELDERLY

CHRISTOPHER R. BLAGG, M.D., F.R.C.P.

CHRONIC RENAL FAILURE IN THE ELDERLY

The function of the kidney and other organs declines gradually with advancing age. With aging of the general population, much more attention is being paid to the medical problems of the elderly; and in nephrology the ready availability of dialysis and transplantation has brought a renewed interest in renal disease in the elderly.

AGE AND RENAL FUNCTION

In evaluating elderly patients, one must consider the normal decline of renal function with age. Glomerular filtration rate, as measured by inulin or creatinine clearance, decreases with age starting in early adult life (1,2), and the mean inulin clearance declines to 65.3ml/min/1.73m^2 in patients in their 80's. Creatinine clearance does not change significantly until the fourth decade of life, but thereafter decreases linearly at about 8ml/min/1.73m^2 per decade (3). Renal plasma flow also declines at about 10% per decade, as a result of both structural and hemodynamic alterations in the renal vasculature and a decrease in cardiac output (4). Renal tubular functions also diminish, including concentrating ability, sodium handling, and glucose transport.

Frequently elderly patients consume a lower dietary protein intake and they also usually have less muscle mass than younger adults. In consequence, the serum creatinine level or blood urea nitrogen level may not give an accurate assessment of renal function; hence the best clinical measurement of renal function in the elderly is endogenous creatinine clearance (5).

RENAL DISEASE IN THE ELDERLY

The literature and perusal of death certificates do not provide reliable data on the incidence of primary renal disease in the elderly, and perhaps the best information is obtained from registries such as those of the Medicare End-Stage Renal Disease (ESRD) Program in the United States and the European Dialysis and Transplant Association. Table I shows the increasing number of patients aged 55 and older starting treatment in the Medicare ESRD program between 1978 and 1980, and Table II shows that the incidence rate per million population for treated end-stage renal disease is highest in the age group 65-74 years (6). The overall incidence of end-stage renal disease in the U.S. in 1980 was 82 new patients per million population, but in the age group 65-74 years, the incidence was 241 patients per million population. As might be expected, the incidence was higher in males aged 60-80 years, averaging 260 new patients per million population, as compared to about 170 new patients per million population in females of the same age. However, the incidence rate was even higher in

Table I: Medicare ESRD program incidence by age, sex, and race:

	1978-80 (6)			
Age, sex and race	1978	1979	1980	Percent change 1978-80
Total	15,584	17,243	18,279	17
Age (years)				
0-14	309	302	345	12
15-24	1,076	1,069	1,013	-6
25-34	1,793	1,885	2,088	16
35-44	2,076	2,113	2,221	7
45-54	2,789	3,107	3,097	11
55-64	3,580	4,034	4,334	21
65-74	3,096	3,496	3,739	21
75 and over	865	1,237	1,442	67
Sex				
Male	8,755	9,658	10,256	17
Female	6,829	7,584	8,023	17
Race				
White	10,725	11,568	12,418	16
Black	3,935	4,593	4,680	19
All Other	464	535	601	30
Unknown	460	547	580	26

Table II: Medicare ESRD program incidence rates per million

Population by age, sex, and race: 1978 80 (6)				
Age, sex and race	1978	1979	1980	Percent change 1978-80
Total	71	78	82	15
Age (years)				
0-14	6	6	7	17
15-24	26	26	24	-8
25-34	53	54	58	9
35-44	85	84	86	1
45-54	120	135	136	13
55-64	173	193	204	18
65-74	208	230	241	16
75 and over	96	134	153	59
Sex				
Male	82	90	95	16
Female	61	67	70	15
Race				
White	59	63	67	15
Black	159	184	185	16
All other	118	131	140	19

nonwhites of both sexes in the 60-80 age group, averaging almost 600 new patients per million population. Presumably the true incidence of end-stage renal disease in the elderly is even higher than these figures suggest because not all patients are referred for treatment by dialysis.

These age, sex, and racial variations in the incidence of end-stage renal disease treated by dialysis closely parallel the population trends for hypertension. For example, the rate of hypertension is 69% greater in blacks than in whites, and 39% higher in white males than white females, while in blacks there is little sex difference (7). Historical discrepancies in access to health care for whites and blacks may explain in part this difference, but these figures point up the opportunity to reduce the incidence of end-stage renal disease by improving the control of hypertension in the general population, and especially in blacks.

With regard to the more common causes of end-stage renal disease in the elderly, Table III shows data from the Medicare ESRD program in 1980, which illustrates the increased frequency of primary hypertensive disease, acquired obstructive uropathy, and multiple myeloma in the elderly (6). Similarly, Table

Table III: Medicare ESRD program incidence, by diagnosis and age, 1980 (6)

Diagnosis	0-14	15-24	25-34	35-44	45-54	55-64	65-74	75 years
Number of persons	137	472	1,060	1,113	1.530	2,126	2,065	807
All Causes	100	100	100	100	100	100	100	100
Glomerulonephritis	37.2	40.0	30.7	24.0	17.6	15.2	14.6	12.6
Primary hypertensive disease	0.0	5.9	11.9	20.0	24.4	25.0	29.1	36.7
Diabetic nephropathy	0.7	5.5	30.8	28.1	24.3	25.9	17.4	10.4
Polycistic kidney disease	6.6	1.1	2.3	7.5	10.7	7.4	4.5	2.0
Collagen vascular disease	2.2	4.7	2.5	2.1	1.4	0.6	0.8	0.4
Interstitial nephritis, hereditary	2.9	4.4	2.2	0.9	0.5	0.7	0.3	0.4
4.4 other	8.1	5.1	4.1	5.6	6.6	7.1	9.3	
Analgesic abuse nephropathy	0.0	0.2	0.1	1.3	1.2	1.7	1.3	0.2
Obstructive uropathy acquired	0.7	1.1	0.7	0.4	1.4	2.4	4.2	5.8
18.2 congenital	9.1	2.0	0.6	0.1	0.1	0.1	0.0	
Amyloidosis	0.0	0.0	0.0	0.4	0.7	0.7	0.8	0.5
Multiple myeloma	0.0	0.0	0.0	0.4	0.6	1.3	1.9	2.1
Gouty nephropathy	0.7	0.2	0.2	0.2	0.7	0.5	0.6	0.7
Other, unspecified	20.4	13.1	6.4	3.6	3.5	4.3	12.7	4.2
Etiology unknown	5.8	6.6	5.2	6.5	7.2	7.7	4.4	14.6

Table IV: Causes of renal failure by age in 2,000 patients - NKC, Seattle

Aged 15-64	Age 65+	
Chronic glomerulonephritis	23.7%	16.8%
Rapidly progressive glomerulonephritis	1.1	2.7
Collagen vascular diseases	2.3	0.8
Diabetic nephropathy	28.9	8.4
Polycystic kidney disease	8.4	7.1
Congenital diseases	4.8	0
Acquired obstruction	2.2	6.3
Myeloma	1.2	3.3
Nephrosclerosis	10.2	24.7
Progression of acute renal failure	1.0	3.3
Pyelonephritis and interstitial diseases	3.7	4.6

IV illustrates causes of renal failure by age in a population of some 2000 patients treated at the Northwest Kidney Center in Seattle (8), and Table V shows the increased frequency of associated diseases in patients over the age of 65.

However, impaired renal function in the elderly often has more than one cause. Many have other serious medical illnesses, and many receive multiple

Table V: Frequency of associated diseases by age in 2,000 patients - NKC, SEATTLE

Number of associated diseases	*Aged 15-64*	*65+*
0-1	34.0	16.9
2-3	42.4	46.7
4-5	23.6	36.4

drugs and are at greater risk of drug-induced nephropathy because of kidneys that already are compromised by age. Elderly patients are also more likely to have acute disturbances of fluid and electrolyte balance following surgical stress, and associated with infection.

Less common in the elderly are such kidney lesions or diseases as congenital anomalies, hereditary interstitial nephritis, medullary cystic disease, acute proliferative glomerulonephritis, IgA nephropathy, lipoid nephritis, membranoproliferative glomerulonephritis, lupus nephritis, hypertension due to fibromuscular hyperplasia of the renal artery, and malignant hypertension. On the other hand, certain kidney diseases are more frequent, for example, prerenal azotemia, acute renal failure, obstructive uropathy, membranous nephropathy, myeloma kidney, renal vascular disease due to atheroma, adult-onset diabetes mellitus, and benign nephrosclerosis.

PRERENAL AZOTEMIA AND ACUTE RENAL FAILURE

The elderly are sensitive to changes in fluid and electrolyte balance and elderly patients have less functional reserve to cope with cardiac failure, salt loading, or fluid deprivation (9). They may be relatively incapacitated as a result of age or illness, and this may interfere with their oral intake of fluids. Two other common causes of prerenal azotemia in the elderly are overuse of diuretics and the decreased renal perfusion associated with congestive heart failure. Volume depletion in the elderly may present as apparent acute renal failure, and it is important to recognize that in many patients, this may be reversible. Acute renal failure in the elderly is even more serious than in younger patients, and the mortality in patients over the age of 70 approaches 80%. Consequently, if it is possible, prevention is most important (9).

The elderly patient appears to be at greater risk of dye-induced renal failure (10), and the incidence is also high of drug-induced renal failure, particularly aminoglycoside toxicity. This increased risk may result in part from the physician's reliance on the serum creatinine level as a guide to renal function, because this may overestimate actual glomerular filtration rate and he may not make appropriate modifications in drug dosage. Also, elderly patients frequently

are volume depleted and may be receiving several drugs. Drug-induced acute renal failure may not be associated with low urine volume in the eldery (11).

OBSTRUCTIVE UROPATHY

Obstructive renal disease is particularly common in the elderly, chiefly due to prostatic enlargement in males. Other causes include neurogenic bladder, carcinoma of the bladder or ureter, clots or calculi, and retroperitoneal fibrosis. Clinically, the classic symptom of obstructive uropathy is anuria alternating with polyuria, but, in many patients, this manifests itself as polyuria, and others have no significant urinary symptoms (12). In all elderly patients with renal failure, it is important to examine the prostate and bladder, and to use sonography to look for dilatation of the urinary tract. Whenever possible, urography should be avoided. In men, prostatectomy should be done for obstruction affecting the bladder and upper urinary tract, in the presence of recurrent gross hematuria, bladder calculi or recurrent infections, or when there is a postvoiding residual urine of more than 100 ml.

BACTERIRURIA AND URINARY TRACT INFECTION IN THE ELDERLY

Bacteriuria is relatively common in the elderly, and occurs in about 25% of asymptomatic individuals over the age of 70 (13). Bladder drainage may be impaired by bladder-neck obstruction from prostatic disease in males in association with perineal relaxation and cystocele in females and in persons with neurologic defects. Glycosuria, diabetes, and an acidification defect associated with early renal failure predispose to bacterial proliferation and infection is particularly common after catheterization.

It is important to identify and treat bacteriuria in the elderly because in nursing-home patients aged 70-79, bacteriuria is associated with a reduction of expected survival from 4-6 years to less than 3 years (14). Generally, at the time of study, patients with bacteriuria had a lower mean creatinine clearance and, over the follow-up period, this more often decreased than in nonbacteriuric patients.

Symptomatic urinary-tract infections in the elderly should always be treated, and probably asymptomatic bacteriuria also should be treated. In infections limited to the bladder, single-dose oral antibiotic therapy may be effective, and is cheaper, has fewer systemic side effects, and less frequently is associated with the emergence of resistant organisms. Failure of single-dose therapy often indicates renal infection and the eradication of bacteria may require longer courses of antibiotics which produce significant renal tissue levels. In nursing-home patients with indwelling catheters, hydration and scrupulous catheter care

are more important in the prevention of symptomatic urinary tract infection than are prophylactic antibiotics.

MEMBRANOUS NEPHROPATHY

Membranous nephropathy is the major cause of nephrotic syndrome in the elderly, and the characteristic findings are proteinuria, edema, and hypertension. Usually, membranous nephropathy is idiopathic but, in 25% of patients over age 65, it is associated with an underlying malignancy (15). One should search for such underlying disease with a chest X-ray, upper gastrointestinal series, barium enema and bone marrow biopsy because removal of a tumor may produce remission of the nephrotic syndrome.

MYELOMA KIDNEY

Multiple myelomatosis is a disease of the elderly, and 50% of such patients have overt renal insufficiency (16). The usual renal manifestations include proteinuria, acute or chronic renal failure, and amyloidosis. Almost all patients have proteinuria, usually light chain, and the presence of significant albuminuria suggests amyloid deposition in the glomeruli. Patients with myeloma may develop acute renal failure secondary to volume depletion, hypercalcemia, increased plasma viscosity, or following intravenous urography. Renal findings include tubular atrophy, the intraluminal precipitation of Bence-Jones protein casts, nephrocalcinosis and deposition of uric acid. Generally, the prognosis is poor, even with use of dialysis (17).

ATHENOMATOUS RENAL VASCULAR DISEASE

Elderly patients develop atheromatous embolic disease particularly after aortic sugery or aortography (18). An embolus, consisting primarily of cholesterol crystals, may separate from the arterial wall and become lodged in a renal artery. Symptoms include painless hematuria and abdominal pain in a patient with generalized atherosclerosis, usually after aortic sugery or aortography. Kidney size is normal and urinalysis shows minimal proteinuria with profuse red blood cells (19).

TREATMENT OF CHRONIC RENAL FAILURE IN THE ELDERLY

Survival with dialysis and transplantation is clearly related to age (6,8). Nevertheless, patients aged 65 and over have a significant extension of life with dialysis, and the experience of all dialysis programs suggests that many elderly patients may do extremely well for up to several years.

Table VI: Quality of life and functional impairment in dialysis
Patients from the national kidney dialysis and transplant study (20)

Mean adjusted quality of life indicator scores	
Life satisfaction (1 = Dissatisfied; 7 = Satisfied)	
Transplant patients	5.66
Home hemodialysis patients	5.19
In-center hemodialysis patients	5.11
CAPD patients	5.30
General population	5.55
Patients aged less than 65	5.10
Patients 65 or older	5.49
Psychological affect (1.0 = low; 6.0 = high)	
Transplant patients	5.62
Home hemodialysis patients	5.42
In-center hemodialysis patients	5.15
CAPD patients	5.24
General population	5.68
Patients aged less than 65	5.26
Patients 65 or older	5.32
Index of well-being (2.1 = low; 14.7 = high)	
Transplant patients	11.83
Home hemodialysis patients	11.12
In-center hemodialysis patients	10.77
CAPD patients	11.05
General population	11.77
Patients aged less than 65	10.86
Patients 65 or older	11.34

No good information is available on the quality of life in the elderly population as a whole, or in those who have early chronic renal failure. Nevertheless, studies of the quality of life of elderly dialysis patients can be projected to elderly patients who have not yet reached end-stage renal disease. A recent study reviewed quality of life in patients treated by various forms of dialysis and transplantation (20). This data base has been analyzed again to compare scores in various quality-of-life indicators in the general population, and in dialysis patients aged less than 65, and 65 and older. Remarkably, on quality-of-life indicators, patients 65 and older generally scored higher than the younger patients (Table VI), despite more functional impairment as measured by the Karnofsky Index (Table VII). As would be anticipated, ability to work and frequency of employment were significantly lower in the elderly patients. Clearly, many elderly patients find the quality of life on dialysis very acceptable.

Table VII: Functional impairment among ESRD patients from the national kidney dialysis and transplant study (20)

(Karnofsky Index 1 = normal; 10 = moribund)	
Under 65	2.73
65 and older	3.61

2 = Able to carry on normal activity; minor signs and symptoms of disease.
3 = Able to carry on normal activity with effort; some signs and symptoms of disease.
4 = Care for self; unable to carry on normal activity or do active work.

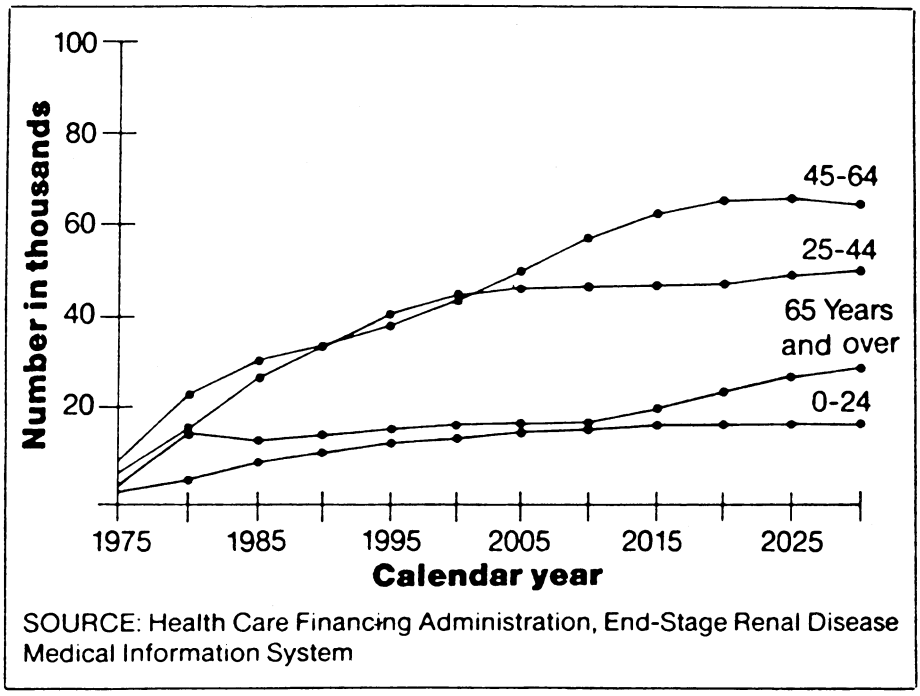


Figure 1
Projected Medicare End-Stage Renal Disease program enrollment, by age: 1975-2030 (6).

THE FUTURE

Chronic renal failure in the elderly will assume even greater imporance in the future with further aging of the general population. Figure I shows projected Medicare End-Stage Renal Disease Program patient enrollment by age group between 1975 and 2030. The number of new patients in the age group 0-24 appears to have plateaued already, and the number of patients in the 25-44 age

group is in process of plateauing. In contrast, patients in the age group 45-64 will not plateau until approximately 2020, and patients in the age group 65 and over will continue to increase through the year 2030. This forecast is important in the planning of services for end-stage renal disease treatment for the future, and also as a spur to increased efforts to prevent chronic renal failure in the population. Paramount among the preventive measures, as is clear from the existing data on the causes of renal failure, is the control of hypertension, particularly in the black population.

REFERENCES

1. Davies DF, Shock NW: 1950, Age changes in the glomerular filtration rate, effective renal plasma flow, and tubular excretory capacity in adult males. J Clin Invest, 29:496-597.
2. Friedman SA, Raizner AE, Rosen H, Solomon NA: 1972, Functional defects in the aging kidney. Ann Intern Med, 76:41-45.
3. Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW: 1976, The effect of age on creatinine clearance in men: a cross-sectional and longitudinal study. J Gerontol, 31:155-163.
4. Samiy AH: 1983, Renal disease in the elderly. Med Clin North Am, 67:463-480.
5. Rowe JW, Andres R, Tobin JD: 1976, Letter: Age-adjusted standards for creatinine clearance. Ann Intern Med, 84:567-569.
6. Eggers PW, Connerton R, McMullan M: 1984, The Medicare experience with end-stage renal disease: Trends in incidence, prevalence, and survival. Health Care Financing Review, 5:69-88.
7. Rowland M, Roberts J: 1982, Blood pressure and hypertension in persons aged 6-74 years: United States, 1976-80. Advance Data from Vital and Health Statistics, No. 84. DHHS Pub. No. (PHS) 82- 1250. National Center for Health Statistics, Public Health Service, Washington, D.C., U.S. Government Printing Office.
8. Blagg, CR, Wahl PW, Lamers JY: 1983, Treatment of chronic renal failure at the Northwest Kidney Center, Seattle, from 1962 to 1982. ASAIO J, 6:170-175.
9. Parsons V: 1977, What decreasing renal function means to aging patients. Geriatrics, 32:93-99.
10. Mudge GH: 1980, Nephrotoxicity of urographic radiocontrast drugs. Kidney Int 18:540-552.
11. Erickson SB: 1980, A rational approach to nephrotoxic drugs in the elderly. Geriatrics, 35:55-63.
12. Mukamel E, Nissenkorn I, Boner G, Servadio C: 1979, Occult progressive renal damage in the elderly male due to benign prostatic hypertrophy. J Am Geriatr Soc, 27:403-406, 1979.
13. Reihle RA, Jr., Vaughan ED, Jr.: 1983, Genitourinary disease in the elderly. Med Clin North Am 67:445-461.
14. Dontas AS, Kasviki-Charvati P, Papanayiotou PL, Marketos SG: 1981, Bacteriuria and survival in old age. N Engl J Med, 304:939- 943.
15. Row PG, Cameron JS, Turner DR, Evans DJ, White RH, Ogg CS, Chantler C, Brown CB: 1975, Membranous nephropathy: Long-term follow-up and association with neoplasia. Q J Med 44:207-239.
16. Kyle RA: 1975, Multiple myeloma: Review of 869 cases. Mayo Clin Proc, 50:29-40.
17. Johnson WJ, Kyle RA, Dahlberg PJ: 1980, Dialysis in the treatment of multiple myeloma. Mayo Clin Proc, 55:65-72, 1980.
18. Kassirer JP: 1969, Atheroembolic renal disease. N Eng J Med, 280:812-818.
19. Varanasi UR, Moorthy AV, Beirne GJ: 1979, 'Spontaneous' atheroembolic disease as a casue of renal failure in the elderly. J Am Geriatr Soc 27:407-409.
20. Evans RW, Manninen DL, Garrison LP, Jr., Hart GL, Blagg CR, Gutman RA, Hull AR, Lowrie EG: 1985, The quality of life in patients with end-stage renal disease. N Engl J Med, 312:553- 559.

14. NUTRITIONAL NEEDS FOR THE ELDERLY HEMODIALYSIS PATIENT

JOEL D. KOPPLE, MARY B. GROSVENOR AND CHARLOTTE E. ROBERTS

Virtually no data have been published concerning the specific nutritional problems and nutritional requirements of the elderly maintenance dialysis patient. There is, however, substantial information concerning the nutritional status and needs of the nonuremic elderly patient. The data suggest that nutritional requirements and nutritional status change with aging, and that many diseases commonly associated with aging are influenced by the individual's nutritional intake. Since these phenomenae also may apply to the elderly dialysis patient, the data will be reviewed briefly.

Nutrition has a major impact on aging individuals for several reasons. First, the dietary requirements for many nutrients change with aging (1-3). For example, nonuremic elderly individuals have a lower calorie requirement which, on average, falls progressively to about 20% below the values of young adults (1,3). Indeed, if the elderly individual does not reduce his energy intake, obesity may result. On the other hand, because calorie needs are less, they should consume a larger amount of protein and other essential nutrients per kilocalorie of food ingested. Thus, the elderly must select foods with particular concern for their nutrient density i.e., the ratio of essential nutrients (protein, vitamins, minerals, essential fatty acids) to calories in the food ingested. There are also minor downward adjustments in the recommended dietary allowances (RDA) for the elderly with regard to certain vitamins and, in women, for iron (1). On the other hand, to prevent or retard osteoporosis the daily requirement for calcium and vitamin D may be increased in premenopausal and menopausal women and in late middle-aged or elderly men (3-5).

Many studies of the nutritional intake of the nonuremic elderly (6-12) suggest that the nutrients for which dietary intake is most likely to be inadequate are total calories, calcium, iron, vitamin A, thiamin and folate (3). The standards used to assess adequacy of intake vary; in the more recent North American studies, the standards usually were based on the RDA (9). The exact criteria for adequacy of intake for a given nutrient varied but usually were set at between two-thirds and 100% of the RDA (9,11). In general, when total food intake is low, it is most

difficult to maintain adequate intake of essential nutrients, particularly for certain minerals and vitamins. Although in most studies the average protein intake is reported to be adequate, in a substantial number of patients it was low, particularly in low-income white and black males and females, Latin females, and Indian males (3,9,11).

Many of the illnesses or disabilities associated with aging may be affected by nutrient intake. An excessive calorie intake will predispose to obesity - a common disorder in the nonuremic elderly. Obesity can predispose to or accentuate diabetes mellitus - another common disease of the elderly. A high intake of purified sugar will increase the likelihood of glucose intolerance or poor glucose control in the diabetic. Obesity, excessive sodium intake, and possibly low potassium or calcium intake may promote hypertension. A diet high in cholesterol and saturated fatty acids can increase the risk of atherosclerosis and coronary artery disease. Evidence continues to accumulate that diet can predispose to certain kinds of cancer, for example, high-fat and low-fiber diets seem to predispose to adenocarcinoma of the breast and colon. Some of the causes of osteoporosis are endocrinologic or nutritional (4,5). As indicated above, recent studies suggest that a high calcium intake supplemented with vitamin D may prevent or retard the development of osteoporosis in the elderly.

The aging person undergoes many alterations in body composition including a reduction in lean body mass, skeletal muscle and bone mass (4,5,13,14). Basal energy expenditure, the metabolism of glucose and lipids, and many other biochemical processes involving nutrients often are altered in the aging individual (2,15).

Many of the illnesses or infirmities of aging may alter daily nutritional requirements or promote wasting and malnutrition. Psychological depression or organic illnesses that cause anorexia or interfere with food intake may promote malnutrition. Intervening catabolic illnesses may induce wasting. Peptic ulcers or gastrointestinal malignancies can cause iron-deficiency anemia. Thus protein, calorie or protein-calorie malnutrition and vitamin and iron deficiency are not uncommon in elderly people, particularly in those with underlying illnesses. Biochemical assessment of nutritional status in the nonuremic elderly indicate that the nutrients most likely to be low or deficient include vitamin A, thiamine, riboflavin, iron, calcium and vitamin B6 (3,11).

The chronically uremic or dialysis patient has many superimposed nutritional disorders due to chronic renal failure itself which have been reviewed recently (16). The metabolism, biochemistry or renal handling of virtually every nutrient is altered in chronic uremia. There is decreased renal clearance of water, sodium, potassium, magnesium, phosphorus and other minerals, impaired renal ability to conserve nutrients such as sodium and protein, reduced intestinal absorption of certain minerals such as calcium, decreased renal production or utilization of certain amino acids, impaired renal synthesis of 1,25-dihydroxycholecalciferol, and altered extrarenal metabolism of nutrients (i.e., impaired glucose uptake and

decreased metabolic clearance of triglycerides and pyridoxine from plasma). The antagonistic effects of certain medicines may predispose to nutritional deficiencies (i.e., anticonvulsant drugs may promote vitamin D and folic-acid deficiency; isoniazid or hydralazine may lead to vitamin B6 deficiency) and the dialysis procedure removes free amino acids, biologically valuable bound amino acids, protein, carbohydrates and water soluble vitamins, and promotes the uptake of glucose (with peritoneal dialysis) and in some studies trace elements, e.g., aluminum. The metabolism of carbohydrates, lipids and protein also is altered in advanced renal failure.

These observations suggest that the nutritional requirements and the nutritional problems of the elderly maintenance hemodialysis patient are influenced both by the special nutritional problems of aging and the nutritional disorders associated with chronic renal failure and dialysis treatment. Moreover, such patients may be at particular risk for malnutrition because of the factors listed in Table I, although these factors have not yet been demonstrated to predispose to malnutrition in the elderly dialysis patient. Since little data are available concerning the nutritional status of elderly patients undergoing maintenance hemodialysis, we began an investigation of this question. This study was carried out to determine whether the nutritional status of these individuals was different than normal and whether it differed from younger adults undergoing maintenance hemodialysis.

We studied two groups of maintenance hemodialysis patients, 18 elderly patients - 64 years of age or older; and, for comparison, 18 adults who were no more than 50 years old. Studies were carried out in patients treated in the maintenance hemodialysis program at Harbor-UCLA Medical Center or V.A. Wadsworth Medical Center. This evaluation included all elderly patients who

Table I: Factors that Might Predispose the Elderly Dialysis Patient to Malnutrition

1. Few or no teeth
2. Physical debility
3. Impaired taste acuity
4. Chronic anorexia
5. Chronic constipation
6. Chronic illnesses
7. Acute illnesses
8. Frequent and prolonged hospitalizations
9. Low income
10. Patients may respond less aggressively or effectively to medical, psychological or environmental stresses
11. There may be less emotional and financial support or physical assistance from family and friends
12. Patients may become frustrated and depressed more easily when the dietician sets strict goals and encourages the patient to adhere to them

were available for study in these two hemodialysis units. We attempted to match the non-elderly individuals to the elderly patients on the basis of duration of dialysis treatment, sex, and medical diagnoses. Exact matches between the two groups for these variables were not possible. Two of the non-elderly and six of the elderly were women.

For nutritional assessment, serum albumin was measured in clinical laboratories using standard automated procedures. Anthropometric measurements were made as previously described (17). Relative body weight was calculated as the patient's weight X 100 divided by the weight of normal persons of the same age, height and sex. Normal values for relative body weight and mid-arm muscle area were taken from the HANES data (18). Estimated body fat was derived from the triceps and subscapular skinfold thicknesses according to the formula of Durnin and Womersley (19).

The mean ages of the non-elderly and elderly dialysis patients were 37 + 8 (SD) and 71 + 7 years, respectively. The mean duration of dialysis therapy did not differ in the two groups and was 50 and 41 months, respectively. There were no differences in the level of education in the two groups; more non-elderly patients had not married. The number of edentulous patients and the incidence of constipation were similar in the two groups.

The estimated dietary protein and energy intake, calculated per kg body weight, and the phosphorus and potassium intake of the two groups, estimated from one interview at the time of the nutritional assessment, were suprisingly similar. The mean energy intake in each group was below 30 kcal/kg/day. All non-elderly and elderly patients were prescribed a multivitamin supplement, and the vitamin intake in the two groups was similar.

Predialysis serum albumin concentrations were similar in the two groups (Fig. 1). There were no differences with regard to relative body weight, mid-arm muscle area or estimated total body fat (Fig. 1). In comparison to published normal values (18), the relative body weight was significantly lower in both groups ($P < 0.001$ for each group), while mid-arm muscle area was decreased only in the non-elderly patients ($P < 0.001$). Serum albumin concentrations and the estimated total body fat did not differ from normal controls.

The data from the males, if analyzed separately, showed no differences in serum albumin concentrations or in anthropometric values of the non-elderly as compared to the elderly. Similarly, the abnormally low relative body weights and, in the non-elderly patients, the mid-arm muscle areas persisted when the analysis was restricted to men.

This preliminary study suggests that the elderly patient undergoing maintenance hemodialysis, like the younger dialysis patient, is likely to develop mild to moderate wasting or malnutrition, and that the severity of malnutrition is more or less similar in these two groups. The mildness of the malnutrition did not appear to be due to the relative 'youth' of these elderly patients; the youngest was 64 and seven patients were 73 years or older. It is noteworthy that our elderly

patients were not more malnourished even though they had been treated in a county or Veterans Administration medical facility, and many of them may have belonged to low income socioeconomic groups.

The wasting or malnutrition observed in both groups most likely was due to multiple causes (16,20); and in this connection, we should emphasize that this study evaluated only serum albumin and anthropometric parameters. It did not examine for mineral, trace element, or vitamin malnutrition; nor did we evaluate the incidence or severity of osteodystrophy.

Based on these preliminary observations, Table II indicates tentative recommendations for the nutritional intake of our growing population of elderly maintenance dialysis patients. These recommendations, which are based upon studies carried out chiefly in younger adults undergoing maintenance hemodialysis or continuous ambulatory peritoneal dialysis (CAPD) (16,21,22), should be considered very tentative. We decided to make recommendations similar to those we made for non-elderly maintenance dialysis patients because the present study suggests that the nutritional intake and nutritional status of these two groups are similar.

Several aspects of these recommendations deserve comment.

First, the proposed daily energy intake of the elderly dialysis patient is the same as that recommended for younger patients, in contrast to current recommendations for the nonuremic elderly whose energy expenditure is decreased and whose requirements are considered to be lower than those of younger healthy individuals (1,15). We did not decrease the recommended energy intake in the elderly dialysis patient because their relative body weight is below normal, and many of them have low mid-arm muscle area (Fig. 1) and skinfold thicknesses (unpublished data). Also, a higher energy intake may improve the utilization of dietary protein.

Second, it is not clear whether elderly maintenance dialysis patients should take 1,25-dihydroxycholecalciferol routinely. Currently, in patients with renal failure, this compound is recommended only for specific complications such as osteodystrophy, vitamin D-deficient myopathy or hypocalcemia. Normal elderly people are at increased risk for osteoporosis, and a high calcium diet with vitamin D-supplementation has been recommended for these individuals (3,5). Hence, it may be appropriate to give routinely low doses of 1,25-dihydroxycholecalciferol to the elderly maintenance dialysis patient; this question should be the subject of careful study. It should be emphasized that 1,25-dihydroxycholecalciferol should not be prescribed unless the patient's serum phosphorus is within the normal range. Hypercalcemia is a common complication of 1,25-dihydroxycholecalciferol therapy; if this compound is given, the calcium intake probably should be reduced to about 800 mg/day, and the patient should be monitored closely for hypercalcemia and hyperphosphatemia.

Third, in patients with chronic renal failure a diet high in fat (about 55% of

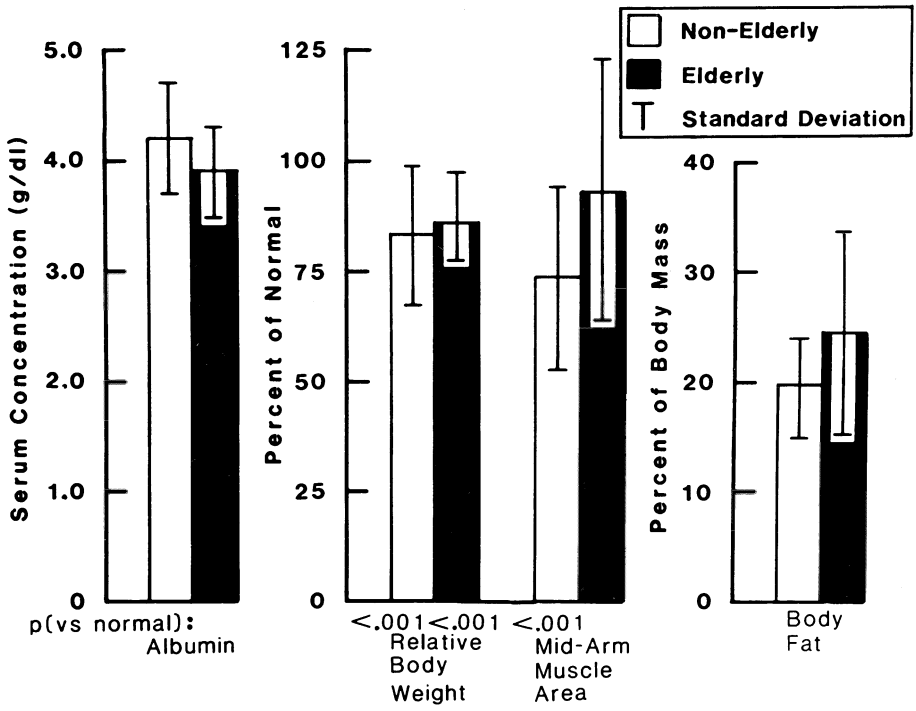


Figure 1. The measured serum albumin concentrations, calculated relative body weight and mid-arm muscle area, expressed as percent of normal values, and estimated percent body fat in 18 non-elderly and 18 elderly patients undergoing maintenance hemodialysis. The p values indicate the probability that the data were not different from normal standard values.

total calorie intake) with a high polyunsaturated-to-saturated fatty acid ratio (2.0:1.0) will keep the serum triglycerides at lower levels (23). Studies in nonuremic individuals suggest that a diet that is high in complex carbohydrates and high total fiber - e.g., at least 20-25 g/day, has health-enhancing effects. The recommendations in this paragraph are less crucial than most of those listed in Table II. Because many of dietary modifications concerning the quantity of fat, complex carbohydrates, and dietary fiber are onerous to the patient, we suggest that these latter factors only be recommended after the patient has shown that he is able to adhere to the other more critical aspects of the diet and only if the physician and dietician believe that he can tolerate and comply with further restrictions. If the diet is too restrictive, the patient may not accept any dietary modifications, and may become alienated, unhappy or depressed.

SUMMARY

Nutritional status was compared in 18 non-elderly and 18 elderly patients

Table II: Tentative Proposal for Nutritional Intake for the Elderly Maintenance Dialysis Patient (a)

Total protein (g/kg/day)(b)	Hemodialysis	1.2
	CAPD	1.2-1.5
High biological value protein	Hemodialysis	$\geqslant$0.60
(g/kg/day)	CAPD	$\geqslant$0.60
Energy (kcal/kg/day)(c)		$\geqslant$35
Water		as tolerated
Sodium		as tolerated
Potassium (mEq/day)		50-70
Phosphorus (mg/day)(d)		600-1000
Calcium (mg/day) (e)		1200-1600
Magnesium (mg/day)		175-225
Zinc (mg/day)		15
Iron (mg/day)		10
Vitamin supplements (f)		
Vitamin A		none
Vitamin E		none
Vitamin K (g)		none(b)
Vitamin D		(see text)
Water soluble vitamins		Recommended Dietary Allowances for each vitamin except for pyridoxine HCl, 10 mg/day, and folic acid, 1.0 mg/day

(a) These values refer to total intake from all sources except for the vitamin intake which refers to supplements. Intakes expressed per kg body weight, in general, refer to the weight of a normal person of the same age, height, and sex (18).
(b) For CAPD patients who do not have protein malnutrition, a protein intake of 1.2-1.3 g/kg/day should be sufficient.
(c) This includes energy intake from dialysate in CAPD patients.
(d) Phosphate binders are usually needed.
(e) Dietary intake must be supplemented to provide these levels.
(f) Diets are to be supplemented with these quantities of vitamins.
(g) Vitamin K, about 10 mg per week intramuscularly or intravenously, may be needed in patients who are not eating and who receive antibiotics.

undergoing maintenance hemodialysis. Estimated dietary intake was similar in both groups. Serum albumin, relative body weight, estimated total body fat, and mid-arm muscle area were similar in both groups. The relative body weight was decreased below normal standards in both groups and mid-arm muscle area was reduced only in the non-elderly dialysis patients. These data suggest that elderly patients undergoing maintenance hemodialysis do not have more severe malnutrition than non-elderly hemodialysis patients. Both groups showed evidence of mild to moderate wasting or malnutrition. This paper makes tentative recommendations concerning the dietary nutrient intake for the elderly maintenance dialysis patient.

REFERENCES

1. Committee on Dietary Allowances Food and Nutrition Board (1980) Recommended Dietary Allowances (9th Ed), Washington, D.C., National Academy of Sciences.
2. Munro HN (1981). Nutrition and aging. Br. Med Bull 37:83-88.
3. Young EA (1983). Nutrition, aging, and the aged. Med Clinics North Amer 67:295-313.
4. Kleerekoper M, Tolia K and Parfitt AM (1981). Nutritional, endocrine, and demographic aspects of osteoporosis. Ortho Clinics North Amer 12:547-558.
5. Parfitt AM, Gallagher JC, Heaney RP, Johnston CC, Neer R and Whedon GD (1982). Vitamin D and bone health in the elderly. Am J Clin Nutr 36:1014-1031.
6. Harill I and Cervone N (1977). Vitamin status of older women. Am J Clin Nutr 30:431-440.
7. Jansen C and Harrill I (1977). Intakes and serum levels of protein and iron for 70 elderly women. Am J Clin Nutr 30:1414-22.
8. Brown PT, Bergan JG, Parsons EP and Krol I (1977). Dietary status of elderly people. J Am Diet Assoc 71:41-45.
9. O'Hanlon P and Kohrs MB (1978). Dietary studies of older Americans. Am J Clin Nutr 31:1257-1269.
10. Garry PJ, Goodwin JS, Hunt WC, Hooper EM and Leonard AG (1982). Nutritional status in a healthy elderly population: dietary and supplemental intakes. Am J Clin Nutr 36:319-331.
11. Bowman BB and Rosenberg IH (1982). Assessment of the nutritional status of the elderly. Am J Clin Nutr 35:1142-1151.
12. Rivlin RS and Young EA, (Editors)(1982). Symposium on evidence relating selected vitamins and minerals to health and disease in the elderly population in the United States. Am J Clin Nutr (Supplement) 36:977-1086.
13. Forbes GB and Reina JC (1970). Adult lean body mass declines with age: some longitudinal observations. Metabolism 19:653-663.
14. Forbes GB (1976). The adult decline in lean body mass. Hum Biol 46:161-173.
15. Consolazio CF, Johnson RE and Pecora LJ (1963). Phychiological measurements of metabolic functions in man. New York, McGraw- Hill, Blakiston, pp. 1-59.
16. Kopple JD (1981). Nutritional therapy in kidney failure. Nutr Rev. 39:193-206.
17. Blumenkrantz MJ, Kopple JD, Gutman RA, Chan YK, Barbour GL, Roberts C, Shen FH, Gandhi VC, Tucker CT, Curtis FK and Coburn JW (1980). Methods for assessing nutritional status of patients with renal failure. Am J Clin Nutr 33:1567-1585.
18. Frisancho R (1984). New standards of weight and body composition by frame size and height for assessment of nutritional status of adults and the elderly. Am J Clin Nutr 40:808-819.
19. Durnin JV and Womersley J (1974). Body fat assessed from total body obesity and its estimation from skinfold thickness: measurements on 481 men and women aged from 16-72 years. Br J Nutr 32:77-79.
20. Kopple JD (1984). Causes of catabolism and wasting in acute or chronic renal failure. In: Nephrology Vol II, RR Robinson (Editor), Springer-Verlag, New York, pp. 1498-1515.
21. Kopple JD (1983). Nutritional management In: Textbook of Nephrology Vol 2, SG Massry and RJ Glassock (Editors), Williams and Wilkins, Baltimore, pp. 8.3-8.12.
22. Kopple JD and Blumenkrantz MJ (1984). Nutrition in adults on continuous ambulatory peritoneal dialysis. Perspectives in Peritoneal Dialysis 2:1-9.
23. Sanfelippo ML, Swenson RS and Reaven GM (1978). Response of plasma triglycerides to dietary change in pateints on hemodialysis. Kidney Int 14:180-186.

15. HEMODIALYSIS OF THE ELDERLY

C. KJELLSTRAND, M.D., F.A.C.P., K. KOPPY, A. UMEN, M.S., S. NESTRUD, B.S., R.N. AND L. WESTLIE, M.D.

I. INTRODUCTION

With the rapid build-up of dialysis facilities in the 1970's and 1980's, the indications for chronic dialysis expanded rapidly and older and more seriously ill patients were accepted for dialysis (1). In many parts of the United States and Europe, the mean age of the dialysis patient is now approaching 60 years. Over the last two decades (2-10) several workers have reported their results and the problems encountered in the management of the older patients by dialysis. The following review will examine changes in attitudes toward the acceptance of the older patient, try to determine how age influences treatment decisions, and analyze survival, risk of hemodialysis, cause of death, risk factors and morbidity, and quality of life.

II. ACCEPTANCE RATES OF ELDERLY PATIENT

The state of Michigan has had a co-operative registry for 10 years (11) and Fig. 1 and 2 illustrate the dramatic change in its acceptance of elderly patients for dialysis. Numerically, there has been an increase in all age groups, but the most dramatic change is in patients older than age 65. In the group 35-54, that accepted the largest number of patients, there was a 32% increase between 1974 and 1978. In the group over age 65, the increase was 350%. In 1974, the group 35-54 years made up 42% of all patients; by 1982 that had decreased to 32%;

that is a 24% decrease. On the contrary, the patients over age 65 had increased from 19 to 27% - a 42% increase. In 1982 the U.S. Health Care Financing Administration projected that in the age group 0-24 years, the number of patients on dialysis would stabilize by the year 1990, by the year 2000 patients age 25-44 would stabilize. The age group 45-64 would stabilize about the year 2010, but at the year 2030, patients accepted at age 65 and over would still be increasing (Fig.3) (12).

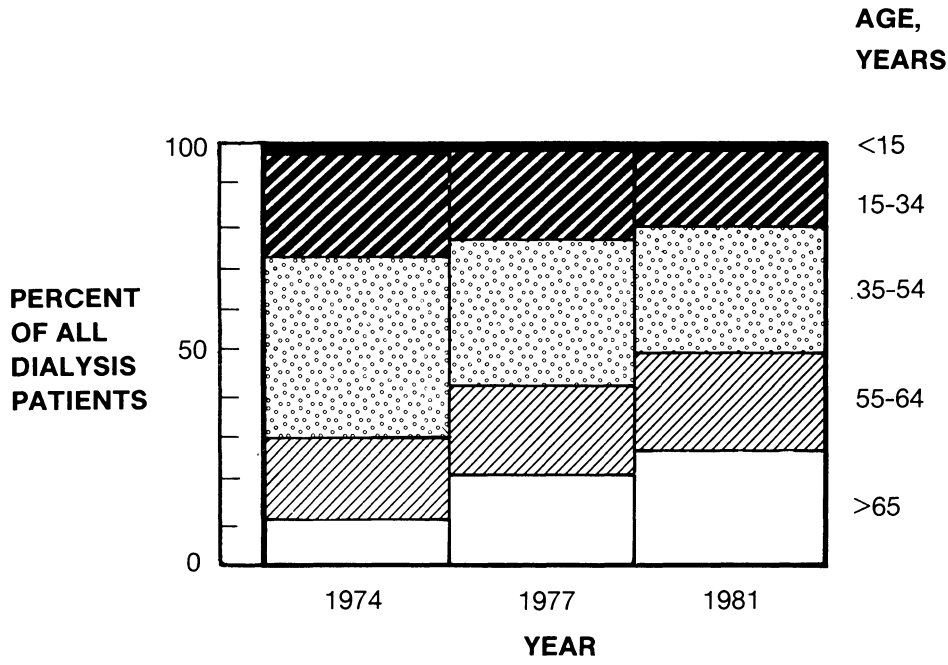


Figure 1: The percent of all dialysis patients in Michigan divided into age groups from 1974, 1977 and 1981 (11). Patients over age 65 show the largest increase. In 1974 these patients made up approximately 10%, now they make up approximately 30% of all patients.

III. DISCRIMINATION

One can develop a 'discrimination index' by dividing the fraction of all patients accepted for dialysis by all those dying of renal failure with the same fraction of patients at a certain age range. The inverse of the discrimination index indicates the chance of dialysis for a certain age group when compared to all others. The discrimination index and chance of being dialyzed for patients in four different

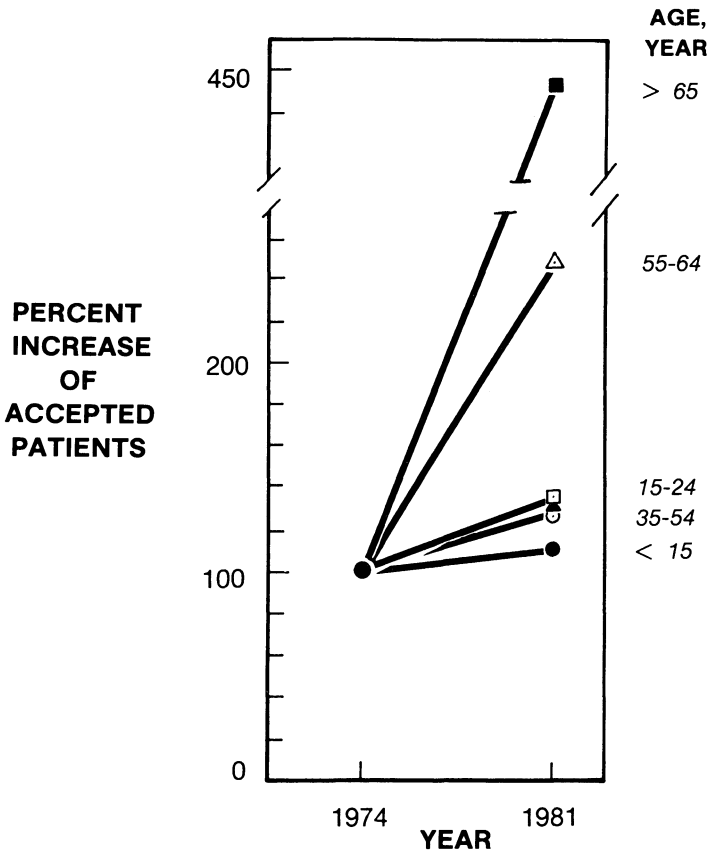


Figure 2: Percent increase from 1974 to 1981 in patients accepted for dialysis in Michigan divided into different age groups (11). All patient groups show an increase but the most startling increase has been in the older patients. In 1981 there were four and one-half times as many patients age 65 on dialysis as in 1974. There has been a 220% increase in patients 55-64 years. Other age groups show a moderate increase and now constitute between 110% and 130% of the numbers in 1974.

age groups is presented in Table I. These figures are the rates for dialysis and death in the U.S.A. in 1979 (12,13). Dividing the numerical value - chance-of-being-dialyzed for one age group with another allows one to compare the chances patients in different age groups have of being accepted for dialysis. The figures make it clear that the chance of being dialyzed is best at age 25-44 years. The discrimination index is highest, 2.257, for the patient over the age of 65. Put another way, the likelihood of a patient over age 65 being accepted for dialysis is only one-fifth of that of the patient aged 25-44 years. Discrimination against the old has decreased considerably in the last decade. However, even with Eggers

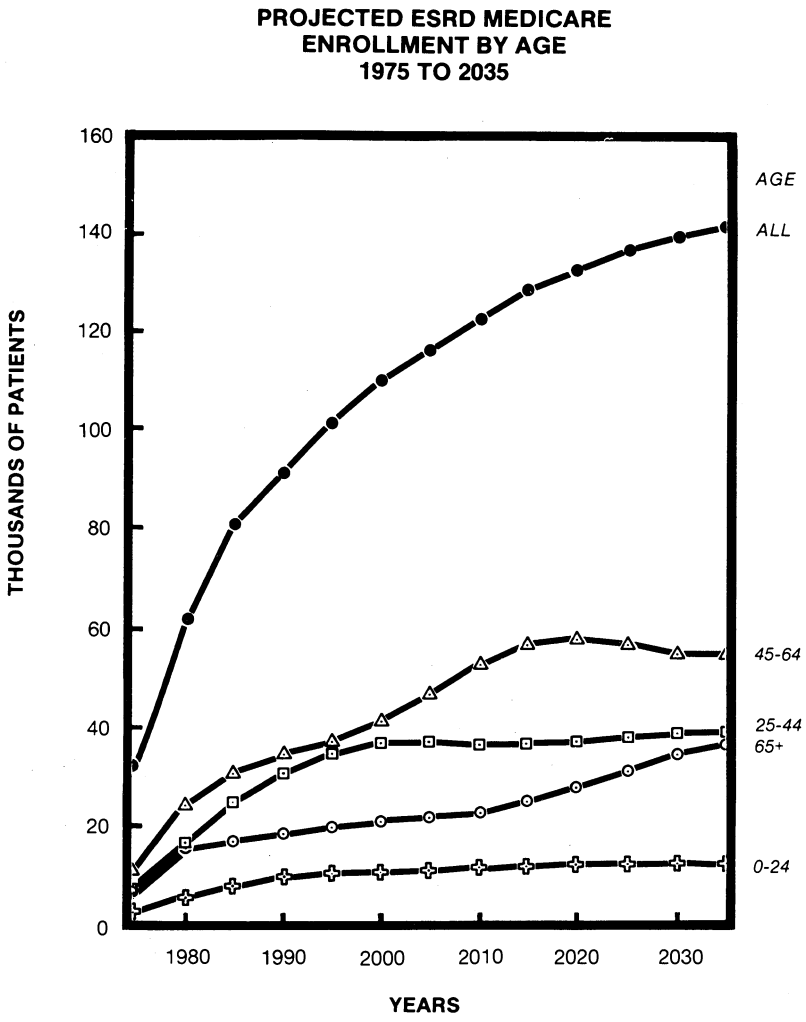


Figure 3: Projected number of patients on dialysis, divided into four age groups, from 1975 till 2035. All age groups, except those over age 65 years, have stabilized around year 2010, but the older patients continue to increase beyond 2035. Figure from reference 12, reproduced with permission of P.W. Eggers.

Table I: Discrimination and chance of dialysis in various age groups

Age range, years:	0-24	25-44	45-64	>65
Discrimination index:	0.493	0.451	0.574	2.257
Chance of being dialyzed:	2.03	2.22	1.74	0.44

et al, (12) projection concerning the relative increase in acceptance of older patients, considerable inequities remain. In the year 2035, patients over age 65 will make up 29% of all dialyzed patients but patients in this age group will make up 59% of those who die of uremia.

Obviously these numbers must be used with caution; many biological factors may explain acceptance rates. Older persons suffer from other diseases such as cancer, heart disease, and vascular disease which might make dialysis futile, because it would correct only one defect in a spectrum of diseases. We will continue our efforts to develop a more efficient discrimination index.

IV. RESULTS OF HEMODIALYSIS

The results of hemodialysis of all patients, including the elderly, has improved with time. However, most of this improvement seems to have taken place in the late 1960's and early 1970's (1,15). Figure 4 illustrates first, third, and fifth-year cumulative survival as reported by the E.D.T.A. registry for the last 15 years. The 1968 report gave no age division and since 1974, the report has included only patients 65 years and older. Since the mid-1970s it is clear that the first and third-year survivals have stabilized at approximately 75 and 50%. There seems to have been a continued improvement of fifth-year survival. Figure 5 summarizes cumulative survival for four age groups over the age of 60 years. When one analyzes a large number of patients, one can discern survival difference with each half decade of advancing age. However, even in the oldest patients - those over age 75, some 10% survive more than six years.

V. RISK OF HEMODIALYSIS

One can estimate the risk of hemodialysis and the complications during dialysis by dividing the chance of dying for a certain age group on hemodialysis with that of the same age group in the population from which the hemodialysis patients are recruited (Fig.6). In this figure the five-year mortality rate of eight age groups from 0-14 years to those over age 75 is divided by the five-year mortality for the same age groups in the general population. It is obvious that the risk of hemodialysis decreases with advancing age. In patients younger than 44 years, the risk of hemodialysis increases the chance of dying 20 times. On the contrary, it increases the risk only five times in patients age 65-74 years, and only doubles it (approximately) in patients over age 75 (14).

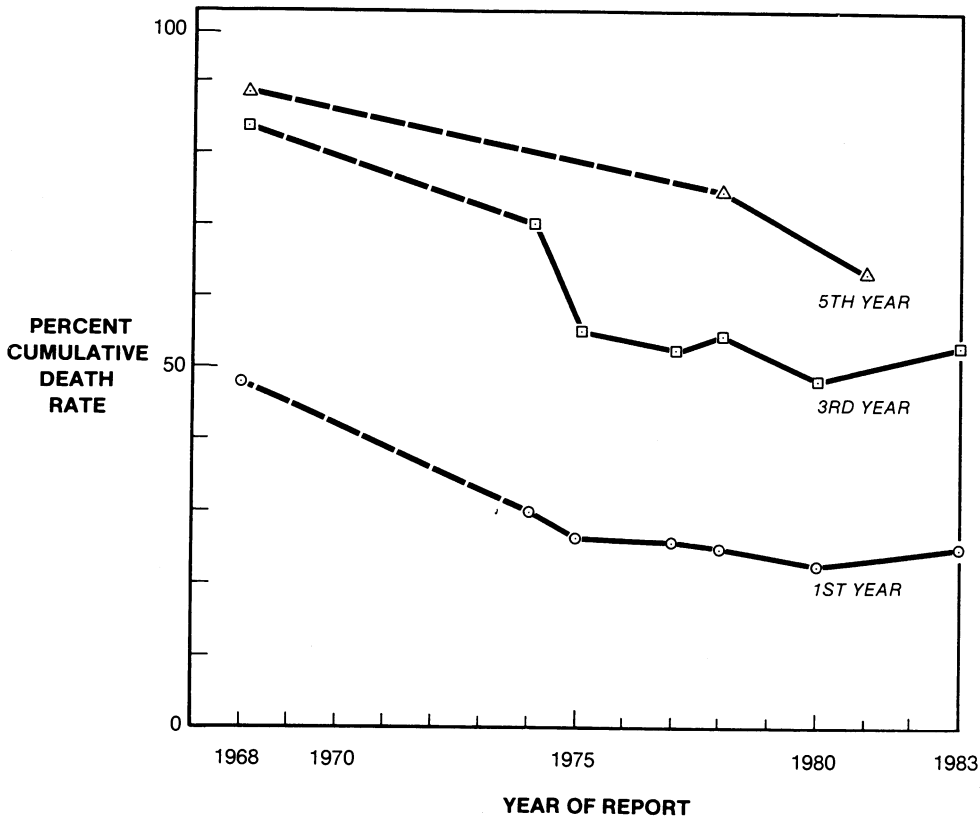


Figure 4: Graph depicting first, third, and fifth-year cumulative death rate as reported in the EDTA registry for the last 15 years. There has been a marked decrease in all mortality but almost all improvement occurred before 1975. The survival rates for 1968 include all age groups. The later survival rates include only patients over the age of 65.

VI. CAUSES OF DEATH

Figure 7 shows the causes of death in the Regional Kidney Disease Program for various age groups, as reported by Shapiro and Umen (15) for patients below and above 61 years of age, and in an analysis of 124 deaths in 227 patients aged 71 years and older, dialyzed at the Regional Kidney Disease Program between 1966 and 1983. The most common cause of death in the patient younger than 61 is vascular disease. The most common cause in patients over 70 years is stopping dialysis. In this age group, 38% of all deaths were due to discontinuing dialysis *versus* 35% due to vascular deaths. In approximately one-half of the 'withdrawals', the patient requested it; in the other one-half, the patient was incompetent and the decision was made by family and physician (16). Although the frequency of stopping dialysis has increased over the years, this increase has been due mainly to the increase in patients of high risk, such as the older and the diabetic patient. There seems to be no difference in the decision-making process in the patients over age 61 compared to younger patients, but this is being analyzed separately for patients over age 70.

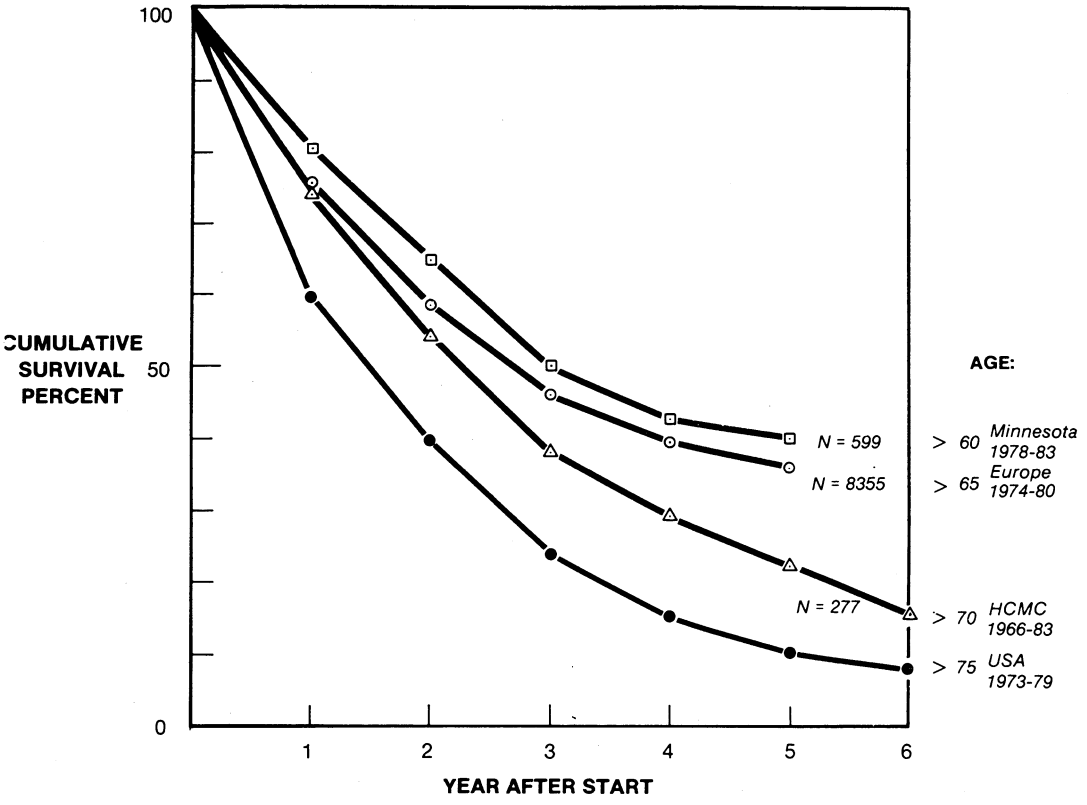


Figure 5: Cumulative survival rates for various age of elderly dialysis patients.

VII. RISK FACTORS FOR DEATH

Ten risk factors, present before the start of hemodialysis, have been analyzed for the older patient using the Cox proportional hazards analysis (7,15). Of pre-existing comorbid conditions in 157 patients over the age of 70 accepted for in-center or home dialysis (but excluding satellite dialysis) between 1966 and 1983, we carried out two analyses; one treating start-of-dialysis year as a continuous variable, the other one treating year of start of dialysis as a dichotomous variable, before or after 1976. The entry year was important in both analyses. Using time as a dichotomous variable, the relative risk was 2.4 before 1976 *versus* after 1976. When the entry year was treated as a continuous variable, the relative risk decreased 0.86 per year. It may be significant that age over 70 years increased the risk 1.07 per year, and that, in the continuous variable analysis, in-center dialysis increased the risk 1.71 over home dialysis. In the dichotomous entry time analysis, only arteriosclerotic heart disease was of importance - it increased the risk 1.5 times. Thus, entry time seems to be a definite risk variable; possible risk

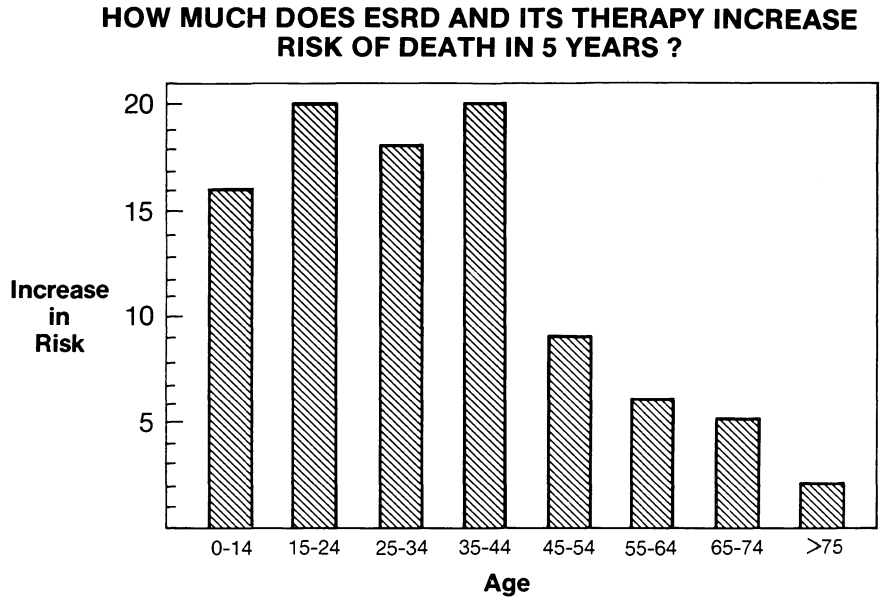


Figure 6: Graph illustrating the risk of dialysis (15). Here death rates for various age groups on dialysis have been divided by the five-year death rates for all individuals. The risk of dialysis decreases with advancing age. In patients below age 45, the chance of dying on dialysis is 20-times that of the general population. In the patients over age 75 the rate is only twice that of the general population.

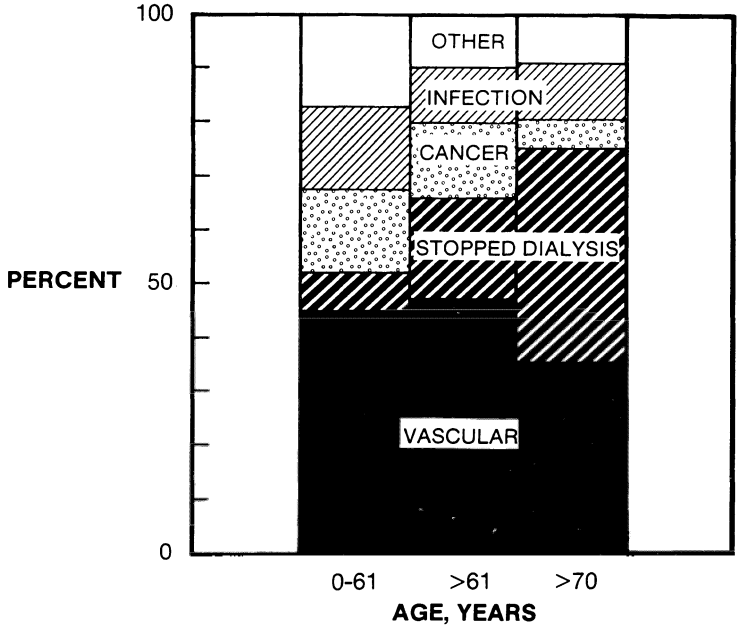


Figure 7: Causes of death of patients on dialysis at the Regional Kidney Disease Program, 1966-1983. Stopping dialysis is the most common cause of death in the older patient. For all younger patients, vascular deaths are the most common.

variables are arteriosclerotic heart disease, advancing age over 70 years, and in-center dialysis. On the other hand, six variables - diabetes, sex, cerebrovascular accident, chronic obstructive pulmonary disease, peripheral vascular disease, and cancer imposed no additional risk if they were present at the start of dialysis (7,15).

VIII. MORBIDITY

In an analysis of patients over the age of 70 at the Regional Kidney Disease Program, we found a hospitalization rate of 1.74 hospitalizations per year (7). These older patients spent a mean of eighteen days of the year in the hospital versus ten days per year in a controlled population of patients aged 20-60 without any premorbid conditions. In an analysis by Carlson, *et al*, of the Minnesota dialysis population, there was a direct relation between the number of days per year spent in the hospital and age. The patient age 0-20 years was hospitalized a mean of 5.25 days versus 13.45 days for the patient older than 71 years (17).

IX. QUALITY OF LIFE

In 1984 we carried out a thorough evaluation of the quality of life in the elderly hemodialysis patient (7). This evaluation included all 79 in-center and home patients alive and oriented during the week of Sept. 1, 1983. Of the 79 patients, three were excluded because they were confused or seriously ill. A personal interview included evaluation of living characteristics, social contacts, desire for other treatment, activity when off dialysis, enjoyment of life and depression (both measured on a six-point scale), the perceived health questionnaire and physical performance using a modified Karnofsky scale. The evaluation included the opinions of both the patient and the patient's nurse practitioner. We found no difference between the findings of the patient and the nurse or between home and in-center dialysis (Tables 2 and 3). Obviously most of the patients were doing well, were at home, having good contact, spending much time outdoors, enjoying life, and ranking very high on the Karnofsky scale. On the negative side, between 3 and 10% of the patients needed nursing homes, had considered stopping all treatment, and were depressed. Of all these patients, 40% wished for a renal transplant. Of the in-center patients, 20% wished they were on home dialysis. Somewhat astonishingly, 40% of the patients on dialysis believed they were in better health than other 70-year-old people. Only 25% regarded their health as worse, and 35% believed they had about the same health as other 70-year-olds.

Table II: Dialysis patients >70 years, quality of life, positive

At home	93%
Good social contact	90%
Much outdoors	86%
Enjoy life	71%
Karnofsky >80	73%
Health better than others	40%

Table III: Dialysis patients >70 years, quality of life, negative

Depressed	10%
Wish for transplant	40%
Consider stopping treatment	5%
In nursing home	7%
Needs nursing home	3%
Health worse than others	25%

X. CONCLUSIONS

The numbers of elderly dialysis patients show the most rapid increase both absolute and relative to the younger patient. In many parts of the world the mean age of the dialysis patient now exceeds 60 years.

The result of hemodialysis has improved for the older, as it has for all dialysis patients, but there seems to be no marked improvement since the mid-1970's. Five-year survival is now between 40% in patients over age 60 to 10% for the patient over age 75. Apart from the year of start of dialysis, there seems to be no other clearly identifiable risk factor. Arteriosclerotic heart disease, in-center *versus* home, and advancing age possibly may be important risk factors. Diabetes, sex, cerebrovascular accident, chronic obstructive pulmonary disease, peripheral vascular disease, and cancer are not important variables.

Vascular disease remains, as for other patients, a common cause of death, but withdrawal of dialysis is the most common cause at least in the patient over age 70. The morbidity in these patients is low and the quality of life high. Most are at home, quite mobile, and enjoy life.

It is obvious that dialysis is a worthwhile treatment even for very old patients, but gaining access to the process is two to six times more difficult than for the younger ones.

It is important to broadcast these results because certain elements in Western society seem to be trying to limit treatment for the old and sick. In England, this policy has almost excluded patients over the age of 55 from dialysis for no valid medical reasons for such exclusion (18).

REFERENCES

1. Kjellstrand CM: Hemodialysis - the gold standard. Proc 8th Int Congr Nephrol: 708-714, 1981.
2. Figueroa JE: Management of uremia in older patients: hemodialysis and renal transplantation. J Am Geriatric Soc 16:1323-1330, 1968.
3. Rathaus M, Bernheim JL: Are your elderly patients good candidates for dialysis? Geriatrics 33:55-61, 1978.
4. Ghantous WN, Bailey GL, Zschaeck D, Hampers CL, Merril JP: Longterm hemodialysis in the elderly. Trans Am Soc Artif Intern Organs 17:125-128, 1971.
5. Cohen SL, Comty CM, Shapiro FL: The effect of age on the results of regular hemodialysis treatment. Proc Eur Dial Transplant Assoc 7:254-260, 1970.
6. Chester AC, Rakowski TA, Argy WP Jr, Giacalone A, Schreiner GE: Hemodialysis in the eighth and ninth decades of life. Arch Intern Med 139:1001-1005, 1979.
7. Westlie J, Umen A, Nestrud S, Kjellstrand CM: Mortality, morbidity, and life satisfaction in the very old dialysis patient. Trans Am Soc Artif Intern Organs 30:21-30, 1984.
8. Siemensen H, Schlamp R, Tachezy H, Bischoff K, Remmecke J: Uberlebenszeit und todesursachen bei dialysepatienten. Dtsch Med Wochenschr 109:1833-1836, 1984.
9. Mallinson WJW, Fleming SJ, Shaw JEH, Baker LRI, Cattell WR: Survival in elderly patients presenting with uraemia. Q J Med 210:301-307, 1984.
10. Taube DH, Winder EA, Ogg CS, Bweick M, Cameron JS, Rudge CJ, Williams DG: Successful treatment of middle aged and elderly patients with end stage renal disease. Br Med J 286:2018-2020, 1983.
11. Weller JM, Wu SH, Ferguson CW, Hawthorne VM: End-stage renal disease in Michigan: incidence, underlying causes, prevalence, and modalities of treatment. Am J Nephrol 5:84-95, 1985.
12. Eggers PW, Conerron R, McMullan M: The Medicare experience with endstage renal disease: trends in incidence, prevalence and survival. Health Care Manage Rev 5:69-88, 1984.
13. Vital Statistics of the United States 1979 Vol II Part B DHHS Publ No (PHS) 84-1101, Washington DC, 1984.
14. Hellerstedt WL, Johnson WJ, Ascher N, Kjellstrand CM, Knutson R, Shapiro FL, Sterioff S: Survival rates of 2,728 patients with end-stage renal disease. Mayo Clin Proc 59:776-783, 1984.
15. Shapiro FL, Umen A: Risk factors in hemodialysis patient survival. Am Soc Artif Intern org J 6:167-184, 1983.
16. Neu S, Kjellstrand C: Stopping chronic dialysis--an empirical study of passive euthanasia. Submitted for publication.
17. Carlson DM, Duncan DA, Naessens JM, Johnson WJ: Hospitalization in dialysis patients. Mayo Clin Proc 59:769-775, 1984.
18. Callah S, Wing AJ, BAuer R, Morris RW, Schroeder SA: Negative selection of patients for dialysis and transplantation in the United Kingdom. Br Med J 288:1119-1122, 1984.

16. PERITONEAL DIALYSIS IN THE ELDERLY

ALLEN R. NISSENSON, M.D., FACP, DOMINICK E. GENTILE, M.D., ROBERT E. SODERBLOM, M.D. AND CHARLENE BRAX

INTRODUCTION

Most investigators agree that CAPD is equivalent to hemodialysis for non-diabetic 'standard' patients - age 21-60, and without associated medical problems (1-4). In addition, most pediatric nephrologists consider CAPD or CCPD the dialysis modality of choice for children awaiting renal transplantation (5). Though the outcome of CAPD in the elderly seems favorable (6,7,8), no large experience with such individuals has been reported. This is particularly surprising because the prevalence of ESRD is increasing most rapidly in this age group (4,9), and overall, 50-60% of patients starting dialysis in the United States are over 60 years of age. This paper reviews experience in Southern California/Southern Nevada with chronic peritoneal dialysis in patients over 60 years of age.

SUBJECTS AND METHODS

The largest ESRD network in the United States, NCC #4 encompasses Southern California and Southern Nevada, and contains 90 outpatient dialysis facilities and 5300 dialysis patients - 7% of all such patients in the United States. The NCC #4 CAPD study includes cumulative patient data on all patients ever on CAPD or CCPD* at NCC #4 facilities. Since 1979, 42 of the 90 facilities provided care

*The term 'CAPD' will be used to describe the combined CAPD and CCPD groups for purposes of this analysis.

to a total of 775 CAPD patients up to Dec. 31, 1983. Patients enter the study when they complete training and initiate CAPD as their only form of treatment. A registration form is completed to collect basic demographic and rehabilitation data. Patient status update forms are completed quarterly to provide data on selected outcome measures. When appropriate, demographic data is tabulated and standard life-table analyses performed (10).

The 775 CAPD study patients had a total of 10,542 months experience on CAPD, with a mean of 12.3 months (range 1-49 months). The 183 patients (23.6% of the total CAPD population) over 60 years of age at the time of initiation of CAPD had accumulated a total experience of 2451 patient-months. For this elderly group, mean time on CAPD is 11.6 months (range 0.5-46 months).

RESULTS

Demographic Analyses:

59.2% of the elderly patients were male and 40.8% female, comparable to the overall CAPD patient sex distribution.

74.3% were white, 13.1% Mexican-American, and 7.9% black compared with 65.8%, 16.5%, and 11% for the same racial groups respectively in the overall CAPD population. 25.1% of the elderly patients had ESRD because of chronic glomerulonephritis, 22% because of nephrosclerosis, 14.1% because of polycystic kidney disease, and 12.6% because of diabetes mellitus, similar to the overall CAPD population.

PATIENT OUTCOME

At the end of the study period, 32% of the elderly patients were still on CAPD, 39% had transferred to hemodialysis and 22% had died.

Table I: Patient Outcome

	(%)
Still on CAPD	32
Transferred to hemodialysis	39
Died	22
Recovered renal function	2
Lost to follow-up	4
Unknown	1

By comparison, in the total CAPD population, 47% were still on CAPD, 26% had transferred to hmeodialysis, 14% had died and 7% had received renal transplants by the end of the study.

When assessed by life-table analysis (Fig.I), 53% of elderly patients overall were still on CAPD at 1 year, 24% at 2 years and 15% at 2½ years. Significantly fewer elderly patients remained on CAPD at these periods then did younger patients.

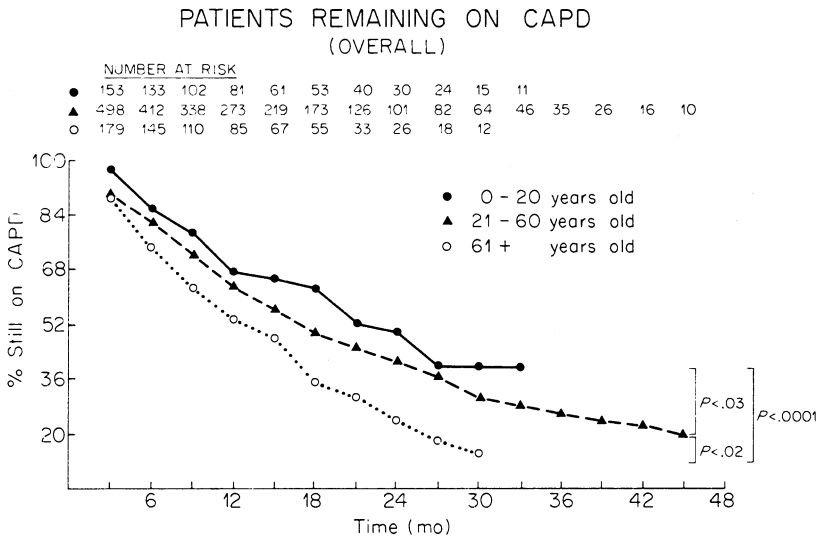


Fig. I. Per cent of patients remaining on CAPD by age group.

TECHNIQUE SUCCESS

When assessed by life-table analysis (Fig.II) and death and transplantation are excluded (treated as 'lost to follow-up'), 67% of elderly patients were still on CAPD at one year, 37% at two years and 29% at two and one-half years. Technique success was significantly lower in the elderly than in the 0-20-year old patients, but not different from that in the 21-60 year olds.

Of the elderly who switched to hemodialysis, 37% did so because of recurrent peritonitis, while 13% did so because of tunnel infection. Only 18% switched because of patient or family preference and 7% because of inadequate clearances. All of these figures are comparable to those seen in the overall CAPD population.

PATIENT SURVIVAL

Elderly patient survival was 79% at one year, 63% at two years and 52% at two and one-half years (Fig. III). Survival was significantly lower, as expected, in the elderly than in the younger patients. The causes of death in the elderly are outlined in Table II. 62% died of vascular causes (MI, other cardiac, or cerebrovascular) while 12% died of septicemia, compared to 52% and 9% for these causes in the overall CAPD population. The remainder of deaths were attributable to a wide variety of causes and occurred with similar frequency in elderly and younger patients.

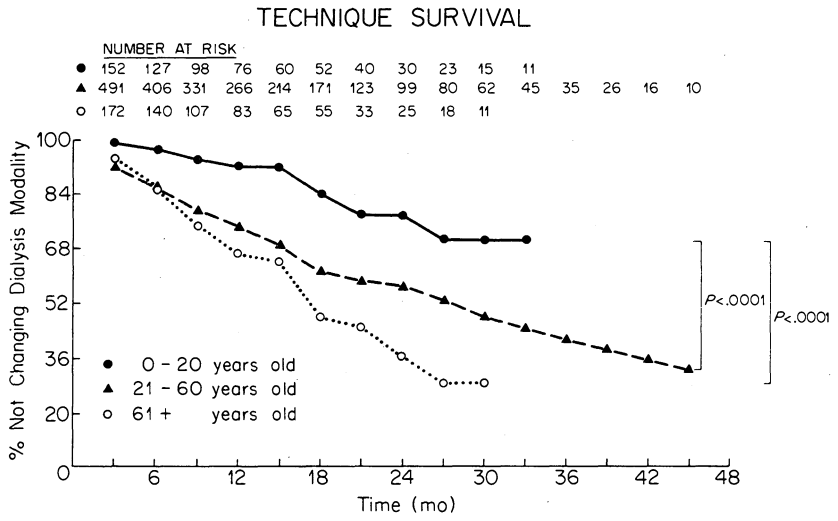


Fig.II. Technique survival on CAPD-death and transplantation are considered 'lost to follow-up'.

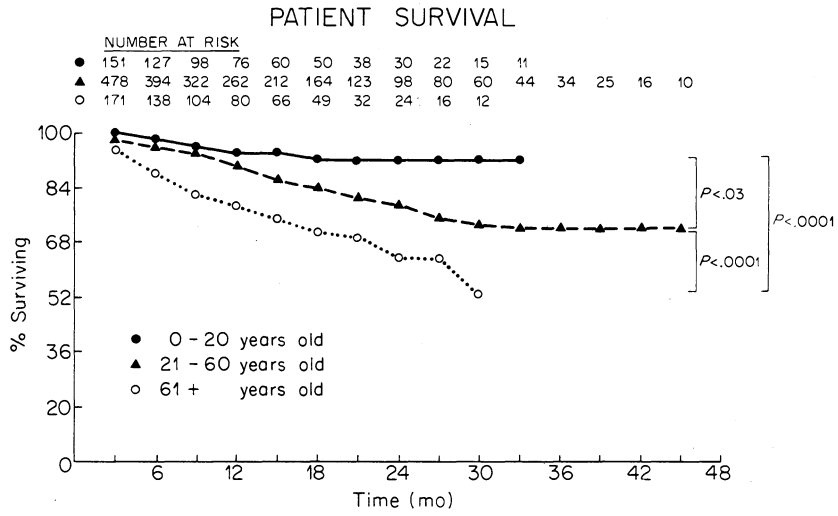


Fig. III. Patient survival for each age group on CAPD

Table II: Cause of Death

	(%)
Acute myocardial infarction	33
Cardiac (excluding MI and pericarditis)	21
Septicemia	12
Unknown	10
Cerebrovascular	8
GI hemorrhage	6
Other	6
Pulmonary infection	2
Withdrawal from dialysis	2

PATIENT MORBIDITY

Three specific areas of patient morbidity were evaluated - peritonitis, catheter placement and hospitalization:

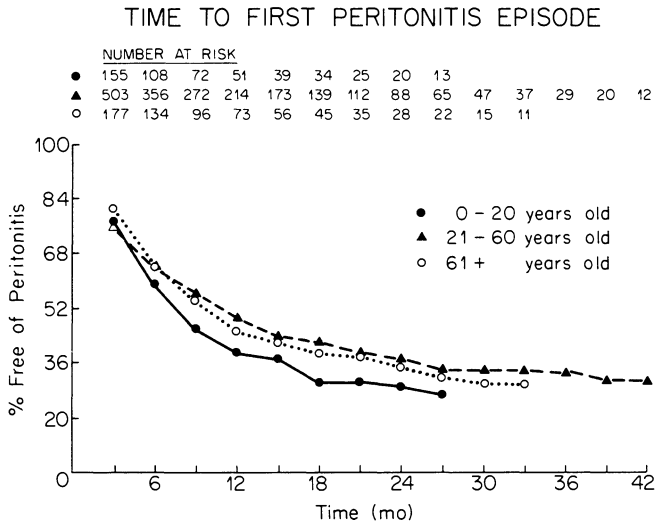


Fig. IV. Per cent of patients free of peritonitis for the first time by age group.

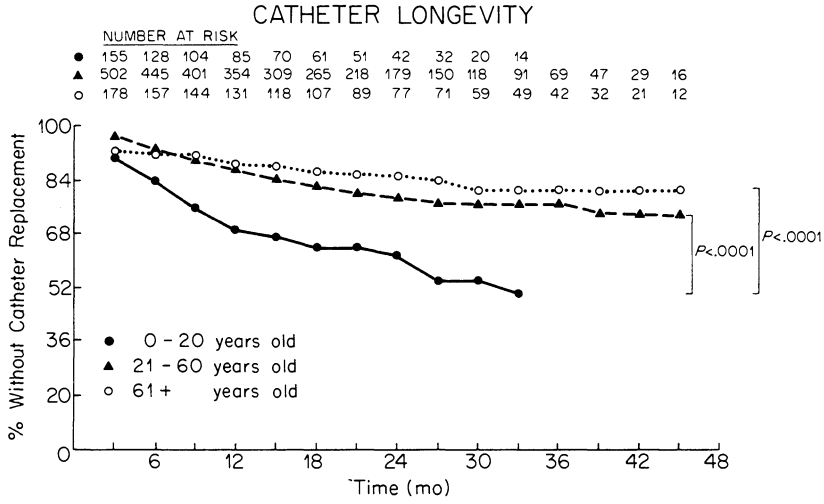


Fig. V. Per cent of patients without a catheter replacement by age group.

Peritonitis: By the end of one year, 55% of the elderly patients had their first episode of peritonitis, 65% by the end of two years, and 70% by the end of two and one half years. No differences were seen in time to first peritonitis episode among the three age groups (Fig. IV). In addition, the overall incidence of peritonitis, averaging 1.5 episodes per patient per year, was not different in the elderly compared to the younger patients.

Catheter replacement: By the end of one year, 88% of elderly still had their original catheter, 86% at the end of two years and 81% at the end of two and one-half years. The elderly had significantly better catheter longevity than did patients age 0-20 (Fig. V).

Hospitalizations (Table III): Elderly patients spent an average of 19.1 days per patient-year in the hospital compared to 17.8 days per patient-year for the overall CAPD population. CAPD-related problems including peritonitis accounted for 60% of all hospital days in both groups.

Table III: Hospitalization

Reasons for Hospitalization	Total # Hosp Admissions	Total # of Hosp Days	Total # Hosp Days/Pt. Yr.
Peritonitis	142	1317	6.5
CAPD related problems other than peritonitis	130	957	4.7
Vascular problems	68	630	3.1
Other problems	97	989	4.8
All reasons	437	3893	19.1

PSYCHOSOCIAL FUNCTIONING

Four specific areas of psychosocial functioning were addressed - marital status, living arrangements, mobility and work status.

76% of elderly patients were married, 11% widowed, 8% divorced and 3% never married. In the overall CAPD population, 32% are unmarried, reflecting the large pediatric population on CAPD.

63% of elderly CAPD patients live with a spouse, 24% live with another relative and 11% live alone. Again, because of the large pediatric population on CAPD, the figures for the overall CAPD group are 30.6%, 54.3% and 8.6% for the same living arrangements respectively.

78% of elderly CAPD patients are ambulatory without assistance, 17% require some assistance, 3% are home-confined, and 3% are bedridden. These figures are similar to that in the overall CAPD population, except slightly fewer of the elderly are ambulatory without assistance than in the younger groups.

49% of the elderly CAPD patients are not working - paid jobs, school hours

or housework, 10% work up to 10 hours per week, 9% up to 10-20 hours per week, 16% up to 20-30 hours per week, and 8% up to 30-40 hours per week. More elderly are not working or work fewer hours than younger CAPD patients, though the differences are not great.

DISCUSSION

In the six years since the widespread application of CAPD, much data has been published on outcome of large heterogenous populations (1-4,11,12). Little has been written, however, on the elderly patient, a rapidly growing segment of the ESRD population. This type of data is highly pertinent, because in some countries, age is a major factor excluding patients from dialysis (13).

Recently, Taube *et al* (8) described their experience with 55 patients over 55 years of age with end-stage renal disease who were placed on dialysis in the United Kingdom. Ten of these were treated with CAPD and the overall five-year patient survival was 63%. In addition, 68.8% were working or 'retired but fit'. These outcomes were not subdivided by dialysis modality.

Kaye *et al* (6) described 18 patients age 65 or older on CAPD in Montreal, and compared them to 26 younger CAPD patients. In most respects - biochemical control, complications, and failure rate, elderly patients were comparable to younger ones. Although more elderly died than younger ones during the period of observation, the difference was not statistically significant.

Nicholls *et al* (7) described 38 patients over 60 years of age treated with CAPD. Most were considered unsuitable for hemodialysis by the criteria applied in the United Kingdom before the availability of CAPD. Subsequently two patients transferred to hemodialysis while the remainder stayed on CAPD. Patient survival was 72% at one year and 61% at two years, and 21% of the 23 survivors were 'fully rehabilitated'.

In the most recent report of the National CAPD Registry of the NIH, Cutler *et al* (14) reported that of all CAPD patients in the registry, 31% were over 60 years old. Other than the expected higher mortality rate in this group, they noted no differences for other outcome variables compared to younger patients.

Finally Mallinson *et al* (15) reported retrospectively on 93 patients aged 60 years or greater who presented with uremia to St. Bartholomew's Hospital in London. 65% of these patients were dialyzed (both hemo and peritoneal dialysis) and overall survival in the dialysed and non-dialyzed groups was 40% at two years. Again, assessment by type of dialysis was not possible because of the small number of patients.

CAPD has had a major impact on ESRD therapy in Southern California/Southern Nevada. Whereas in 1978 only 3% of all NCC #4 patients were on home dialysis (88% home hemodialysis, 12% IPD or CAPD), by 1983 this number had tripled, almost entirely because of the growth of CAPD - 82% CAPD

or IPD, 18% home hemodialysis as of Dec. 31, 1983 (4).

In the United States, the NIH CAPD Registry has been the major source of data on large numbers of patients undergoing CAPD (14). We have had the opportunity, because of the early and rapid growth of CAPD in NCC #4, to collect similar data in one region of the country, using the existing Network to obtain information directly from each facility performing CAPD. In this way we have collected data on all patients started on CAPD in NCC #4, and have verified any incomplete or ambiguous quarterly status update forms.

The present report is the largest series of elderly CAPD patients yet described other than in the NIH Registry. The demographic features of this group, other than age, were similar to those of the overall NCC #4 CAPD population. Overall patient and technique success are comparable to the previous reports, but patient survival was significantly lower compared to the overall NCC # 4 CAPD population. Technique success, hospitalization rate, peritonitis rate and catheter survival rates were similar in our young and older patients, although the latter was somewhat better in the elderly.

Of considerable interest and importance were the findings related to psychosocial functioning, because some have suggested that nephrologists may overtreat older patients to benefit themselves financially, rather than to improve the patient's quality of life (16). In our experience, however, the vast majority of elderly CAPD patients are married and living satisfying lives with a spouse. In addition, nearly 80% are ambulatory without any assistance and one-half are engaged in some form of gainful work. These data suggest that the elderly can lead gratifying, productive lives in spite of their ESRD.

In summary, CAPD offers certain specific advantages and disadvantages to the elderly (Tables IV, V). The advantages are related to the gradual fluid and solute removal and the avoidance of vascular access or anticoagulants. The disadvantages are that the elderly are over-represented among CAPD patients suffering from back pain, hernia formation, fluid leaks and vascular ischemia of the lower extremities. However, these findings need to be confirmed in larger numbers of patients.

Table IV: Advantages of Peritoneal Dialysis in the Elderly

Less abrupt solute and fluid removal than HD.
No anticoagulant needed.
Can be performed at home.
Better cardiovascular stability than HD.
Avoids need for a vascular access.

Table V: Disadvantages of Peritoneal Dialysis in the Elderly

Requires adequate eyesight and dexterity.
Back pain.
Vascular ischemia.
Hernia formation.
Fluid leaks.
Poor tolerance of peritonitis.
Higher incidence of diverticulosis may lead to more frequent bowel leak - peritonitis syndrome.

In conclusion, CAPD is a reasonable alternative for the elderly patient with ESRD. Except for the expected increase in mortality in this group, the elderly compare favorably in other aspects of morbidity to younger patients receiving this therapy.

REFERENCES

1. Khanna R, Wu G, Vas S, Oreopoulos DG: Mortality and morbidity on CAPD. ASAIO J. 6:197, 1983.
2. Mion CM, Mourad G, Canaud B, et al: Maintenance dialysis: A survey of 17 years' experience in Languedoc-Rousoillon with a comparison of methods in a 'standard population'. ASAIO J. 6:205, 1983.
3. Wing AJ, Broyer M, Brunner FP, et al: The contribution of CAPD in Europe. ASAIO J. 6:214, 1983.
4. Nissenson AR, Gentile DE, Soderblom RE, Brax C, Medical Review Board, NCC #4: Morbidity and Mortality of CAPD. Regional Experience and Long Term Prospects. In press (Am. J. Kd. Dis., 1985).
5. Baum M, Powell D, Calvin S, et al: CAPD in children. New Engl. J. Med. 307:1537, 1982.
6. Kaye M, Pajel PA, Somerville PJ: Four years' experience with CAPD in the elderly. Perit. Dial. Bull. 3:17, 1983.
7. Nicholls AJ, Waldek S, Platts MM, Moorehead PJ, Brown CB: Impact of CAPD on treatment of renal failure in patients aged over 60. Brit. Med. J. 288:18, 1984.
8. Taube DH, Winder EA, Ogg CS, Bewich M, Cameron JS, Rudge CJ, Williams DG: Successful treatment of middle aged and eldery patients with end-stage renal disease. Brit. Med. J. 286:2018-2020, 1983.
9. Weller JM, Wu SH, Ferguson CW, Hawthorne VM: End-stage renal disease in Michigan. Am. J. Nephrol. 5:84-95, 1985.
10. Cutler SJ, Ederer F: Maximum utilization of the life table method in analyzing survival. J. Chron. Dis. 8:699, 1958.
11. Nissenson AR, Gentile DE, Soderblom R, Brax C, et al: Long-term outcome of CAPD - regional experience. Dialysis and Transplant 13:34, 1984:
12. Diax-Buxo J: Intermittant, continuous ambulatory and continuous cycling peritoneal dialysis. Chapter in *Clinical Dialysis* (ed. Allen R. Nissenson, Richard N. Fine, and Dominick E. Gentile), Appleton-Century-Crofts, Norwalk, Conn., 1984, pp. 263-307.
13. Challah S, Wing AJ, Bauer R, Morris RW, Schroeder SA: Negative selection of patients for dialysis and transplantation in the United Kingdom. Brit Med. J. 288:1119, 1984.
14. Cutler SJ, Steinberg SM, Novak JW, Nolph KD: Report of the National CAPD Registry of the

NIH. Characteristics of participants and selected outcome measures for the period January 1, 1981, through December 31, 1983. Bethesda, Maryland, 1984.

15. Mallinson WJW, Fleming SJ, Shaw JEH, Baker LRI, Cattell WR: Survival in the elderly patients presenting with uremia. Quart. J. Med., New Series LIII, 210:301-307, 1984.
16. Relman AS, Rennie D: Treatment of end-stage renal disease. Free but not equal. New Engl. J. Med. 303:996-998, 1980.

17. RENAL TRANSPLANTATION IN THE MIDDLE-AGED AND ELDERLY UREMIC PATIENT

THE RECENT UNITED STATES EXPERIENCE AND RESULTS FROM A SINGLE INSTITUTION

BRUCE G. SOMMER, M.D., DAVID M. MANDELBAUM, M.D., MITCHELL L. HENRY, M.D. AND RONALD M. FERGUSON, M.D.

INTRODUCTION

Renal transplantation in the uremic patient with advancing age either has been denied or undertaken at a presumed high risk. Currently over 50% of uremics on some form of chronic dialysis in the United States are 50 years of age or older (1). The comparatively poorer results achieved with renal transplantation in the elderly have been previously attributed to excessive infectious and cardiovascular complications and intolerance of immunosuppressive therapy. However, recent advances in immunosuppressive techniques have produced a dramatic improvement in patient and allograft survival for the older renal allograft recipient, especially following cadaveric transplantation.

This report reviews cadaveric renal transplantation in the middle aged and elderly uremic in the Unites States, and examines the experience at The Ohio State University Hospital, where patients over the age of 50 years old constitute one-quarter of all patients transplanted. Since previous authors (1,2) have stated that living related donors can cancel the 'high risk' of renal transplantation for the elderly uremic, this report will focus on the current status of cadaveric renal transplantation.

PATIENTS-METHODS-RESULTS

Between January 1982 and June 1984, 680 cadaver renal transplants in recipients 55 years of age or older were reported to the United States Registry of the Health Care Finance Administration. The general characteristics of this population are shown in Table I. Recipients were predominately white males with a mean age of 59 years. The majority of patients received pretransplant blood transfusions and did not have a splenectomy before transplantation. During this period, cyclosporine was being evaluated at a few institutions in the United States and only 29% of these recipients received cyclosporine as maintenance

Table I: HCFA: UNITED STATES TRANSPLANT REGISTRY CHARACTERISTICS OF 680 CADAVERIC RENAL TRANSPLANT RECIPIENTS

Mean Age (Yr.) (x + S.D.)	59 + 3 (Range 55-80)
Percent male	67
Percent black	15
Percent with diabetes	6
Percent with pretransplant splenectomy	12
Percent given pretransplant blood transfusions	85
Percent given cyclosporine	29
Mean HLA AB antigens matched	1.3 ± 0.9
Mean Dr antigens matched	0.5 ± 0.7
Length of allograft storage prior to transplant (hours)	18 + 16

immunotherapy. One hundred ninety-eight recipients received cyclosporine and 482 recipients were treated with various regimens of conventional immunosuppression. Unfortunately, the 680 elderly recipients transplanted during this 2 1/2 year period represent only 6% of the total cadaveric renal transplants done in the United States during that time.

Patient and renal allograft survival (3) one year following transplantation for cadaver donor recipients 55 to 60 years old receiving conventional immunosuppression was 84% and 59% respectively. At one year, recipients 60 to 65 years old had a patient and allograft survival of 85% and 57%, and recipients over 65 years had survivals of 63% and 43% respectively with conventional immunotherapy (Figs. 1A & B). Allograft survival in the elderly has increased with cyclosporine and the results are closer to that seen with younger recipients. At one year, patient and allograft survival with cyclosporine is 89% and 55% respectively for recipients 55 to 60 years of age. Recipients 60 to 65 years have a patient and allograft survival of 79% and 67%, and recipients over 65 had survivals of 100% and 75% respectively with cyclosporine (Figs. 2A & B). The middle-aged recipient tends to have a slightly better allograft longevity than the elderly recipient; however, no statistical differences are present.

A review of a selected series of cadaveric renal transplants in elderly recipients shows an improvement in recipient survival over the past 10 years with use of conventional immunosuppression. Allograft survival has improved, however, only with the recent use of cyclosporine (Table II). Yet, important lessons have been learned with conventional immunosuppressive therapy. The elderly patient was shown to tolerate poorly high-dose steroids, and both mortality and morbidity decreased when the dose of steroids was reduced, without sacrificing allograft survival (14). Post-transplant survival in the elderly uremic on chronic

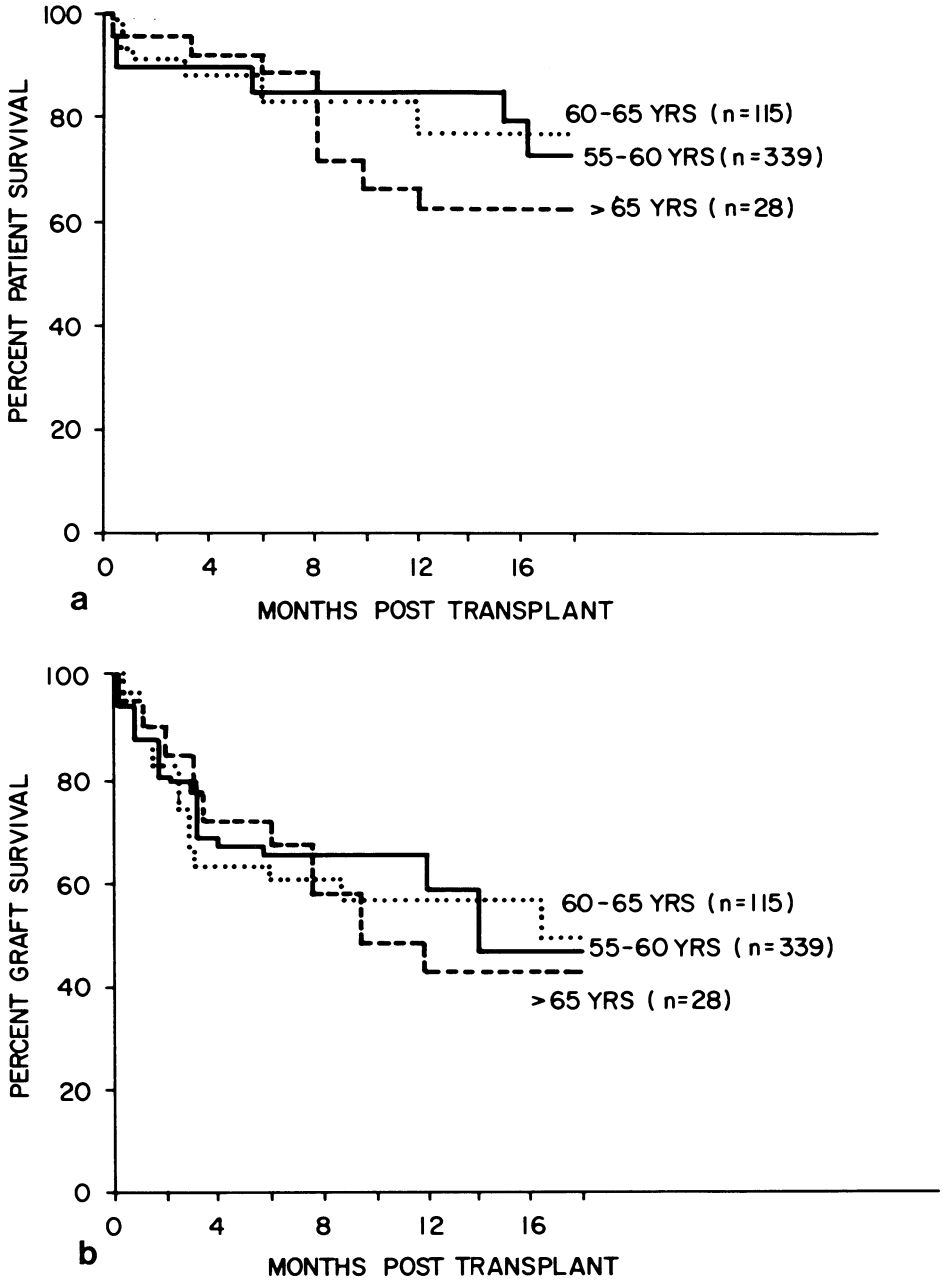


Figure 1: Patient survival (A) and renal allograft survival (B) following 482 cadaveric renal transplants in the elderly using conventional immunosuppression. Data is from the HCFA: United States Transplant Registry and includes renal transplants performed between January 1982 and June 1984.

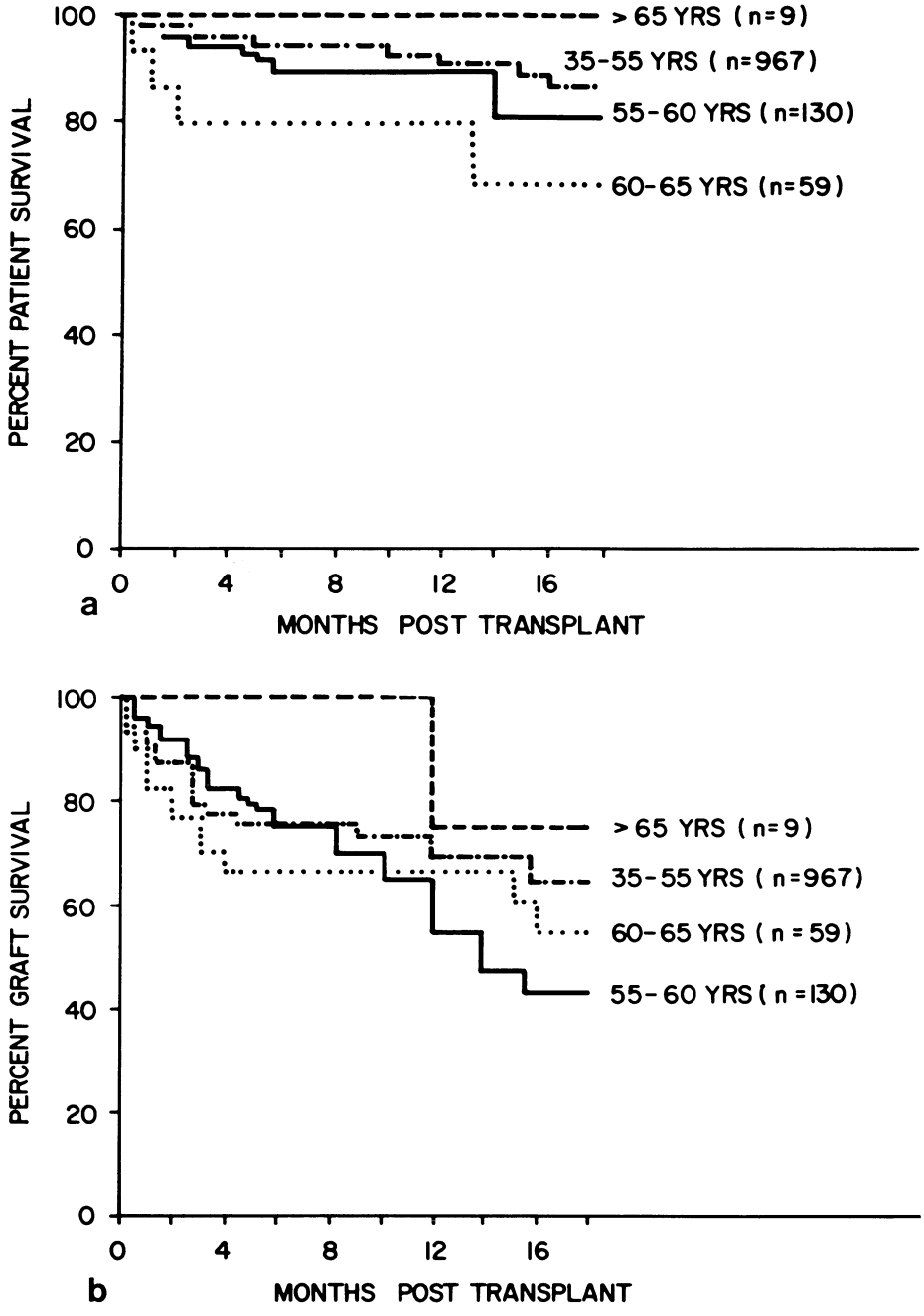


Figure 2: Patient survival (A) and renal allograft survival (B) following 198 cadaveric renal transplants in the elderly using cyclosporine compared to patient and graft survival in 967 younger recipients. Data is from the HCFA: United States Transplant Registry and includes renal transplants performed between January 1982 and June 1984.

Table II. Cadaver renal transplantation in recipients 50 years of age or older

YEAR STUDIED	REPORT & REFERENCE	AGE	NO. OF PATIENTS	IMMUNO SUPPRESSION	PERCENT SURVIVAL AT ONE YEAR RECIPIENT	ALLOGRAFT
1974	Delmonico 4	⩾50	23	AZA*	57	--
1976	Kjellstrand 5	⩾50	33	AZA	66	--
1977	Golper 6	⩾50	30	AZA	75	58
1978	Wedel 7	⩾60	38	AZA	60	60
1978	Kock 8	⩾60	38	AZA	66	62
1978	SCASTS 9	⩾50	89	AZA	82	49
1979	Sommer 10	⩾50	62	AZA	60	51
1982	Oiye 11	⩾50	29	AZA	73	61
1982	Taube 12	⩾55	38	AZA	83	67
1983	Ringden 13	⩾55	29	CSA	85	73
1985	Sommer (current)	⩾50	52	CSA	92	86

*AZA--Azathioprine, CSA--Cyclosporine

TABLE III. Original kidney disease necessitating renal transplantation for 71 elderly recipients at the Ohio State University

Cause of renal disease	Number of recipients	Percent
Glomerulonephritis	26	37%
Polycystic kidneys	11	15%
Hypertension	9	13%
Diabetes	7	10%
Intersititual nephritis	5	7%
Other	13	18%

dialysis also has improved allowing the transplant surgeon to accept graft failure, that is, the high incidence of septic deaths declined when we stopped the efforts to prolong allograft longevity (12,15). During the last 10 years, the elderly uremic, who had an extremely high risk following renal transplantation, now has no greater risk than any other age group when treated properly.

At the Ohio State University Hospitals, we have taken a special interest in rehabilitating the elderly uremic and have used renal transplantation as the primary mode of therapy. Fully one-quarter of all renal allograft recipients at our institution are 50 years or older. Table III shows the original kidney disease

Table IV. The effect of blood transfusions following cadaver renal transplantation in recipients 50 years of age or older treated with cycosporine

Number of transfusions	Number of patients	Number of deaths	Number of allograft losses
0	14	1	2
1-4	17	2	3
5 +	21	3	4

necessitating transplantation in this age group. Compared to a younger population, polycystic kidney disease accounts for a large proportion of renal transplants in the elderly. Interestingly, all nine patients with renal failure on the basis of hypertension were black.

Between September 1982 through to March 1985, 71 renal transplants were performed in patients 50 years of age or older. Twelve recipients received maintenance immunotherapy with azathioprine (16). Cyclosporine (10 mg/kg/day) was used for maintenance immunotherapy in 59 recipients. After transplantation, all patients received prednisone (2 mg/kg/day) which was tapered to 0.3 mg/kg/day at one month and 0.2 mg/kg/day by three months. Rejection episodes were treated by recycling the same immediate post-transplant prednisone taper. Thirty recipients were between 50 and 55 years, 21 between 55 and 60 years, and 20 were older than 60 years of age. Donor and recipient pairs were matched only on the basis of ABO-blood compatibility and a negative warm T-cell crossmatch before transplantation. Mandatory preoperative blood transfusions are not a part of our protocol and absence of transfusions before transplantation has not correlated with an increased incidence of allograft losses when cyclosporine is used for maintenance immunosuppression (Table IV).

Figure 3 shows patient and allograft survival for 52 cadaveric recipients treated with cyclosporine. At 18 months, 88% of the elderly transplants were alive and 82% had functioning renal allografts. All seven recipients who received living related-donor renal allografts are alive with functioning kidneys at 18 months. Unfortunately, most recipients in this age group do not have potential related donors and must seek cadaveric sources. It is the elderly cadaveric recipient who shows the benefits of cyclosporine over that seen with conventional immunotherapy. Figures 4A & B shows patient and allograft survival following cadaveric renal transplantation (47 primary, five second, and one third renal allograft) according to age grouping when cyclosporine is used for immunotherapy. As previously shown by results obtained from the United States Transplant Registry, recipients closest to 50 years of age have a slightly better patient and allograft survival, yet no individual group can be designated as 'high risk'.

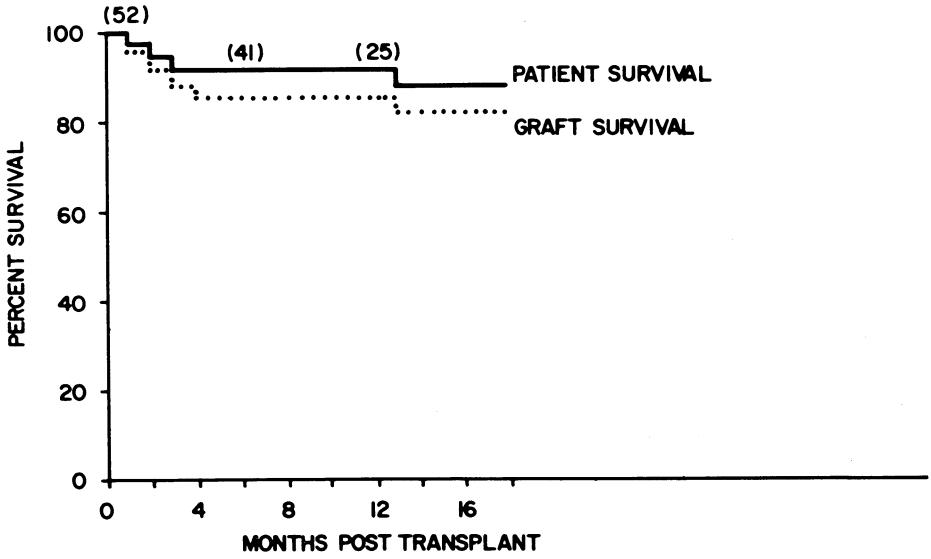


Figure 3: Overall patient and renal allograft survival following 52 cadaveric renal transplants for recipients 50 years or older treated with cyclosporine at The Ohio State University between March 1983 and March 1985.

When cyclosporine is used for immunotherapy, drug associated renal dysfunction following transplantation is common in the elderly. However, multiple episodes of cyclosporine-associated nephrotoxicity are not as common as that seen in the younger transplant population (16). Eighty-eight per cent of elderly cadaveric renal recipients treated with cyclosporine had at least one episode of renal dysfunction as measured by a 25% rise in serum creatinine from a stable baseline. Cyclosporine-associated nephrotoxicity was more common during the first year following transplantation than was rejection (Fig.5). Therefore in dealing with allograft recipients treated with cyclosporine, one needs a management strategy which gives a consistent approach to episodes of renal dysfunction. We have elected to titrate the cyclosporine dose to renal function without the use of cyclosporine levels. A rise in the serum creatinine over baseline is managed first by a decrease in cyclosporine dose, leaving the prednisone dose unchanged. If renal function does not improve or worsens, the patient is biopsied to rule out rejection. If rejection is present on biopsy, the prednisone dose is increased. It is apparent, three months following renal transplantation, rejection episodes become less common in relationship to nephrotoxic episodes (Fig.5). Nephrotoxicity, also, becomes less frequent with increasing time after transplantation; however, nephrotoxic episodes still occur after one year. Our management policy allows us to separate most nephrotoxic from rejection episodes on an outpatient basis.

In the elderly recipient, septic and cardiovascular causes remain a frequent cause of death after renal transplantation. In the first 18 months, four deaths

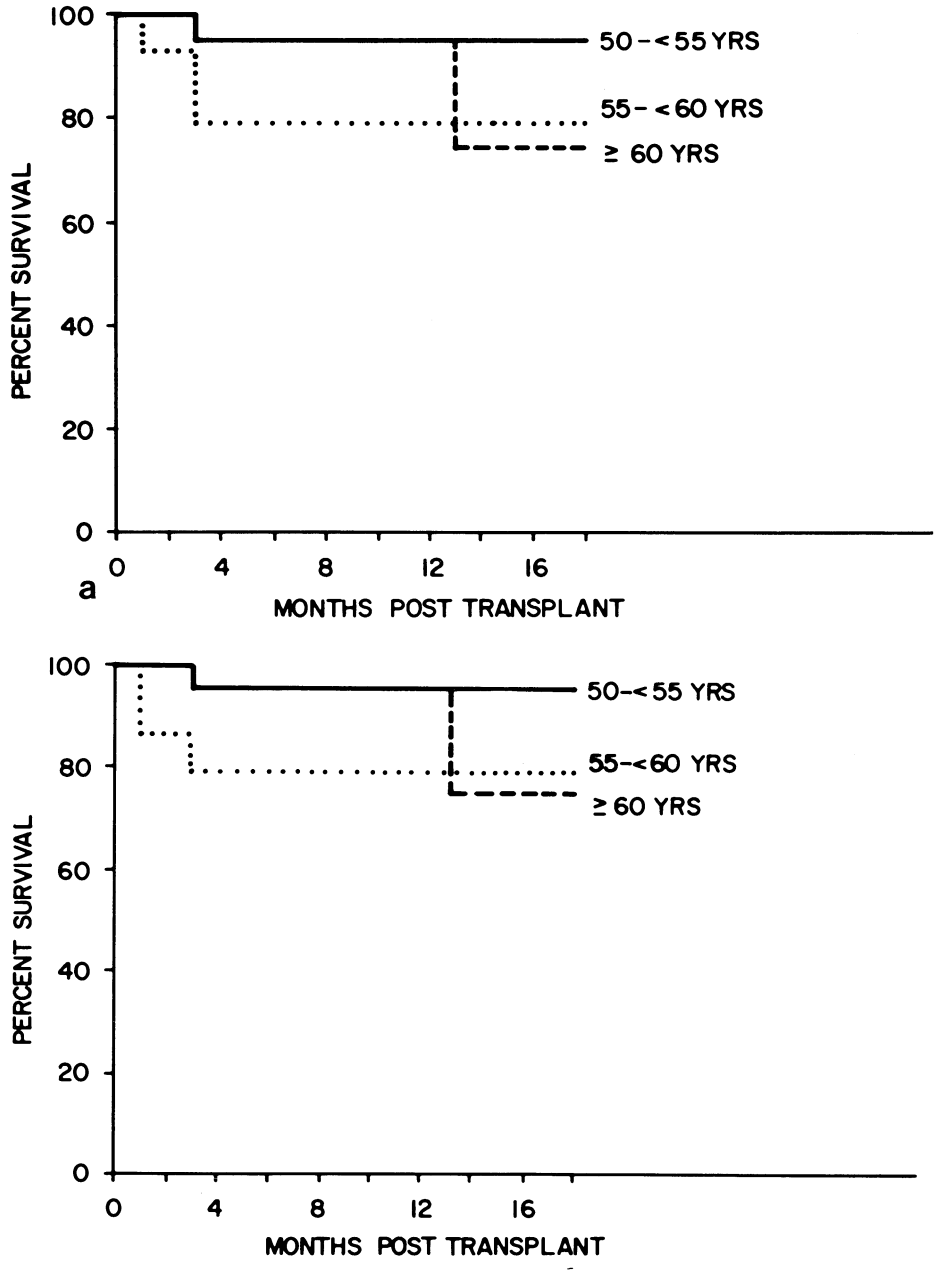


Figure 4: Patient survival (A) and allograft survival (B) according to age group for 52 cadaveric renal recipients 50 years or older treated with cyclosporine at The Ohio State University between March 1983 and March 1985.

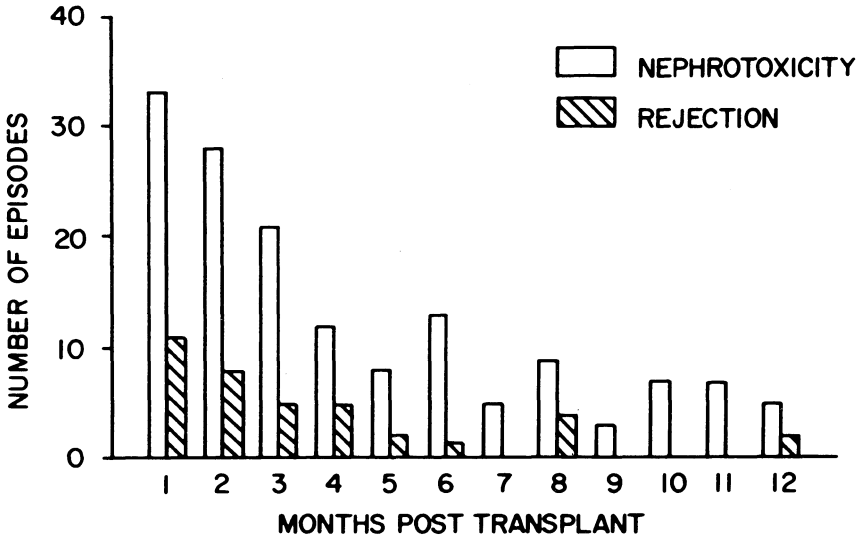


Figure 5: Monthly relationship and number of nephrotoxic and rejection episodes in 52 elderly cadaveric renal-transplant recipients treated with cyclosporine.

resulted from septic complications and five from cardiovascular causes. Even though recipient mortality is relatively low in this series, recipient death remains the most frequent cause of graft loss. Table V shows the etiology of infectious complications in the elderly recipient treated with maintenance azathioprine, and with maintenance cyclosporine. The cyclosporine group had a lower incidence of infectious complications than the azathioprine group. However, zoster infections and urinary tract infections seem to be more common in the cyclosporine group.

Hypertension is reported to be common in allograft recipients receiving cyclosporine maintenance, and this side effect may lead to an increased incidence of cardiovascular complications in elderly recipients. Table VI lists the mean blood pressures of cadaveric renal recipients treated with cyclosporine. Twenty-two per cent of recipients are normotensive without antihypertensive therapy, and 45% of allograft recipients require a diuretic alone or a diuretic plus a beta-blocker. More aggressive therapy was needed in 33% of the recipients to maintain normal blood pressure control. Although the incidence of hypertension following transplantation with cyclosporine is higher than that found with conventional therapy, the hypertension has been easily manageable and cyclsoporine has not produced an increase in cardiovascular deaths.

Table V. Etiology of infections in elderly renal transplant recipients according to immunotherapy

	VIRAL			BACTERIAL			FUNGAL		TOTAL
HVZ	HSV	EBV	CMV	E.COLI	STAPH	PSEUDO	CANDIDA	HISTO	
Azathioprine n=12	1		1		1		1	1	5
Cyclosporine n=59	1	3		3	2	1	1		11

LEGEND

HVZ – Zooster
HVS – Simplex
EBC – Ebstein Barr
CMV – Cytomegalovirus
STAPH – Staphlococcus
PSEUDO – Pseudomonas
HISTO – Histoplasmois

Table VI. Blood pressure following cadaveric renal transplantation with cyclosporine

Group	*Percent*	*Mean + S.D.* *Systolic*	*Diastolic*	*Treatment*
I	22%	151 ± 12	82 ± 9	None
II	12%	144 ± 12	84 ± 6	Diuretic
III	33%	146 ± 16	78 + 7	Diuretic ± Beta Blocker
IV	33%	152 ± 19	81 ± 10	Other

DISCUSSION

Although renal transplantation was initially withheld from the elderly because of associated high risks, over the past 10 years patient survival and, recently, allograft survival have improved dramatically. During the past decade, the number of patients over 50 maintained on hemodialysis has steadily increased, and by 1983, 56% of all dialysis patients in the United States were 50 years of age or older (1). This increase of older uremics has led to a reassessment of transplantation as a therapeutic alternative. The high risk of renal transplantation for the elderly was decreased initially by use of living related-donors (1,2). However, recipients in this age group usually do not have potential related donors, leaving them to await cadaveric grafts. Recently, with the advent of cyclosporine for maintenance immunosuppression and rejection prophylaxis, the high incidence of cardiovascular and septic complications associated with conventional immunosuppression has decreased and allograft longevity has

increased significantly. Patient and allograft survival for the elderly recipient now is almost equal to that achieved with younger recipients. However, sepsis and cardiovascular complications after renal transplantation remain an important, though small, cause of death in the elderly recipient. As we identify greater numbers of older patients with renal failure, vigorous efforts will be needed to fully rehabilitate these patients. The recent success of transplantation in this area is due in part to an awareness that the older recipient requires less aggressive immunosuppression and, most importantly, the widespread use of cyclosporine for maintenance immunotherapy. Currently the elderly patient with end-stage renal disease can undergo safe and effective transplantation using cyclosporine; mortality and morbidity now are notably less than previously reported with conventional immunosuppression (4-12). In view of these results, the elderly patient's choice whether to undergo transplantation or to remain on dialysis should be based on the chance for ultimate rehabilitation and the effect of treatment on his family and social responsibilities. The elderly uremic should not be excluded from renal transplantation, because their prognosis following transplantation equals that of the elderly uremic restricted to hemodialysis. In addition, the potential for total rehabilitation following successful transplantation exceeds that achieved with hemodialysis.

REFERENCES

1. Krakauer H, Grauman JS, McMullan MR, et al. 1983. The recent U.S. experience in the treatment of end-stage renal disease by dialysis and transplantation. N Engl J Med 308:1558-1563.
2. Simmons RL, Kjellstrand CM, Buselmeier TJ, et al. 1971. Renal Transplantation in high risk patients. Arch Surg 103:290-298.
3. Cutler SJ, Ederer F. 1958. Maximum utilization of the life table method in analyzing survial. J Chronic Dis 8:699-712.
4. Delmonico FL, Cosimi AB, Russel PS. 1975. Renal transplantation in the older age group. Arch Surg 110:1107-1109.
5. Kjellstrand CM, Shideman JR, Lynch RE, et al. 1976. Kidney transplants in patients over 50. Geriatrics 31:65-73.
6. Golper TA, Barry JM, Bennet WM, et al. 1978. Primary cadaver kidney transplantation in older patients: Survival equal to dialysis. Trans Amer Soc Artif Intern Organs 24:282-287.
7. Wedel N, Brynger H, Blohme L. 1980. Kidney transplantation in patients 60 years and older. Scand J Urol Nephrol (Suppl) 54:106.
8. Kock B, Kuhlbach B, Ahonen J, et al. 1980. Kidney transplantation in patients over 60 years of age. Scand J Urol Nephrol (Suppl) 54:103.

9. Standards Committee of the American Society of Transplant Surgeons. 1981. Current results and expectations of renal transplantation. JAMA 246:1330-1331.
10. Sommer BG, Ferguson RM, Davin TD, et al. 1981. Renal transplantation in patients over 50 years of age. Transplant Proc 13:33-35.
11. Okiye SE, Engen DE, Sterioff S, et al. 1983. Primary renal transplantation in patients 50 years of age and older. Transplant Proc 15:1046-1052.
12. Taube DH, Winder EA, Ogg CS, et al. 1983. Successful treatment of middle aged and elderly patients with end stage renal disease. Br Med J 286:2018-2020.
13. Ringden O, Ost L, Klintmalm G, et al. 1983. Improved outcome in renal transplant recipients above 55 years of age treated with cyclosporine and low doses of steroids. Transplant Proc (Suppl) 15:2507-2512.
14. McGeown MG, Douglas JF, Brown WA, et al. 1980. Advantages of low dose steroids from the day after renal transplantation. Transplantation 29:287-289.
15. Mallinson WJ, Fleming SJ, Shaw JEH, et al. 1984. Survival in elderly patients presenting with uraemia. Quart J Med 210:301- 307.
16. Mandelbaum DM, Henry ML, Sommer BG, et al. Renal transplantation in patients over 50 years of age. Amer J Surg (In Press).

18. RENAL TRANSPLANTATION IN THE ELDERLY: THE CANADIAN EXPERIENCE

CARL J. CARDELLA, M.D., F.R.C.P. (C)

SUMMARY

The Canadian experience with transplantation in the elderly is limited to two Canadian reports both of which indicate that this can be a successful and relatively safe therapy for ESRD in the elderly. The first, from the Canadian Renal Failure Registry, reported that 27 patients over 60 years of age have been transplanted; 21 of these have functioning grafts and have been followed for 10+8 months after transplantation. The second report, also favourable, came from a Canadian centre that transplanted 36 patients who were 60 years of age or older at the time of operation. The one, two and three-year actuarial graft survival in younger patients (less than 60 years of age) was 73%, 64% and 60% respectively. The one, two and three year actuarial graft survival in older patients (greater than or equal to 60 years) was 72%, 61% and 55% - similar to that in younger patients. Patient mortality rates in younger and older patients were not significantly different. Older patients appeared to have a lower incidence of rejection and a higher infection rate.

In spite of these two reports, the transplantation rate in 1983 in Canada for new uremic patients, 65 years of age or older, was only 0.6%, compared to 6.0% for new patients who were 45-64 years of age, and 19.7% for new patients who were 15-44 years at the time of presentation ($p < 0.0001$). Canadian nephrologists appear to favor dialysis, especially CAPD, for end stage renal disease in the elderly.

The indications for renal transplantation have broadened over the last several years. The morbidity and mortality associated with such transplantation have decreased because of the successful control of rejection using less toxic antirejection drugs and improved management of medical problems before and after transplantation (1). As a result more patients and in particular, more of the elderly, are being considered for transplantation. This report discusses the safety, efficacy and role of transplantation in the management of elderly patients with end stage renal disease in Canada.

Table I: *Comparison of transplant rates in various age groups (1983)*
*age (years)

	15-44	*45-64*	*65+*
Not transplanted in 1983	380	470	310
Transplanted in 1983 (%)**	*93 (19.7%)*	*32 (6.4%)*	*2(0.6%)*
Total new patients 1983	473	502	312

*Age at presentation
**Age *versus* no. transplanted $P < 0.0001$
Data extracted from reference (2).

In Canada in 1983, 1,313 new patients started treatment for end-stage renal failure (2). Of these, 814 (62%) were 45 years of age or older; 502 (38.2%) were between 45 and 64 years of age, and 312 (23.8%) were 65 years or older at the start of treatment. Over the years 1981, 1982 and 1983, the percentage of new patients 65 years of age or older entering renal failure programs in Canada has remained at approximately 25% of the total but the percentage of elderly patients on dialysis is considerably higher. In one metropolitan Canadian centre, the percentage of elderly patients on dialysis is 46% (3). This increase in the proportion on dialysis compared to the percentage entering renal failure treatment programs suggests that Canadian nephrologists favor dialysis over transplantation as optimal therapy for the elderly.

The bias towards dialysis and against transplantation is evident from the statistics concerning the management of uremic patients entering treatment in 1983. The transplantation rate was significantly higher in younger than in older patients (Table I). In 1983, approximately 20% of new patients between 15 to 44 received a transplant whereas only 6% of those 45 to 64 years and only 0.6% of those over 65 years were transplanted in that year. Furthermore, of the two forms of dialysis, Canadian nephrologists appear to favor peritoneal over hemodialysis for the elderly but the reverse is true for younger patients (2). In 1983, over 275 patients between 15 to 44 were placed on hemodialysis but only 160 in this age group were placed on peritoneal dialysis. In the 45-64 age group, 300 were placed on hemodialysis compared to 200 on peritoneal dialysis. For patients 65 years or over, however, approximately 160 were placed on peritoneal dialysis compared to 140 on hemodialysis. CAPD appears to be the most popular form of peritoneal dialysis for the elderly (3). In summary, for the elderly uremic, Canadian nephrologists appear to favor dialysis (especially CAPD) rather than transplantation.

We have no explanation of this attitude towards dialysis and transplantation in the elderly. Elderly patients may prefer dialysis and not wish to proceed with

transplantation. Physicians may feel kidneys are a scarce resource and should not be given to the elderly. Nephrologists may favor dialysis for the elderly perhaps because of the perceived high risks involved with transplantation in them.

The evidence that the elderly do poorly after transplantation is controversial and difficult to interpret. Should we compare results of transplantation in the elderly to those of dialysis or to the results of transplantation in younger patients? Several studies have concluded that transplantation should be offered to the elderly even though the risks may be higher than those in younger patients (4-8). Others suggest that there is no increased risk in the transplanted elderly patient and that a living related transplant is the optimal therapy for elderly patients with renal failure.

Canadian experience is limited with renal transplantation in the elderly. In 1983, according to the Canadian Renal Failure Registry only 34 patients 45 years or older received a renal allograft and only two of these were 65 years or older (2). Outcome of transplantation in this cohort of patients is unknown. Two reports - that from the Canadian Renal Failure Reigistry (12) and from an urban Canadian centre (13) - suggest that transplantation is a safe and effective in elderly Canadians with end stage renal failure. As of November 1984, 27 patients 60 years or older had received a transplant and were registered with the Canadian Renal Failure Registry (12). Of these, 21 are alive with a functioning graft and have been followed for a mean of 10 + 8 months. Four patients died and two had a failed transplant; the causes of these complications is unknown.

Cardella and colleagues recently reported (13) the largest Canadian experience with renal transplantation in patients over 60 years of age. They compared results of transplantation in 36 patients 60 years of age or older to that in 371 persons less than 60 years of age. All patients were transplanted in one centre; had similar immunosuppressive protocols (azathioprine and prednisone), and were cared for by the same surgical and medical teams. In the older group, only one of 36 received a graft from a living related donor, compared to 60 in the younger group. Thus this report was able to compare and assess only the results of cadaveric transplantation in the elderly.

The effect of cadaveric transplantation on overall patient survival was similar in younger and older patients but the authors found important differences. In the older patients, the one, two and three year patient survival rate was 80%, 71% and 65% respectively compared to 86%, 82% and 78% in the younger patients (p = N.S.). At one year older patients showed a 6% increase in mortality compared to younger patients; by three years this had increased further to 13%. Although these differences were not statistically significant, the small number of patients in the study may have concealed the clinical significance. Of the seven deaths in older patients, four were related to infection and none of the seven were being treated for rejection when they died. This observation suggests that these deaths were related to baseline immunosuppressive therapy and not to overtreatment of rejection. It is likely, but not yet proven, that a reduction in

baseline immunosuppression would reduce mortality in older patients (14).

Similar in the two groups were graft survival, the effect of blood transfusions, a primary or secondary graft, HLA matching and cytotoxic antibody levels on graft survival. The one, two and three year graft survival in primary, transfused cadaveric older recipients was 72%, 61% and 55% respectively; these survivals were similar to those obtained in younger patients - 73%, 64% and 60% respectively. In older patients, 24% of grafts were lost to early rejection, compared to 15% in younger patients. The rejection rate was not statistically significantly different but the lower rate in older patients and their apparent susceptibility to infection suggests that the elderly need less immunotherapy.

No criteria have yet been established to determine the suitability of older patients for transplantation. In the Canadian experience (14), as in the other studies (5, 10), a large number of patients had pre-existing heart disease. Unquestionably a selection bias is operating which chooses some older patients for transplantation but not others. The presence of pre-existing cardiovascular disease probably is not a contraindication to transplantation but other factors, such as exercise status, mobility, desire for a change in life style and biological fitness may have been applied to select patients for transplantation; however, these are difficult to quantitate and most of the reports do not give this information. More data is needed to establish the criteria clinicians apply to decide the suitability of older patients for transplantation.

In summary, the Canadian experience has been favorable with renal transplantation in the elderly. Cadaveric donors are suitable and azathioprine and prednisone are effective for baseline immunosuppression. Overall patient and graft survival results in older patients are similar to that in younger but the causes of morbidity and mortality may differ. Fatal infections seem to develop in the absence of excessive immunotherapy, and rejection rates may be lower in the older patients suggesting that we may need immunotherapy protocols specific to the elderly in order to reduce mortality. The selection criteria for renal transplantation in the elderly remain to be established but the presence of pre-existing stable cardiovascular complications do not appear to be a contraindication.

REFERENCES

1. NL Tilney, TB Strom, GC Vineyard, JP Merrill. Factors contributing to the declining mortality rate in renal transplantation. N Engl J Med 1978;299:1321-1325.
2. Canadian Renal Failure Register, 1983 Report. Published by the Kidney Foundation of Canada, December 1984.
3. DG Oreopoulos. Editorial, Geriatric Nephrology. Perit Dial Bull 1984;4(4):197.
4. WN Ghantous, GL Bailey, D Zschaeck, et al. Long-term hemodialysis in the elderly. Trans Am Soc Artif Int Organs 1971;17:125.
5. R Tersigni, CM Kjellstrand, RL Simmons, JS Najarian. Renal transplantation in high risk patients older than sixty years. Am J Surg 1976;131:648-652.

6. N Wedel, H Brynger, I Blohme. Kidney transplantation in patients 60 years and older. Scand J Urol Nephr (Suppl) 1980;54:106-108.
7. L Ost, CG Groth, B Lindholm, G Lundgren, G Magnusson, A Tillegard. Cadaveric renal transplantation in patients of 60 years and above. Transplantation 1980;30(5):339-340.
8. BG Sommer, RM Ferguson, TD Davin, CM Kjellstrand, DS Fryd, RL Simmons, JS Najarian. Renal transplantation in patients over 50 years of age. Transplant Proc 1981;13(1):33-35.
9. FL Delmonico, AB Cosimi, PS Russell. Renal transplantation in the older age group. Arch Surg 1976;110:1107-1109.
10. CM Kjellstrand, JR Shideman, RE Lynch, TJ Buselmeier, RL Simmons, JS Najarian. Kidney transplants in patients over 50. Geriatrics 1976:65-73.
11. B Kock, B Kuhlback, J Ahonen, O Lindfors, BL Lindstrom. Kidney transplantation in patients over 60 years of age. Scand J Urol Nephr (Suppl) 1980;54:103-105.
12. GA Posen. Personal communication. 1984.
13. CJ Cardella, DG Oreopoulos, PR Uldall, GA deVeber, RJD Honey, GA Cook. Renal transplantation in patients 60 years of age or older. Manuscript submitted for publication 1985.
14. G Lundgren, I Fehrman, R Gunnarsson, B Lindholm, A Tillegard, L Ost, CG Groth. Cadaveric renal transplantation in patients over 55 years of age with special emphasis on immunosuppressive therapy. Transplant Proc 1982;14(3):601-604.

19. NURSING ASPECTS OF THE ELDERLY PATIENT ON DIALYSIS

SHARRON IZATT, R.N.

INTRODUCTION

The elderly patient on dialysis requires more nursing care than those tasks assigned by the dialysis procedure; he needs more than the obvious physical care. The dialysis nurse needs to be aware of the aging process and the psysiological changes which come with advancing years and how the dialysis procedure and the response to it differs from that in the younger patient. Beyond the physical needs of the elderly dialysis patient, lie the complex emotional and psychosocial demands of complete care. It is a privilege to care for the elderly. We can learn much from them. We must be willing to give of ourselves and be prepared to learn.

THE NURSE CAN MAKE A DIFFERENCE

The logo chosen for this conference showed an elderly patient, who obviously is in need of care. He is in a wheelchair, he is supporting his head on his hand. He looks tired and discouraged. The shadowy kidneys indicate renal failure.

The caregiver pictured there is the nurse. Her hand on his shoulder conveys an image of caring at an interpersonal level, which transcends words and offers constant reassurance, encouragement and a sense that 'You are not alone'. She sees in her patient understandable fears and concerns for the present - today's dialysis treatment and upcoming tests - and the anticipation of trouble in the future, whether to sell the house and move in with 'the kids' *or* go into a nursing home. She recognizes that he is coming to terms with certain losses - beyond his loss of renal function. Despite these things, she senses his determination to carry on, to adapt, to continue. In some way she wants to help him through this transition.

In this paper I hope to show you *how* the nurse can make a difference.

SENESCENCE - THE BIOLOGIST'S DEFINITION OF AGING

The biologist in his definition of aging describes it as a 'deteriorative' process. In its study we seek to measure a decrease in viability and an increase in vulnerability. Senescence shows itself as an increasing probability of death with increasing chronological age. Sooner or later we must all face the progressive loss of our energies and our ability to resist disease. Eventually, no matter how well we look after ourselves, this loss will progress to the point where we *will* die. It is decidedly unpleasant to discover that we must decline in this way - that even if we escape wars, accidents and diseases still we will die.

AGING AND DEATH

This grim note is essential because thát, important as physical care is, our elderly patients need emotional care. In rendering this care, the nurse *must* be aware of his/her own feelings about aging and death. In nursing the elderly, the nurse must recognize and become comfortable with the imminence of death. In fact, as Robert Atchley points out in his book 'The Social Forces in Later Life' - the very appearance of the elderly reminds us of death - skeleton-like, wrinkled skin, gray hair - ßandß it is their own fear of death which causes some health care workers to shrink from involvement with the aged.

THE WILL TO SURVIVE

The elderly patient with ESRD and beginning chronic dialysis does not have as good a prognosis as his/her younger counterpart. He will likely NOT be on dialysis for 10 years but we face the challenge of how to best care for him for the one, two or three years he has left. The nurse must be aware of the patient's physical vulnerability and of the energy he will need to continue with life. However, the will to survive - at any age - is incredibly strong. One of our patients was 89 when she started dialysis. She had been a professor of art at the university. Suffering from severe osteoarthritis and chronic bronchitis, she travelled back and forth to her dialysis from her home, where she lived alone, by way of ambulance. She had been on dialysis for 3 1/2 years and with every birthday celebration, we grew to love her more and more. When complications increased and she could continue no more, she left us. She will be remembered for a long time as a fighter - and a friend.

PHYSIOLOGICAL CONSIDERATIONS

Nurses must be mindful of important physiological considerations when dialysing the elderly. In addition to renal disease and dialysis, they may have the physical limitations associated with the normal aging, such as cardiovascular disease, degenerative joint disease and visual and hearing loss.
Here are some points to remember:

The older ESRD patient, like most renal patients, will present with lower hematocrit levels - a handicap that will be aggravated by diminished cardiac reserve. Also, the aged ESRD patient responds suddenly and profoundly to cardiovascular changes, for example while on dialysis, he may have frequent hypotensive episodes sometimes with no prior signs. The elderly tend to have precarious fluid reserves and frequently will slip into congestive heart failure.

For these reasons, careful predialysis assessment is essential; this is a nursing responsibility because the nurse is present at the commencement of dialysis. Close monitoring and accurate observations are as essential as carrying out the doctor's orders to transfuse, dialyse with hypotonic solution, hold antihypertensives and so on.

NUTRITION

Assessment of nutritional status is an important nursing function because the nurse knows better than anyone else how well or how poorly a patient is eating and perhaps *why*. Maintaining adequate nutrition can be difficult in the elderly. However, in the presence of renal failure, it is vital to achieve a satisfactory nutritional status. The elderly's appetite and eating habits often may be impaired by physical changes directly associated with the act of eating, such as tooth loss, decreased saliva secretion and impaired taste and smell. One-half of all Americans will have lost their teeth by age 65 and this increases to two-thirds by the age of 75. Tooth loss often leads to dentures, which in some patients may suppress appetite, because they cannot chew in the usual manner. The elderly tend to avoid foods which are difficult to chew and swallow. Loss of acuity of taste and smell which is common in the elderly, decrease the pleasure of eating.

The aging process may be accompanied by marked atrophy of the tongue which lessens the ability to distinguish sweet and salty foods. Thus it is common for the aged to complain that food tastes bitter or sour. A reduction in the number of taste and olfactory nerve endings encourages them to add more sugar, salt or spices to compensate for the loss of taste.

We should view the nutritional requirements of the elderly from their own psychosocial context. Anxiety, depression, dependence on others, loss of spouse and lowered income - all affect eating habits. The elderly are more prone to depression because of the many social and psychological changes they face. They

may become depressed because they are no longer able to do the things they used to do. Depression diminishes appetite. Eating becomes a chore. Lack of food choice makes eating tiresome and thus contributes to poor intake. Also, a shrinking income may force them to choose inexpensive foods that may have a low nutritional value. Food intake may also reflect the older person's preferences and culture; many have developed strong likes and dislikes over the years and they associate certain foods with 'remedies'.

Dietitians and nurses are practical people and much of good nutrition is simple and practical. First, dietary changes should be made gradually and should be tailored to the individual. It's possible to arrange counselling, which, if it involves family members, is most helpful. Each nurse must become familiar with dietary restrictions. Because the nurse is readily available, the patient often directs his questions to her. Her knowledge of foods that ARE and are NOT allowed, helps to convince him that diet is an important part of his management.

Patients coming for centre dialysis should be informed that they can bring some of their most cherished but hitherto forbidden food and eat it while on dialysis. Remembering to give patients permission for such 'treats' can mean a great deal to the patient and to the family.

It should be remembered that the elderly often enjoy breakfast more than any other meal of the day. The foods served then usually are easy-to-chew and this may explain the greater food intake at that meal. Easy-to-chew protein foods such as eggs and cheese should be encouraged at breakfast. The patient should not be forced to eat only certain foods over and over again; variety helps to ensure an adequate intake of the essential nutrients and it prevents boredom and the appetite loss often associated with it.

It should be explained to the patient or family-member, who will be doing the cooking, that the appearance and smell of food are important because they stimulate salivation and the secretion of gastric juices, thus preparing the stomach to receive the food. Foods that taste *good* increase salivation - *unpleasant* foods suppress it. Many elderly patients cannot afford or tolerate high biological proteins. Then a dietary protein supplement can be recommended to avoid the muscle-wasting which accompanies a negative nitrogen balance. With respect to medications, it should be remembered that day-time drowsiness may interfere with adequate intake.

CONSTIPATION

Intake is important, but output is equally important and if constipation concerns the patient, it should also concern the nurse. Constipation often is a major concern because of diminished peristalsis in the elderly and the need for phosphate binders and limited dietary bulk in the diet.

The nurse needs to recognize this as a legitimate problem and know that

chronic constipation can lead to obstruction. She will find it necessary to work with the patient - documenting the frequency and regularity and nature of his bowel movements. Usually, bowel softeners, such as colace or metamucil are a must. Laxatives such as lactulose often are required. Dosages need to be adjusted and re-adjusted to suit each individual. Patients are warned to avoid favourite over-the-counter laxatives such as chocolate Ex-Lax or magnesium-containing preparations.

Before dialysis begins, patients coming for centre dialysis should be assessed for prolonged constipation. At the Western, the patient receives a soap suds enema if he has been constipated for more than four days or if he is complaining. Usually we avoid fleet enemas because of their phosphorus composition and because they do not get high enough into the bowel and usually return as clear fluid.

Patients on peritoneal dialysis especially need to avoid constipation, because it may impair dialysis outflow.

Patients on PD can be dialysed with magnesium free Dianeal solution and may use Maalox (instead of Amphogel) as a phosphate binder, and take Mognalax as a prn laxative. This has proved most effective.

POOR VISION

The function of the lens and iris decline with increasing age, and vision on the whole gets poorer. Most common is the loss of ability to focus on nearby objects, which hampers the ability to read. With advanced years, it becomes difficult to distinguish between levels of brightness and color vision often is affected. About 25% of people over the age of 70 have cataracts. If home dialysis is being considered, the older patient should have an eye test before the training begins. Also, large-print instructions may be most helpful.

Whether or not the elderly patient is a home dialysis candidate reading is a popular pastime. The nurse can talk to the patient and his/her relatives and emphasize the importance of good lighting for the visually-impaired patient. Low-vision clinics have many aids for such patients.

The patient who has recently lost or is losing vision undergoes a grieving process, which must be acknowledged. The nurse can do much to help the partner and the patient come to terms with this loss. The adjustment takes time and much patience, because it is both frustrating and depressing for the patient. All available support groups should be used to help the patient maintain his independence.

HEARING LOSS

About 13% of the older population have severe hearing loss. Gradually, as people get older, they lose their ability to hear certain frequencies and to discriminate among adjacent frequencies. This type of hearing loss is considerable for high-pitched sounds. When speaking to the older patient, one should speak clearly and deliberately and lower the voice pitch. A decline of either sight or hearing can be partly compensated for by using the other sense but when both decline simultaneously the older patient faces a major adaptation to his environment. Those who deal one-to-one with such people must take these new limitations into account in order to help them make maximum use of their capabilities.

One unfortunate patient of ours was blind, had impaired hearing, was diabetic, and a bilateral amputee. She had been on IPD for two years. Fitted with a hearing aid, she could hear again and smiled in wonder the first time she used it. This patient was cared for by a devoted daughter who worked hard to keep her mother orientated to her surroundings and interested in life.

THE ELDERLY PATIENT AS A LEARNER

The nurse views her elderly patient as a learner. Nesselbroade and group have demonstrated that intelligence is made up of several dimensions - some do not change with age, some improve and some decline. Most older people can learn effectively. Memory does decline with age. The chief defect appears to lie in the retrieval function. Also, aging seems to reduce ability to categorize and to make logical inferences. Motives guide and direct action toward specific goals. There is some indication that, as people grow older, they become less motivated toward growth and expansion goals and more motivated toward reducing anxiety and perceived threat. However, even in older people, motives can be changed.

In our home dialysis unit, we have found that older people may take a little longer to learn the technique and absorb the information. They should not feel pressured or rushed, and you may need to repeat yourself more than with the younger learner. They should be encouraged to get involved in planning the rate of learning so that the lessons are long enough to challenge him without being frustrating. To continue instructions after mental fatigue has set in invites confusion, which is reflected in excessive talking or frequent changes in the subject. It should be reinforced to the patient that mastering the procedures is what counts, not how long it takes.

Because of physiological aging, the older adult may have a moderately lowered sense of pride and dignity. He feels less able to master his environment and now can make less impact on his surroundings. With chronic renal failure and the growing awareness that dialysis is permanent, depression may deepen.

Family counselling and the support of a specialized dialysis social worker and the nurse is vital. Now all need a positive attitude. The elderly patient entering the home dialysis program needs a lot of reassurance that he is NOT too old, that he CAN do it. The older person who has spent much of his life trying not to make mistakes, may over-react to errors that are just part of mastering new techniques. The nurse-teacher must plan so to minimize error, build confidence and provide a sense of security and mastery. As practice continues, errors decrease and the patient feels the satisfaction which comes from the learning process itself.

TERMINATION OF DIALYSIS

Sometimes at the patient's request and, occasionally, at the doctor's suggestion, the decision is made to terminate dialysis. Usually this comes after a long trial on dialysis, when the patient seems to be deteriorating and complications are making life unbearable.

This is a difficult and emotional time for the nurses especially if they have come to regard this patient as a family member. Difficult as it is, however the nurse plays an important role in this critical decision because of her intimate relationship with the patient. The patient may have confided his wishes to the nurse and she has a responsibility to speak on his behalf.

It is important that nurses make a record of remarks which patients make concerning their future, for example - 'If I am ever mentally incompetent, I would not want to continue with dialysis.' They may make this as a categorical statement when they observe a fellow patient who is demented, incontinent, and whose family is suffering.

On occasions such as this, when the patient is suffering and the team feels there is no hope, dialysis may be discontinued. At this point, the family members particularly will need our sympathy and support.

WHAT 'CARE' MEANS

The elderly need our care. Basically care means 'to grieve, to experience sorrow, to cry out with'. When you consider which person in your life means the most to you, you find that it is the one who, instead of giving advice, solutions or cures - chooses rather to share your pain and touch your wounds with a tender hand. The friend who can be silent in a moment of despair or confusion, who stays with us in an hour of grief and bereavement, who can tolerate the frustration of 'not-knowing, not-curing, not-healing' and face the reality of our powerlessness, *that* is the friend who cares. Learning to care, to be present, to listen - that is what nurses most need to do for their elderly patients. With all our technical knowledge and expertise, our patients sometimes need *us* most, not *what* we do.

Our tendency is to run away from the painful realities *or* to try to change them as quickly as possible. However, cure without care makes us preoccupied with quick changes, impatient and unwilling to share each other's burdens.

Since we are all at some stage in the aging process, we would do well to remember that some day we shall all be at the receiving end - you can count on it. We shall be the ones in need of affirmation, encouragement, a gentle touch of tenderness.

REFERENCES

Atchley RC. The Social Forces in Later Life, Third edition. Wadsworth Publishing Company: Belmont, California;1980.

Canadian Renal Failure Register, 1983 Report. Published by the Kidney Foundation of Canada.

Lesch E. The Geriatric ESRD Patient. A unique problem in patient care. Nephrology Nurse 1982;July-August:42-44.

Marshall VR. Aging in Canada: Social Perspectives. Fitzhenry and Whiteside 1980.

Murray JT. Geriatric Hemodialysis. AANNT 1977;4.

Raab D, Raab N. Nutrition and aging: an overview. The Canadian Nurse 1985;58:24-26.

Rife M. Open Forum: The Dependent Elderly on Dialysis. Dialysis and Transplantation 1979;8:867-878.

Chronic Care and the Elderly. The Renal Family 1983;Vol. 5.

Roy C., Flynn E. Atcherson E. Home Hemodialysis and the Older Patient. AANNT 1980;Vol 7.

20. THE ELDERLY PATIENT ON DIALYSIS--PSYCHOSOCIAL CONSIDERATIONS

STEPHEN A. KLINE, M.D., HOWARD J. BURTON, DR. P.H. AND MUMTAZ AKHTAR, PH.D.

INTRODUCTION

There is an unprecedented increase in the number and proportion of elderly people in all industrial nations. Barring catastrophes such as nuclear war, pandemic infections, or an overheating of our planet, at the beginning of the next century the United States and Canada can expect to have more than 40 million old people.

Currently, the median age in the United States has surpassed 31, with the middle aged and the very old becoming the fastest growing segments of society (1). While the population in the United States grew 4.2% between 1980 and 1984, the age group 75-84 grew by 11.5% and those aged 85 and over increased at a rate of 19.4%. Canadian population projections (2) indicate that the number of people over 65 will increase from 1.7 million in 1971 to approximately 3.3 million in 2001 and 6.2 million in 2031. This represents a projected proportional increase of the elderly in the general population from 8.1% in 1971 to 22% in the year 2031. These demographic changes will continue to aggravate the problems related to health care of the elderly.

While aging *per se* is not a disease, the process of aging often is complicated by one or more diseases which may impair physiologic, cognitive and psychosocial function, especially in those suffering from renal insufficiency. With the aging of the post-war baby boom generation, and with concurrent improvements in medical care extending the typical lifetime, the total number of elderly patients with end-stage renal disease (ESRD) will increase worldwide. If, in addition, the practice of excluding those over 60 from renal transplantation continues and if the total annual death rate of those with chronic renal failure remains at 19%, the number of elderly dialysis patients will increase dramatically. This increase, coupled with extended long-term survival, will force medical practitioners to re-evalute the need for more dialysis centres and the rights of this burgeoning population to open access to all forms of renal replacement therapy.

Physicians and others (3-6) have made impassioned pleas for empirical evidence supporting the discontinuance of age restrictions for those receiving dialysis. In the absence of convincing studies of the quality of life of elderly patients compared to other age groups, we have reviewed our data from a retrospective study on adaptation to home dialysis (7), and extracted data which allows us to compare the psychosocial profile of the elderly to those younger.

Very few articles have been published solely on the rehabilitation of the elderly dialysis patient (8-14). For the most part, the methodologies of these studies suffer from two major problems. First, the elderly are considered to be that group of patients over 50-55 years of age. Secondly, the authors make no methodical investigation of psychosocial adaptation ('quality of life') in this age group except in anecdotal form. Despite these limitations, the findings of these studies are consistent. As a group, the elderly show more acceptance of dialysis as a treatment, and they rehabilitate impressively well. Also, they appear to be more compliant with the treatment regimen. Psychologically, elderly patients often are more able to adapt to chronic dialysis than their younger counterparts. Finally, the frequency of complications seems to be related more to the co-existing extrarenal disease than to age itself.

Gerontological research has advanced two opposite positions with respect to the intellectual and neuropsychological changes of advancing age (15-17). The traditional position is that intelligence decreases with age, and the newer view denies such a relationship. However, neither is absolute. Various intellectual and neuropsychological abilities change at different rates with age. Therefore, in testing the elderly, one must apply reliable, broad-based assessment batteries to measure abilities that are likely to change, and those that are likely to be stable. Wide-ranging assessment tools, whatever their drawbacks, span a variety of abilities and when they are known to be reliable, are to be preferred. Besides, one is more likely to detect subtle changes with these tests than with more crude techniques.

After reviewing the instruments in current use, we found them wanting in the assessment of elderly ESRD patients. Most were designed for use in younger people and do not have normative or standardized data beyond age 60. Those with a clinical focus have the advantage that their administration is less physically taxing but their scope tends to be narrow and they do not define normal behaviour.

MULTIMETHOD ASSESSMENT OF CHRONIC RENAL FAILURE

The primary data sources for this paper are research instruments revised and scaled on the basis of a seven year study of 451 chronically ill renal patients. To assure the appropriateness of the testing tools, cohort specificity was obtained by assessing prospectively all individuals over the age of 17 from 16 renal units

in Ontario (Canada) who commenced a home-dialysis training program between July 1979 and June 1980.

The constructed scales and indices captured several dimensions of quality of life specific to chronic renal failure. Each scale was pre-tested and standardized with data obtained from an independent study on end-stage renal disease (18). From a multi-item test battery, scales were selected to measure the dimensions of psychological functioning, stress, support systems and leisure time activities.

ASSESSING PERSONALITY DYSFUNCTION

The chief measure was the basic personality inventory developed by Hoffmann, Jackson and Skinner (19). This 12-scale, 240-item true/false inventory uses modern principles of test construction for item writing and selection procedures (20,21). These scale constructs are based on a multi-mehtod factor analysis of the Differential Personality Inventory (22), and the Minnesota Multiphasic Personality Inventory. The BPI scales represent relatively independent aspects of traditional dimensions of psychological dysfunction (19). The scale has been shown to have suitable psychometric properties (23-26).

ASSESSING DIALYSIS STRESS

The dialysis stress scale (DSS), which consists of subscales developed to analyze end-stage renal disease and dialysis stress, is comprised of 13 items that were selected on the basis of observed clinical symptoms (27). The respondent indicates whether the event described constitutes a personal concern or worry. The degree of stress caused is recorded on a scale of 0 (no stress) to 5 (high stress). Items reflect fears and concerns generally related to chronic renal failure - being physically weak, fear of death, fear of blood clotting, up and down health, etc., and those more specific to the dialysis procedures - cramps, headaches, pain or discomfort during dialysis, etc. The reliability of the global dialysis scale as measured by Cronbach's alpha is .81 (14).

ASSESSING STRESSFUL LIFE CRISES

Our life event stress scale (LESS) is a modified version of Holmes and Rahe's social readjustment scale (28), which purports to measure stress associated with life crises. The concept of 'stressful life events' implies that the social environment is a complex structured, cultural, interpersonal and psychological system with adaptive and adjustive properties. Life events within this system, whether desirable or undesirable, are conceived of as a life change, which may

induce stress and invariably require readjustment. A prolonged series of changes (life crises) predisposes a person to illness, accidents and injuries (29). Reliability based on separate dialysis populations - CAPD and hemodialysis, is in the range of .70 (14).

ASSESSING STRESSES OF DAILY LIVING

While the life event stress scale detects the stress associated with major life events, the psychosocial stress scale (PSSS) measures the daily stress a dialysis patient could encounter in personal and family life on an ongoing basis. The eight item scale has a range of scores from 0 (no stress) to 6 (high stress). Scale reliability is 0.68 (14).

ASSESSING SOCIAL SUPPORT

Social support is defined as information received by the respondent that he is loved, wanted, respected, valued, and a part of a context he can count on should the need arise. The social support scale (SSS) which is based on the work of Cobb (30) and Kaplan (31), is comprised of seven sets of vignettes from the original 16 developed by Kaplan using a story identification technique. The evidence suggests that social - support mechanisms function as moderators of stress and as independent variables in determining health status (30,31). Scale reliability is .78 with a chronic renal failure population, and ranges from .78 to .83 in nonrenal failure populations (32).

ASSESSING PRIMARY GROUP SUPPORT

Primary groups may include one's family, friends, fellow workers, and neighbours. Primary group support is assessed by a dialysis interpersonal relationship index (DIPI). The index requires the respondent to assess the amount of mutual understanding, perceived support, closeness and level of satisfaction with the relationship. The global index divides itself into four separate subscales each containing four items. The reliability of the scale as measured by Cronbach's alpha is .88 (14).

ASSESSING LEISURE AND RECREATIONAL ACTIVITY

Viewed as a social indicator, social/leisure time activity is an objective measure. As a concept, it is relevant to social norms and is a common measure of the well

being of a society or a population strata within society. Spare time (non work) activities are most strongly related to a global index of well being (33). The social leisure activities inventory (SLAI) reflects the degree to which patients participate in various activities - physical, sedentary, informal and formal, in a typical month. The items represent a cross section of active and passive activities which the patient can engage in alone or with others. Because it is an inventory rather than a scale, reliability co-efficients are inappropriate (14).

PSYCHOSOCIAL ADAPTATION TO CHRONIC RENAL FAILURE

In patients with ESRD, emotional and personality makeup has an effect on both state of health and survival (34,35). Studies of personality traits have found that serious psychological problems interfere with successful adjustment and contribute to self-destructive behavior (36,37). This section will discuss the trait symptoms of depression, anxiety, hypochondriasis, social introversion and denial.

ANXIETY

Anxiety, a frequently observed reaction (38-40), shows high levels in all ESRD patients. As a group, they show significantly higher levels than normal individuals (41). Much of the anxiety is related to fear of dying, fear of peritonitis, psychological stress, financial worries, changes in life style and the physical distance between the patient and the hospital support staff (42).

Sex differences are clearly evident. Women are more likely to be anxious than are men, irrespective of mode of treatment (43). With CAPD, age has little influence on how a patient group experiences anxiety. Anxiety in patients over 65 does not differ significantly from that in those between 45 and 64 and those under 45 (Table I). Patients in the middle years manifest greater anxiety than

Table I: Emotional well being of a CAPD population by age groups

Personality trait	<45 (N = 12)	45-64 (N = 48)	>65 (N = 20)	P
Depression	3.08	5.83	3.60	.01
Denial	6.92	8.58	9.95	.02
Anxiety	5.08	6.85	5.40	NS
Self depreciation	2.25	3.38	2.60	NS
Social introversion	4.67	4.92	4.10	NS
Hypochrondriasis	6.50	7.81	8.05	NS

Table II: Emotional well being of a home dialysis population proportional representation (%) for low scores by age groups

Personality trait	<39 (N = 124)	40-59 (N = 173)	>60 (N = 118)	P
Depression	46	41	53	.09
Anxiety	52	51	64	.09
Hypochondriasis	61	51	51	NS
Social introversion	49	35	58	.006

those older and younger. The young and old patients show marginal differences. In contrast, if we include all modes of home dialysis and divide the sample into high and low depression scores, we find that those over 60 have proportionately lower anxiety levels than those in the 40 to 59 category or those under 40 (Table II).

Despite the minimal differences in expressed anxiety, the renal team should be aware that as a group, the elderly show significantly higher levels of anxiety than individuals in the normal population (41). They will also experience anxiety states with greater frequency than the elderly in the general population. These attacks usually are transient and commonly occur in response to sudden changes in the environment or in health status.

DEPRESSION

Of all the psychiatric syndromes of old age, the most common is depression (44). The incidence and prevalence are highest in those 55 to 70 (45). Depression often is secondary to the stress of physical illness, isolation, and loss of spouse, friends and income. It is among the most frequently observed reactions of dialysis patients (46-48). Particularly during the first three to six months after beginning dialysis, most patients experience intense awareness of and vulnerability to the stresses inherent in their situation (49-52).

We found, as have others, that depression in ESRD patients is significantly deeper than in the general population (52-54). They may experience severe depressive reactions even after they have been stabilized through dialysis (48,55). These reactions often are accompanied by apathy and suicidal ideation and can be sufficiently severe to impede cooperation in self care and adherence to dietary restrictions. Of vital importance to the treatment team, we found that, among all psychosocial and physiological parameters examined, depression distinguishes most clearly those who failed, succeeded, or died while on a home program (56-58).

Most patients show a slight increase in depression after three months home

dialysis - a trend unrelated to treatment choice (43). In CAPD, we found that patients over 65 were significantly less depressed than those in the middle years, and were slightly more depressed than those under 45 (Table I). Among those on home-hemodialysis, depression was proportionately lower in patients over 60 than in those under 40 and those between 40 and 59 (Table II).

In elderly patients with chronic renal failure, the clinical picture of depression is similar to that in elderly individuals in general. Yet, it has many similarities with clinical depression seen earlier in life, particularly in its episodic nature, its tendency to remit and its potential for a favorable outcome (59). The elderly dialysis patient also may manifest an atypical picture of masked depression. Here, the clinical presentation may be one of apathy, withdrawal, somatic complaints and functional slowness (59).

Staff should also be aware that the depression of old age may be complicated by paranoid reactions, which in turn may be associated with an acute confusional state or with a chronic organic brain syndrome. We should make every effort to seek out any underlying causes and to weigh carefully the degree of maladaptation imposed by this distorted ideation.

Like their counterparts in the general population, elderly dialysis patients are less likely than young persons to admit to the symptoms of depression itself. They are more likely to complain of the symptoms of anziety, somatization, hypochondriasis, or to a loss of concentration and memory deficit (60). Counselling, psychotherapy and environmental structuring are usual methods of treatment. Antidepressants may have a role in depressions where the patient is more obtunded clinically or where there is suicidal risk.

HYPOCHONDRIASIS

In the elderly, excessive preoccupation with physical functions may be a sign of depression. Alternatively, it may represent an exaggeration of a normal response to the increase in physical disability and the limitations associated with aging and progressive chronic illness. For the elderly, somatic complaints often are the only acceptable avenue of asking for attention. Unfortunately, for renal team members, frequently it is hard to determine whether somatic complaints are primarily physical, psychological, or a combination (59).

In our assessment of hypochondriacal traits in a CAPD population, we found a tendency for those older to complain more regularly and to be more preoccupied with peculiar pains and bodily dysfunctions. Differences between age groups, however, were not statistically significant (Table I). We obtained similar results from our analysis of combined treatment groups (Table II).

These findings suggest that the hypochondriacal old person appears to be one more unverifiable mythical figure in peoplesideas of aging. Not only is hypochondriasis less common among older people than presumed, but when

elders do complain, they are likely to have important diseases more often than younger nonhypochondriacal individuals (61). Also, it should be kept in mind that the somatic complaints in the elderly which have a psychological basis may be a feature of anxiety or the expression of masked depression.

SOCIAL INTROVERSION

Understandably, those with chronic renal insufficiency often react in a passive and dependent manner (62). They may withdraw from pleasurable interpersonal activities and lose interest in their environment (63,64). Patients have feelings of estrangement, loneliness, guilt, shame and feelings of failure. They experience diminshed financial, occupational, community and social status. They avoid family and friends and feel incapable of participating according to others' expectations (53,65-67).

Surprisingly, we found that the elderly CAPD patient is likely to be more outgoing than younger CAPD patients (Table I). Modalities aside, proportionately fewer home-dialysis patients 60 and over are found among those with high social introversion scores (Table II). This indicates a more socially integrated personality.

Patients handle the crises of social isolation individually. Their manner of coping is a function of previous personality development, the resolution of the normal anxieties of childhood and the meaning that they attach to their illness (68).

DENIAL

Dialysis patients use denial more than any other group of the chronically ill (52). For most, it is their major mechanism of defense (69,70). It assists them in coping with the stresses of dialysis, and helps them to co-operate with the treatment and to carry with them previous life styles (27,53,71,72). Some clinicians believe that denial is a blessing and that no one should attempt to substitute a more realistic attitude (73).

On the other hand, excessive denial may have dangerous consequences for patients, leading among other things to non-compliance or even delusional thinking (38,74,75). It can prevent patients from hearing instructions or information (42) or from recognizing emotional conflicts and difficulties (76). Massive denial disrupts basic reality testing and can lead the patient to view any sort of psychiatric intervention with suspicion, negativity and indifference (50,77).

Denial appears to be employed differently across dialysis age groups but in a consistent way. For instance, in our CAPD population, we found that it

significantly increases with age but has no relationship to gender, mode of dialysis or length of time on a home program (43).

The best hope for achieving successful adjustment and for tolerating the stresses and anxieties of chronic renal failure is the use of denial and other coping strategies. However, the relationship between denial and other coping processes is precarious at best. If denial frees the individual to focus on the problems to be mastered, the relationship is positive. If denial is ineffective or overpowering, anxiety ensues. If denial is massive, dominating the patient's function, it will seriously restrict the ability to concentrate on external or internal threats and to deal with them effectively.

In our clinical experience, there is an intermediate range of defensive strength in the use of denial which allows optimal coping, while extreme deviations on either side have adverse effects. This delicate dilemma seems to have been solved most successfully by the elderly who, as we shall see, experience much less stress than do younger people.

THE IMPACT OF STRESS ON PSYCHOSOCIAL FUNCTION

Renal failure precipitates innumerable stresses. Dietary and liquid restrictions obviate stress outlets such as smoking, drinking of alcohol, or excessive eating (37,53). There are frequent stresses related to cannula care, survival or infection, hemorrhage, clotting and disengagement (39,42). Additionally, stresses associated with erratic physical functioning arouse great emotional tension, disrupt the patterns of daily behavior, and reduce mental efficiency, thus producing painful, unpleasant effects (78).

We have documented elsewhere (4,54,79) the stresses associated with home dialysis and noted the general trend for males to experience less stress than females (43). Our findings support clinical impressions concerning the differentiation and specificity of foci of stress in hemodialysis and CAPD populations (80). We suggest that age is a modifier of stress, especially as it relates to concerns about the chronicity of the illness and treatment related procedures (41).

STRESSORS OF ILLNESS AND TREATMENT

As dialysis patients get older, they experience far less stress associated with the chronic nature of ESRD and its incumbent regimen. This is true irrespective of the length of their illness (79). We found that, in an older CAPD population, patients experienced less dialysis stress - both in the illness itself and the treatment procedures (Table III).

Compared to those younger, they were significantly less concerned by cramps,

Table III: Stress intensity of a CAPD population by age groups

Stress scale	<45 (N = 12)	45-65 (N = 48)	>65 (N = 20)	P
Psychosocial stress	8.92	5.89	3.10	.04
Life event stress	13.58	12.15	13.60	NS
Dialysis stress	17.92	19.95	10.00	.01

pain or discomfort during dialysis, headaches, fear of death, fear of blood clotting, fear of loss of dialysis sites, being physically weak and up and downhealth. In the home dialysis experience, we also found proportionately fewer patients over 60 who experienced high stress with the treatment process and with the consequences of chronic illness. This is in marked contrast to that reported by those younger or in their middle years (Table IV).

STRESSORS OF LIFE CRISES AND DAILY LIVING

The stresses inherent in life crises and daily events reflect the onset, intensity, incidence and prevalence of a wide range of health disorders (81,82). Most studies of health care and human behaviour conceptualize the social system as inducing or reducing stress (83,84). Events within this system, whether desirable or undesirable, invariably require the individual to adjust - a notion which illuminates the common view of stress as a condition of perceived imbalance between environmental demands and the capability of the individual to meet these demands (85).

We sought to determine whether age would be a prime factor in deciding how an individual would cope with life crises. We found major age differences in the coping capabilities of our dialysis patients. At the start of a home training program, the stress associated with life crises in those under 40 is proportionately higher than those 60 and over, or those in their middle years (Table IV). This finding held true after three months of home therapy, even with an overall increase in stress among all patients (43).

Table IV: Stress intensity of a home dialysis populatiion proportional representation (%) for low scores by age groups

Stress scale	<39	40-59	>60	P
Psychosocial stress	37	48	64	.0001
Life event stress	30	45	44	.02
Disease process stress	44	45	59	.02
Treatment regimen stress	46	38	64	.001

During these initial months, stressful life events generally increase, especially with respect to changes in personal, recreational and sleeping habits, living conditions, spouses beginning or stopping work, trouble with in-laws, arguments with spouses, death of a close friend, major financial changes, sexual difficulties, changes in health of other family members and stress related to personal injury or illness. These findings confirm those of others (37,86-89).

Age is a more obvious mitigator of the psychosocial stresses of daily living. The proportional distribution of this stress as seen in different home dialysis groups shows that those younger than 60 reported much more stress than those older. As with major life events, those under 40 experience the most psychosocial stress (Table IV). This same pattern can be found in our CAPD smaple population (Table III).

Thus, our data affirms that the older home dialysis patient handles stress better. Their use of denial may provide them with a more effective means of dealing with stressors. It is equally probable that many of their developmental tasks have been achieved. As a group, they are less likely to be in financial need and to be free of parental and community obligations. Possibly, the elderly are more prone to contemplation, integration and acceptance.

SOCIAL SUPPORT AND THE ELDERLY PATIENT WITH RENAL FAILURE

In explaining the predisposition for elderly home dialysis patients to fare as well as, and sometimes better than, those younger, we cannot disregard the importance of their support systems. Social support satisfies basic needs, buffers stress, prevents disorders of all types and moderates the effects of illness and psychological distress (90-96).

Social support decidedly affects the experience, course and outcome of a renal regimen (97-100). The absence of a support system is detrimental to the patients' well-being while its presence is crucial to long term adjustment (101-103). The question remains, however, whether patterns of support differ in young and old dialysis patients.

When we analyzed age specific groups for perceived social support, differences failed to materialize. Home dialysis patients' perceptions were similar across all age categories (Table V). Their proportions were distributed evenly between those with perceptions of low support and high support. A previous analysis of 90 individuals over 65 showed that social support contributed positively to emotional well-being (104). Levels of depression, anxiety, self-depreciation and social introversion were reduced. Social support not only mediated the annoying concerns of daily living but also the stresses associated with treatment.

Table V: Perciption of social support of a home dialysis population
Proportional representation (%) by age groups

Support level	<39 (N = 124)	40-59 (N = 173)	>60 (N = 118)	P
Low	42	48	43	NS
High	58	52	47	

PRIMARY GROUP SUPPORT

In times of illness, perceived social support and meaningful social networks are of undeniable importance. Social support from primary group affiliates such as family members, friends, neighbours, or one's work mates provides resources for dealing with both stressful life situations and the emotional disturbances related to them (105). A deficiency in primary group ties is associated with increased vulnerability to disease - both medical and psychiatric (106-108). Personal relationships and community ties also act as a protective buffer against the noxious impact of stress on the individual (106,109). In fact, a cluster of studies show that persons who maintain contact with a least one confidant, even in the face of reduced social contacts with others over time, report more positive mood states, greater life satisfaction and better health status than those without ties (110-113).

Primary group support commonly is assessed by determing the frequency of those who are accessible to provide actual or potential support, the appraisal of satisfaction with support received, and the adequacy of social attachments. With respect to availability, both the middle aged and elderly groups report significantly more spousal support than those under 40 (Table IV). Except for family members at home from whom all age groups receive frequent support,

Table VI: Frequency of primary group support of a home dialysis population
Proportional representation (%) by age groups *

Primary group	<39 (N = 124)	40-59 (N = 173)	>60 (N = 118)	P
Spouse	77	97	97	.0001
Family at home	88	87	91	NS
Family elsewhere	75	68	88	.0002
Friends	64	57	74	.003
Neighbours	17	32	54	.0001

* Proportions include often and very often

Table VII: Satisfaction with primary group support of a home dialysis population * Proportional representation (%) by age group

Primary group	<39 (N = 124)	40-59 (N = 173)	>60 (N = 118)	P
Spouse	86	99	100	.0001
Household member	94	94	100	NS
Family elsewhere	89	91	98	.0001
Friends	83	88	96	.0001
Neighbours	54	63	82	.0001

* Proportions include the combined categories of very and somewhat satisfied.

those 60 and over report significantly more support from family who live outside the household, as well as from friends and neighbours.

Our findings on satisfaction show that, as a rule, everyone on home dialysis is satisfied with the support they receive, expecially from their spouse, family and friends (Table VII). The elderly, however, were the most satisfied. It is interesting that they also saw their neighbours as more available and more supportive. A corollary of satisfaction with support received is the determination of adequacy of social attachments (114). Our previous findings reinforce the premise that, for the elderly dialysis patient, social support is broadly based within family and friendship networks and is an important factor in emotional well-being (104).

SOCIAL-LEISURE TIME ACTIVITIES

Social participation and deployment of leisure time indicates an individual's sense of well-being (115). From our clinical experience, outside interests provide patients with the opportunity to become absorbed in an activity which distracts from their preoccupation with self and with excessive introspection. Patients who keep personal concerns at a distance recharge their emotional and intellectual apparatus to deal more effectively and objectively with their personal problems.

This is easier said than done. We know that dialysis patients and their families who pursue outside interests show better emotional adjustment (116). Yet there is clear evidence that social interaction and recreation are subject to the necessary modifications imposed by the diaysis regimen. Both social interests and recreation are among the greatest threats to a dialysis patient's sense of well-being (117). Hemodialysis with its complex treatment regimen limits life style and restricts extra-familial social activity (70,118). Even the simpler process of CAPD can diminish physical activity (43). Involvement in leisure activities not only is a matter of individual preference but understandably age related. Non-work

Table VIII: Social-leisure activities of a home dialysis population
Proportional representation (%) of low participation * by age groups

Type of activity	<39 (N = 124)	40-59 (N = 173)	>60 (N = 118)	P
Physical	28	44	55	.0001
Sedentary	41	47	53	NS
Social	30	58	58	.0001
Community	49	50	52	NS

* Low participation is less than two times in a typical month

activities of elderly home dialysis patients show significantly less participation in physical and social activities and a trend towards fewer sedentary and community activities (Table VIII).

CONCLUSION

In conclusion, our findings offer a sharp rebuff to those who denigrate the importance of providing the elderly renal patient with the opportunities of dialysis. As a group, they evidence less psychological dysfunction and a greater capacity to handle a variety of important stressors. They utilize social support as well as, and in some instances, better than their younger cohorts. From our perspective, their right to treatment is irrefutable.

ACKNOWLEDGEMENTS

We would like to thank Ms. J. Gastaud for the preparation of this manuscript and Ms. M. Pollack for her insightful research contributions. We also acknowledge grant support by the Ministry of Health of Ontario (DM 338) and by Physicians Services Inc. for the 'Ontario Adaptation to Home Dialysis Study', which provides much of the current knowledge of psychosocial problems in the dialysis field.

REFERENCES

1. U.S. Bureau of the Census. Current Population Reports: Projections of the population of the United States. Washington, D.C.: U.S. Government Printing Office, 1975.
2. Statistics Canada. Population projections for Canada and the provinces 1972-2001. Ottawa: Information Canada, Catalogue 91- 514:119-133, 1974.

3. DePalma JR: Is patient rationing in our future? Dialysis and Transplantation 12:829-830, 1983.
4. Parsons V: The ethical challenges of dialysis and transplantation. The Practitioner 220:871-877, 1978.
5. Caplan AL: The selection of patients for dialytic therapy - Should treatment be left to change? Dialysis and Transplantation 13(3):155-161, 1984.
6. Berlyne GM: Over 50 and uremic = death. Nephron 31:189-190, 1982.
7. Burton JH, Lindsay RM, Canzona L, et al: Adapting to a home dialysis program: The Ontario experience. Ontario Ministry of Health (DM 338):1-30, 1985.
8. Cohen SL, Comty CM, Shapiro FL: The effect of age on the results of regular haemodialysis treatment. Proc Eur Dial Trans Assoc 7:254-260, 1970.
9. Chester AC, Rakowski RA, Argy WP, et al: Hemodialysis in the eighth and ninth decades of life. Archives of Internal Medicine 139:1001-1005, 1979.
10. Taube DH, Winder EA, Ogg CS, et al: Successful treatment of middle aged and elderly patients with end stage renal disease. British Medical Journal 285:2018-2020, 1983.
11. Walker PJ, Ginn HE, Johnson KH, et al: Long-term hemodialysis for patients over 50. Geriatrics 55-61, 1975.
12. Bailey GL, Mocelin AJ, Griffiths HJ, et al: Hemodialysis and renal transplantation in patients of the 50-80 age group. Journal of the American Geriatrics Society 20(9):421-428, 1972.
13. Ghantous WN, Bailey GL, Zschaech CL, et al: Long-term hemodialysis in the elderly. Transactions - American Society for Artificial Internal Organs 17:125-128, 1971.
14. Rowe JW: Renal System. In: Rowe JW, Besdine RW (eds), Health and Disease in Old Age. Little, Brown and Company, Boston:165-183, 1982.
15. Horn JL, Donaldson G: On the myth of intellectual decline in adulthood. American psychologist 31:701-719, 1976.
16. Horn JL, Donaldson G: Faith is not enough: a response to the Baltes-Schaie claim that intelligence does not wane. American Psychologist 31:701-719, 1976.
17. Baltes PB, Schaie KW: On the plasticity of intelligence in adulthood and old age: where horn and Donaldson fail. American psychologist 31:720-725, 1976.
18. Burton HJ, Canzona L, Lindsay RM, et al: Adaptation to home dialysis: a retrospective look. Toronto: Ontario Ministry of Health (DM338), 1980.
19. Hoffman H, Jackson DN, Skinner H: Dimensions of psychopathology among alcoholic patients. Journal of Studies on Alcohol 36:825- 837, 1975.
20. Jackson DN: A sequential system for personality scale development. In: Spielberger C (ed), Clinical and Community Psychology, Vol. 2, Academic Press, New York, 1970.
21. Jackson DN: The dynamics of structured personality tests. Psychological Review 78:229-278, 1971.
22. Jackson DN, Messick S: The differential personality inventory. Authors, London, Canada, 1971.
23. Jackson DN: Orthogonal components of psychopathology: a fresh appraoch to measuring the constructs underlying MMPI clinical scales. Presented at Society of Multivariate Experimental Psychology, Oregon, November, 1975.
24. Kilduff RA: Reliability and faking susceptibility of the Basic Personality Inventory. M.A. Thesis, University of Rhode Island, 1979.
25. Smiley W: Multivariate classification of male and female delinquent personality types. Ph.D. Dissertation, University of Western Ontario, 1976.
26. Holden RR: Item subtelty, face validity and the structured assessment of psychopathology. Ph.D. Dissertation, University of Western Ontario, 1982.
27. Sviland M: Factors of adaptation and rehabilitation in home hemodialysis. Ph.D. Dissertation, University of Southern California, 1971.
28. Holmes TH, Rahe RH: The social readjustment rating scale. Journal of Psychosomatic Research 11:213-128, 1967.
29. Holmes TH, Masuda: Life changes and illness susceptibility. In: Dohrenwend B, Dohrenwend B

(eds), Stressful Life Events: Their Nature and Effects, John Wiley and Sons, New york, 45-72, 1974.
30. Cobb S: Social support as a moderator of life stress. Psychosomatic Medicine 38(5):301-314, 1976.
31. Kaplan RH, Cassel JC, Gore S: Social support and health. Medical Care 5:47-58, 1977.
32. Turner RJ, Frankel BG, Levin D: Social support: conceptualization, measurement and implications for mental health. In: Greenley JR (ed), Research in community and mental health vol. III. Jai Press, Greenwich, 1985.
33. Campbell A, Converse P, Rodgers N: The quality of American life-perceptions, evaluations and satisfactions. Russell Sage Foundation, New York, 1976.
34. Levy NB: Psychological factors affecting long-term survivorship on hemodialysis. Dialysis and Transplantation 8(9):880-881, 1979.
35. Lynch JJ: The broken heart - the medical consequences of loneliness. Basic Books Inc, New York, 1979.
36. Gombos EA, Lee TH, Harton MR, et al: One year's experience with an intermittent dialysis program. Annals of Internal Medicine 61:462-469, 1969.
37. Shea E, Bogdan DF, Freeman, RB, et al: Hemodialysis for chronic renal failure, IV. Annals of Internal Medicine 62:558-563, 1965.
38. Cummings JW: Hemodialysis - feelings, factors, fantasies. The pressure and how patients respond. American Journal of Nursing 70:70-76, 1970.
39. Hampers CL, Schupak E: Long-term hemodialysis. Grune and Stratton, New York, 1967.
40. Eschbach JN, Barnett BMS, Daly S, et al: Hemodialysis in the home: a new approach to the treatment of chronic uremia. Annals of Internal Medicine 67(6):1149-1162, 1967.
41. Linday RM, Oreopoulos D, Burton HJ, et al: Adaptation to home dialysis - a comparison of continuous ambulatory peritoneal dialysis and hemodialysis. In: Legrain M (ed), Continuous ambulatory peritoneal dialysis. Excerpta Medica, Amsterdam, 120- 130, 1980.
42. Brand L, Komorita NJ: Adapting to long-term hemodialysis. American Journal of Nursing 66(8):1178-1181, 1966.
43. Burton HJ: Survival without the machine: a comparison of the psycho-social effectiveness of continuous ambulatory peritoneal dialysis (CAPD) and home hemodialysis. Dr. P.H. Dissertation, University of Pittsburgh, 1981.
44. Salzman C, Shader RI: Depression in the elderly: I. Relationship between depression, psychologic defense mechanisms and physical illness. Journal of the American Geriatrics Society 26:253-302, 1978.
45. Levy S: The psychosocial assessment of the chronicall ill geriatric patient. In: Prokop CK, Bradley LA (eds), medical Psychology: Contributions to Behavioral Medicine. Academic Press, New York, 119-137, 1981.
46. Levy NB: Psychological complications of dialysis. Bulletin of the Menninger Clinic 48(3):237-250, 1984.
47. Levy NB: Coping with maintenance hemodialysis - psychological considerations in the care of patients. In: Massry SG, Sellers AL (eds), Clinical Aspects of Uremia and Hemodialysis. Charles C. Thomas, Springfield, IL. 53-68, 1976.
48. Lefebvre P, Norbert A, Crombez J: Psychological and psychopathological reactions in relation to chronic hemodialysis. Canadian Psychiatric Association Journal 17:55-59, 1972.
49. Abraham HS: The psychiatrist, the treatment of chronic renal failure and the prolongation of life: II. American Journal of Psychiatry 126:157, 1969.
50. DeNour AK: Psychotherapy with patients on chronic haemodialysis. British Journal of Psychiatry 116:207, 1970.
51. Short MJ, Alexander RJ: Psychiatric considerations for center and home hemodialysis. Southern Medical Journal 62:1476, 1969.
52. Reichsman R, Levy NB: Problems in adaptation to maintenance hemodialysis. Archives of Internal Medicine 130:859, 1972.

53. Wright RG, Sand P, Livingston G: Psychological stress during hemodialysis for chronic renal failure. Annals of Internal Medicine 64:611, 1966.
54. Burton HJ, Klatt h, Conley JA, et al: Stresses associated with sexual adjustment of end stage renal disease patients commencing home diaoysis: a comparison between hemodialysis and CAPD. Contemporary Dialysis 2(6):25-28, 1981.
55. Cramond WA, Knight PR, Lawrence JR: The psychiatric contribution to a renal unit undertaking chronic haemodialysis and renal homotransplantation. British journal of Psychiatry 113:1201, 1967.
56. Wai L, Richmond J, Burton HJ, et al: Influence of psychosocial factors on survival of home dialysis patients. Lancet 2:1155, 1981.
57. Richmond JM, Lindsay RM, Burton HJ, et al: Psychological and physiological factors predicting the outcome of home dialysis. Clinical Nephrology 17:109, 1982.
58. Burton JH, Kline SA, Lindsay RM, et al: Relationship of depression to survival in chronic renal failure. Psychosomatic Medicine (accepted 1985).
59. Epstein L: Symposium on age differentiation in depressive illness. Depression in the elderly. Journal of Gerontology 31:278-282, 1976.
60. Liptzin B: psychiatric aspects of aging. In: Rowe JW, Besdine RW (eds), health and Disease in Old Age. Little, Brown and Company, Boston, 85-96, 1982.
61. Stenback A, Kumpulainen M, Vauhkonen ML: Illness and health behavior in septuagenarians. Gerontologist 33:57, 1978.
62. Dansak DK: Secondary gain in long-term hemodialysis patients. American Journal of Psychiatry 129:352, 1972.
63. Menzies IC, Steward WK: Psychiatric observations on patients receiving regular dialysis treatment. British Medical Journal 1:544, 1968.
64. McKegney FP, Lange P: The decision to no longer live on chronic hemodialysis. American Journal of Psychiatry 128:267, 1971.
65. Wittkower E: Psychological aspects of physical illness. Canadian Medical Association Journal 66:220, 1952.
66. Gentry WD, Davis GC: Cross-sectional analysis of psychological adaptation to chronic hemodialysis. Journal of Chronic Diseases 25:545, 1972.
67. Greenberg RP, Davis G, Massey R: The psychological evaluation of patients for a kidney transplant and hemodialysis program. American Journal of Psychiatry 130:274, 1973.
68. Ballak L: Psychology of Physical Illness. Grune and Stratton, New York, 1952.
69. Beard BH: Fear of death and fear of life. Archives of General Psychiatry 21:373, 1969.
70. Freyberger H: Six years' experience as a psychosomaticist in a hemodialysis unit. Psychotherapy and Psychosomatics 22:226, 1973.
71. Short MJ, Wilson WP: Roles of denial in chronic hemodialysis. Archives of General Psychiatry 20:433, 1969.
72. MacNamera M: Psychosocial problems in a renal unit. British Journal of Psychiatry 113:1231, 1967.
73. Coogan JP: Psychiatry for the slowly dying. Report on a program at Los Angeles County Hospital, SK and F Psychiatric Reporter 45:4-6, 1969.
74. Abram HS: The prosthetic man. Comprehensive Psychiatry 11:475, 1970.
75. Glassman BM, Siegal A: Personality correlates of survival in a long-term hemodialysis program. Archives of General Psychiatry 22:566, 1970.
76. Hollon TH: Modified group therapy in the treatment of patients on chronic hemodialysis. American Journal of Psychotherapy 26(4):501-510, 1972.
77. Goldstein AM, Reznikoff M: Suicide in chronic hemodialysis patients from an external locus of control framework. American Journal of Psychiatry 127:1204, 1971.
78. Janis I: Psychological Stress, John Wiley and Sons, New York, 1958.
79. Lindsay RM, Oreopoulos DG, Burton HJ, et al: The effect of treatment modality (CAPD vs

hemodialysis) in adaptation to home dialysis in Canada. In: Atkins RC, Thomson NM, Farrell PC (eds), Peritoneal Dialysis. Chruchill, Livingstone, Edinburgh, 385-394, 1981.
80. Kline SA, Burton HJ, DeNour AK, et al: Patient's self assessment of stressors and adjustment to home hemodialysis and CAPD. Peritoneal Dialysis Bulletin 5(1):36-39, 1985.
81. Elliot GR, Eisdorfer C: Stress and human health. Springer- Verlag, New York, 1982.
82. Goldberger L, Breznitzs: Handbook of stress. Free Press, New York, 1982.
83. Cassel J: Psychosocial process and 'stress': theoretical formulation. International Journal of Health Services 4:471, 1974.
84. Cassel J: An epidemiological perspective of psychosocial factors in disease etiology. American Journal of Public Health 64:1040-1043, 1974.
85. McGrath JE: Social and psychological factors in stress. Holt, Rinehard and Winston, New York, 1970.
86. Brown HW, Maher JF, Lapierre L, et al: Clinical problems related to the prolonged artificial maintenance of life by hemodialysis in chronic renal failure. Transactions American Society for Artificial Internal Organs 8:281-291, 1962.
87. Tsaltas MD: Children of home dialysis patients. Journal of the American medical Association 236:2764, 1976.
88. Shambaugh PW, Hampers CL, Bailey GL, et al: Hemodialysis in the home - emotional impact on the spouse. Transactions-American Society for Artificial Internal Organs 13:41, 1967.
89. Shambaugh PW, Kanter SS: Spouses under stress - group meeting with spouses of patients on hemodialysis. American Journal of Psychiatry 125:928, 1969.
90. Berkman LF, Syme SL: Social networks, host resistance, and mortality: a nine-year followup study of Alameda County residents. American Journal of Epidemiology 109:186-204, 1979.
91. Gore S: Stress-bufferingfunctions of social supports: an appraisal and clarification of research models. In: Dohrenwend BS, Dohrenwend BP (eds) Life stress and illness. Neale Watson, New York, 1980.
92. Rabkin Jg, Struening EC: Life events, stress and illness. Science 194:1013-1020, 1976.
93. Tolsdorf C: Social networks, support and coping: an exploratory study. Family Process 15:407-418, 1976.
94. Caplan G: Support systems. In Caplan G (ed), Support systems and community mental health, Basic Books, New York, 1974.
95. Dean A, Lin N: The stress-buffering role of social support: problems and prospects for systematic investigation. Journal of Nervous and Mental Disease 165(6):403-417, 1977.
96. Kaplan BH, Cassel JC, Gore S: Social support and health. Medical Care 15(5):47-58, 1977.
97. Sand P, Livingston G, Wright RG: Psychological assessment of candidates for a hemodialysis program. Annals of Internal Medicine 64:602, 1966.
98. Mallard WP: Rehabilitation level of home hemodialysis patients and predialysis training social factors. Dialysis and Transplantation 6:15, 1977.
99. Pentecost RL: Family study in home dialysis. Archives of General Psychiatry 22:538, 1970.
100. Pentecost RL, Zwerens B, manuel JW: Intrafamily identity and home dialysis success. Nephron 17:88, 1976.
101. Palmer S, Canzona L, Conley J, et al: Vocational adaptation of patients on home dialysis - its relationship to personality, activities and support received. Journal of Psychosomatic Research 27:201, 1983.
102. Conley JA, Burton HJ, DeNour AK: Support systems for patients and spouses on home dialysis. Internation Journal of Family Psychiatry 2(1):45-54, 1981.
103. Burton HJ, DeNour AK, Conley JA, et al: Comparison of psychological adjustment to continuous ambulatory peritoneal dialysis and home dialysis. Peritoneal Dialysis Bulletin 2(2):76- 79, 1982.
104. Burton HJ, Kline SA, Lindsay RM, et al: The effect of social networks, integration and support systems in determining quality of life for the ESRD patient. In: Levy NB (ed) Psychonephrology 4, Plenum publishers, New York (in press).

105. Eckenrode J, Gore S: Stressful events and social supports: the significance of context. In: Gottlieb BH (ed), Social networks and social support. Sage Publications, Beverly Hills, 43-68, 1981.
106. Henderson S: The social network, support and neurosis. British Journal of Psychiatry 131:185-191, 1977.
107. Brown G, Bhrolchain M, Harris T: Social class and psychiatric disturbance among women in an urban population. Sociology 9:225- 254, 1975.
108. Hammer M, Makiesky-Barrow S, Gutwirth L: Social networks and schizophrenia. Schizophrenia Bulletin 4:522-545, 1978.
109. Liem GR, Liem JH: Social class and mental health reconsidered: the role of economic stress and social support. Journal of Health and social Behaviour 19:129-156, 1978.
110. Lowenthal Mf, Haven C: Interaction and adaptation: intimacy as a critical variable. American Sociological Review 33:20-30, 1968.
111. Miller P, Ingham JG: Friends, confidants, and symptoms. Social Psychiatry 11:51-58, 1976.
112. Weiss RS: The provisions of social relationships. In: Rbin Z (ed), Doing unto others. Prentice-Hall, Englewood Cliffs, NJ, 1974.
113. Conner KA, Powers EA, Bultena GL: Social interaction and life satisfaction: an empirical assessment of late-life patterns. Journal of Gerontology 34:116-121, 1979.
114. Henderson S, Duncan-Jones P, McAuley H, et al: The patient's primary group. British Journal of Psychiatry 132:74-86, 1978.
115. Campbell A, Converse P, Rodgers W: The quality of American life. Russell Sage Foundation, New York, 1976.
116. Adler D: Psycho-social characteristics of successfully adapted and unsuccessfully adapted hemodialysis. Ph.D. Dissertation, Washington University, 1975.
117. Levenburg S, Campbell L: An Eriksonian approach to long-term adjustment ot hemodialysis. Journal of the American Association of Nephrology Nurses and Technicians 4:19-23, 1977.
118. Goldberg RT: Rehabilitation of patients on chronic hemodialysis and after renal transplantation: a comparative study. Scandinavian Journal of Rehabilitation Medicine 6(2):65-69, 1974.

21. REFUSAL OR TERMININATION OF A LIFE-SUPPORT PROGRAM - LEGAL ASPECTS

BERNARD M. DICKENS

INTRODUCTION

Faced with an elderly patient suffering end-stage renal disease or in danger of imminent renal failure, the attending physician must decide whether to offer invasive or aggressive care, principally dialysis (but perhaps organ transplantation), or to provide only conservative or comfort measures until the patient's anticipated death. Likewise, when dialysis has been initiated, perhaps as a routine institutional response to a patient's condition, the physician must determine whether it should be maintained or discontinued in favor of conservative treatment.

Decisions such as these require sensitivity to the legally imposed duty of care, but the law sometimes admits more than one legitimate treatment option; when it does, the selection is controlled by other factors. The patient's right of choice has to be accommodated, and the patient's wishes exert a strong, if not decisive, influence upon the treatment offered and rendered. The patient's choice must be adequately informed and freely exercised. Elderly, sick patient's may be compromised in their exercise of informed and free choice. At that point, a patient's family may play a significant role in treatment choice. Even when a patient is able to exercise a choice, family members may want to be informed of it, and to challenge it if they disagree. They may even threaten legal action to enforce their preference.

A choice of medical treatment, notably the decision (of a physician, a patient, or a family member for a patient) to refuse or terminate a life-support program, has both objective and subjective components. The objective elements are both scientific and legal. The patient's prognosis involves clinical judgment, which must be based on scientific data and exercised within the range of reasonable professional skill and practice. Legal doctrine distinguishes between mandatory and discretionary means of patient management. The physician and health facility are obliged to offer mandatory care; the patient may be obliged to accept it. Legally discretionary treatment involves subjective elements of choice: the

physician and health facility may offer or withhold it on the basis of individual judgment and competing demands on scarce resources, and the patient (or someone on his or her behalf) may accept or reject it on the basis of personal preference, philosophy and lifestyle.

This paper addresses the interaction of these components. First it discusses the legal duty to provide care and the distinction between mandatory and discretionary care; then it considers the extent to which a patient may refuse or terminate treatment in order to have a natural death. Finally, it examines the role of the patient's family in medical decision-making affecting the patient's care. The paper is oriented towards the general law of Canada and the United States, but, given the highly interactive jurisprudence of the Common law, it reflects approaches which may be taken in associated jurisdictions, such as those of the United Kingdom and, for instance, Australia. Many of the legal judgments cited concern not elderly but young (even newborn) children, but that is of no consequence; the legal principles apply without regard to age of patients. The aim is to present a structure of analysis which may be considered without regard to the traditions of individual jurisdictions.

THE LEGAL DUTY OF CARE

In a medical setting where a patient's life is at risk and death is a real possibility, health professionals should be aware not only of the liability to be sued in a civil action for negligence or malpractice (1) or for inflicting wrongful death, but also of the liability under criminal law to be prosecuted for manslaughter or, for instance, for criminal negligence causing death. In both civil and criminal law, the distinction between ordinary and extraordinary care, first formulated in the field of ethics or moral philosophy, (2), has become particularly important. Briefly, ordinary care is legally mandatory to offer, and perhaps to accept, whereas extraordinary care is discretionary. The latter does not have to be offered; once initiated, it can be withdrawn unless the patient's prognosis improves, and once offered or initiated it can be declined at the patient's discretion. In law, the civil and criminal duty of care is limited to ordinary care; a physician's or health facility's decision to refuse or terminate extraordinary care is not actionable by civil or criminal process even if the patient subsequently dies.

Only in recent years has the law come to apply the distinction between ordinary and extraordinary care. In itself, the distinction does not direct physicians upon the management of specific patients, and its apparent failure to prescribe individual treatment has brought it into some discredit. Disappointment with the distinction's capacity to direct patient care has led to the finding that 'the distinction between ordinary and extraordinary treatments now has become so

confused that its continued use in the formulation of public policy is no longer desirable' (3).

Confusion has arisen because early use of the distinction was based upon a belief in its prescriptive power, whereas now it is considered only a descriptive distinction. The distinction arose with development of mechanical life-support and similar technological means of patient care. When such means first appeared, about 30 years ago, it was asked whether facilities had to use them in individual cases when they were available. The answer was that they were required neither to be available nor to be used when accessible. Ordinary means of medical and nursing care, such as nutrition, warmth, sanitary care and, for instance, routine antibiotics, had to be available and used, it was believed, because patients had a legal right to expect such basic treatment; artificial or mechanical means, on the other hand, were considered extraordinary care, to which patients had no right. These means might be offered, in the discretion of the physician and health facility, but their unavailability or denial violated no legal rights.

Early ethical commentators often translated the ordinary/extraordinary care distinction into one between proportionate and disproportionate care. That language remains in use today in ethical discourse. In 1957, Pope Pius XII observed that '...morally one is held to use only ordinary means - according to circumstances of persons, places, times, and culture - that is to say, means that do not involve any grave burden for oneself or another.' (4). The question of proportion was supposed to relate to the technological equipment: use of some machines was always considered 'extraordinary', whereas other means of treatment, such as nutrition and, for instance, basic antibiotics, were considered, as such, 'ordinary', and legally obligatory to have available and to apply.

The language of proportionate and disproportionate care has cost-effectiveness implications, and seems better suited to health economics than to health ethics. It does, however, draw attention to the significance of macroethics, in contrast to the more individualized microethics which have become predominant in modern ethical analysis. The legal significance of the language is that courts are unlikely to hold a particular means of treatment to be ordinary, and therefore obligatory, if it is not available in the region's health facilities. Courts reserve the residual right to determine whether a patient's care measures up to legally required standards, because determination of legal standards is a matter for the courts and not for individual health professionals or health-facility administrators, (5). Particularly where hospital facilities are provided by public resources, such as Canadian provincial health insurance plans or the large metropolitan hospitals common in the United States, however, their standard of provision will influence what the courts will determine to be mandatory.

The simplistic, prescriptive application of the distinction between ordinary and extraordinary care was changed by the judgment in the well-known *Quinlan* case (6), where the New Jersey Supreme Court made it clear that the distinction is

relative not to equipment or therapy but to the individual patient's prognosis. The court considered the chronically vegetative patient's care in the belief that the patient's life would end if artificial life supports were to be withdrawn, and it recognized the medical need to balance perspectives of life and death. The court observed, however, that:

> ...this balance, we feel, is particularly difficult to perceive and apply in the context of the development by advanced technology of sophisticated and artificial life- sustaining devices. For those possibly curable, such devices are of great value, and, as ordinary medical procedures, are essential. Consequently ... they are necessary because of the ethics of medical practice. But in light of the situation in the present case (while the record here is somewhat hazy in distinguishing between 'ordinary' and 'extraordinary' measures), one would have to think that the uses of the same respirator or life support could be considered 'ordinary' in the context of the possibly curable patient but 'extraordinary' in the context of the forced sustaining by cardio-respiratory processes of an irreversibly doomed patient.' (7).

Accordingly, treatment that will help the patient is ordinary (and therefore mandatory), whereas treatment that will only postpone death is extraordinary: it may legally be offered and rendered, but it is not legally mandatory to be offered, continued or accepted. Understood in this sense, the distinction means that treatment as invasive as surgery can be ordinary (and therefore mandatory) when its performance offers the prospect of a continued life of at least modest but meaningful human function and when its denial might result in a life of pain and distress (8). Similarly, a staple means of care such as nutrition may lawfully be withheld from a newborn child affected by stomach blockage when surgery is clinically contraindicated (9). Antibiotics may be withheld from a patient with advanced malignancy who contracts pneumonia, when the alternative to the patient's peaceful death from that condition would be death a short time later in acute distress or in sedative-induced oblivion. Surgery to amputate a limb affected by gangrene may lawfully be denied by an elderly competent patient who does not want to suffer mutilation and dependency (10).

In the context of geriatric nephrology, the question is whether dialysis or related treatment will prolong a particular patient's life or merely postpone death. Unavoidably this determination depends on the clinical assessment of the attending physician, and upon medical criteria. Dialysis will be ordinary care in some cases and extraordinary in others; the distinction is drawn not by the law but by the physician's prognosis. Some guidance from the law may be found, however, in the provisions of legislation such as California's Natural Death Act, (11), which permits refusal of a life-sustaining procedure where a patient is in terminal condition. The Act provides that:

> 'Terminal condition' means an incurable condition caused by injury, disease, or illness, which, regardless of the application of life-sustaining procedures, would, within reasonable medical judgment, produce death, and where the application of life-sustaining procedures serve [*sic*] only to postpone the moment of death of the patient (12).

and that:

> ' Life-sustaining procedure' means any medical procedure or intervention which utilizes mechanical or other artificial means to sustain, restore, or supplant a vital function, which ... would serve only to artificially prolong the moment of death and where, in the judgment of the attending physician, death is imminent whether or not such procedures are utilized. 'Life-sustaining procedure' shall not include the administration of medication or the performance of any medical procedure deemed necessary to alleviate pain (13).

Another formulation which may be of assistance, based on medical and legal perceptions, is found in the policy on non-resuscitation at the Beth Israel Hospital in Boston, Massachusetts. It observes that:

> The specific issue of the appropriateness of cardio-pulmonary resuscitation arises frequently with the irreversibly, irreparably ill patient whose death is imminent. We refer to the medical circumstance in which the disease is 'irreversible' in the sense that no known therapeutic measures can be effective in reversing the course of illness; the physiologic status of the patient is 'irreparable' in the sense that the course of illness has progressed beyond the capacity of existing knowledge and technic to stem the process; and when death is 'imminent' in the sense that in the ordinary course of events, death probably will occur within a period not exceeding two weeks (14).

Cardiopulmonary resuscitation may differ from geriatric nephrology, for instance in that resuscitation may be a single incident in patient care whereas dialysis is a continuing condition of maintenance. Nevertheless, the Beth Israel Hospital protocol for non-treatment resulting in a patient's immediate death may provide a basis for a protocol for refusing or terminating dialysis resulting in a patient's death within a calculable period.

Whether a patient is in a terminal condition, so that treatment beyond comfort measures is extraordinary, is a matter of clinical prognostic judgment, but courts are respectful of clinicians' assessments and will not discount them simply because other physicians of comparable specialization and experience might have

reached a different conclusion (15). A prognosis must be one which no competent practitioner would reasonably have reached before courts will consider whether it was negligently made. No liability arises simply because the prognosis was, or might have proven to be, incorrect.

Courts have been anxious to deny that principles which justify refusal or termination of life-support programs are based upon considerations of patients' quality of life. It is recognized that what gives life quality is a personal and idiosyncratic matter uniquely determined by each individual for himself or herself. One person, whether a health professional, a member of the clergy or a member, for instance, of a committee or court, cannot credibly assess what affords quality to the life of another person. Accordingly, the courts have made actual or potential capacity to achieve or resume a life of at least minimal human quality or experience the essential precondition for active treatment. In the *Quinlan* case, the court asked if the patient could ever return to 'cognitive or sapient life' (16). This modest neurological or intellectual criterion appears to consist in capacity for awareness of self and of others. Once satisfied that the patient's prognosis excluded the possibility of resumption of such a life of interactive human experience, and that she would remain chronically vegetative, the New Jersey court concluded that mechanical life supports would not assist her care and therefore were extraordinary and legally discretionary. The fact that the unconscious patient was weaned off such supports and survived without them for over a decade does not affect the legal status or strength of that analysis.

Courts have also recognized, however, that conscious patients may exist in a condition in which active care may not assist them. The unconscious patient who has no experience of human life may at least escape pain, but conscious patients may suffer pain and acute distress (17). In 1981 the English Court of Appeal required that consent be given to surgical treatment to remove intestinal blockage of a child affected by Down syndrome, because her prognosis after surgery was a life of human functioning extending for 20 or 30 years (18). The court considered in the circumstances that an operation would help the child, and that it was accordingly ordinary (and legally mandatory) care; it added, however, that there:

> may be cases ... of severe proved damage where the future is so certain and where the life of the child is so bound to be full of pain and suffering that the court might be driven to a different conclusion (19).

In geriatric nephrology, therefore, the attending physician must determine not only whether a patient is in a terminal condition (such that treatment that will merely postpone death is extraordinary), but also whether a non-terminal patient will survive in the certainty of pain and suffering. While courts claim not to apply quality-of-life criteria, judicial recognition that a life of unrelievable pain and suffering may not have to be sought by active means may come close to

recognition of such a factor. How far improvements in palliative care and pain control can relieve a patient's pain is, again, a matter of clinical judgment.

The perception that the legal duty of care owed a patient by a physician and health facility is limited to the duty to provide ordinary care, and that there is no legal duty to offer care that, by the above analysis, is determined to be extraordinary, assists application of legal doctrine. This perception clearly governs the duty of care imposed by negligence law; it also applies to the duty voluntarily assumed under principles of contract law, unless the physician or health facility expressly undertakes to provide extraordinary care. Such express undertaking may be given in language which specifies a particular treatment such as dialysis, rather than through generic language, referring for instance to artificial, mechanical or aggressive care.

Similarly, duties imposed by criminal law appear to be limited to the provision of ordinary care. In the Criminal Code of Canada (20), for instance, section 197 requires parents to provide their children, and spouses to provide each other with 'necessaries of life.' These may include medical aid, (21), but extraordinary care, which by definition is unlikely to assist the child or spouse in question, is unlikely to be a 'necessary'. If such care would assist in prolonging a life of human experience or in relieving pain and distress, it would fall within the category of ordinary care, which parents and spouses are obligated to provide. The same provision also governs a person who has another person, such as a parent, under his or her charge, if that other person '(i) is unable, by reason of detention, age, illness, insanity or other cause, to withdraw himself from that charge, and (ii) is unable to provide himself with necessaries of life.'(22). It is an offence for a person to refuse or neglect to provide care to such a dependant if 'the failure to perform the duty endangers the life of the person to whom the duty is owed or causes or is likely to cause the health of that person to be injured permanently' (23).

Accordingly, if in medical judgment a patient has a favorable prognosis but is temporarily incompetent to consent to dialysis and is under the *de facto* or *de jure* charge of another (such as a spouse or adult child) who declines to consent to such care, a physician or health facility may initiate judicial proceedings for an order to dialyse. Alternatively, either may initiate treatment on the strength of the patient's implied consent to ordinary care, in spite of the spouse's or child's unlawful refusal to consent on the patient's behalf (24).

When the Criminal Code places health professionals and facilities under duties to the patients, the same analysis shows that only ordinary care is included. Section 199, for instance, provides that '[e]very one who undertakes to do an act is under a legal duty to do it if an omission to do the act is or may be dangerous to life.' Physicians and health facilities will be considered only to undertake provision of ordinary care. They may expressly bind themselves by contract to provide extraordinary care too, of course, such as dialysis (where that is unlikely to be of benefit to patients whose deaths it might postpone), and if they fail to

perform their agreements they will be liable to pay damages for breach of contract. Because the omission is not itself dangerous to life, however, their failure to provide agreed extraordinary care will not render them liable to criminal punishment. The danger comes from the patient's predisposing circumstances, not from the omission to perform extraordinary treatment. Such treatment, by definition, would not assist patients' survival or comfort, even if it were provided.

On the other hand, when ordinary care such as dialysis is withheld and a patient consequently dies, it is no defence that the patient would not have lived long even had the treatment been given. Section 209 of the Criminal Code provides that:

> Where a person causes bodily injury to a human being that results in death, he causes the death of that human being notwithstanding that the effect of the bodily injury is only to accelerate his death from a disease or disorder arising from some other cause.

Note that the section refers to 'bodily injury', not to 'bodily assault'. Failure to discharge a legal duty of bodily care can constitute an 'injury'; the word derives from the Latin *in juria*, meaning juridically wrongful action. Hence, failure to discharge a legal duty to provide ordinary care can be the basis of a prosecution for homicide. At this point, however, it is important to consider the role in decision-making of the patients themselves and of their families. One reason why physicians or facilities might refuse or terminate life-support programs is that patients or their families refuse or withdraw consent to their use.

THE PATIENT'S RIGHT TO NATURAL DEATH

A patient who has been assessed, by the criteria outlined above, to be in a terminal condition may refuse the application or continuation of extraordinary care, which may include dialysis, with legal effect; an attempt to administer dialysis despite his or her refusal of consent will constitute civil and criminal wrongs of battery and assault. To that extent, a terminal patient has a right to natural death, in that postponement of death through use of artificial or mechanical means may be resisted. The issue is complicated, however, by the special protection the law affords, as a matter of policy, to rescue attempts, and by the difficulty of expressing involuntarily imposed postponement of death as a legally compensable injury. These issues will be addressed below. The initial issue, however, is whether a non-terminal patient can decline dialysis when that treatment, by legal analysis, would be ordinary care; that is, whether a patient has an unrestricted legal right to die, not just the more limited right to die naturally when in a terminal condition.

It appears that a patient has no right to experience or suffer avoidable death. In the *Bouvia* case, tried in the Superior Court of California in 1983, (25), a mentally competent quadriplegic young woman wanted not to be fed but to be

medically eased into death by starvation in the institution where she resided. Staff members refused to comply and insisted upon supplying nutrition to the patient by voluntary, or if necessary by involuntary, means. The patient sought a court order that her preference prevail, but she was unsuccessful. The court held that she could not insist on substandard care, or on the withholding of ordinary care (which included nutrition), while she remained a patient. She was free, of course, to cease to be a patient by leaving the institution. Equally, the institution had the option of requiring her to leave, and even of having her removed as a trespasser, if she refused to conform to institutional requirements of taking nutrition; the institution, however, made it clear that it had no intention of asking her to leave.

Similarly, in the *Astaforoff* incident, a Doukhobor inmate of a federal penitentiary in British Columbia went on a hunger strike; in response, the Attorney General of Canada asked the court for a declaration that it was mandatory that she be fed. The court ruled that no legal duty existed to feed the inmate in the face of her competent refusal (26). A separate question, not raised in court but considered by lawyers to the Department of the federal Solicitor General, was whether it would be illegal to feed her, by force if necessary. Accepting that there was no duty to feed her, the question was whether there was a power to feed her. The Department's lawyers concluded that it would not be illegal to feed her, and she was fed until she terminated her hunger strike. Clearly, prisoners are not free in the way that patients are. The lesson of the court judgment, however, is that it is legitimate for guardians, in whose care a patient willingly remains, to comply with the patient's competent refusal of ordinary care. This suggests that a homicide charge would fail if brought against a physician or health facility when death followed upon a competent non-terminal patient's refusal or termination of consent to ordinary care. Compliance with the patient's wish is legitimate even though not mandatory.

Geriatric nephrology patients who are not terminal may nevertheless not be capable of leaving the institutions in which they receive care. If physicians or institutions will not allow patients to die avoidable deaths in accordance with the patients' expressed wishes, they may seek court orders which permit dialysis, or they may undertake involuntary care and invoke their legal defences. Before these options are addressed, it may be observed that persons who manifest self-destructive preferences or tendencies on account of mental disorder may become liable to proceedings under mental health legislation. Such proceedings may provide for their involuntary detention, for guardianship (perhaps as judicially approved) and for their restraint and sustenance. Whether persons so detained and managed may be treated involuntarily by therapeutic means is a matter of local legislation and jurisprudence (27). Even if they cannot be treated, however, dialysis may constitute maintenance or restraint of self-destructive tendencies which is justifiable in the short term on grounds of necessity to save human life, and in the long term on the basis of legislation or judicial approval.

Defences available to those who take life-sustaining initiatives over patients' competent objections centre upon rescue principles. These are sometimes called Good Samaritan principles, but that description may be inappropriate. The Samaritan, after all, came to the aid of a person desiring the assistance rendered after his injury by a third party, whereas patients declining dialysis and comparable ordinary care do not want the treatment offered. The threat to their survival comes from their own competent decisions. Nevertheless, the justification for rescue intervention exists in such provisions as section 45 of the Criminal Code of Canada, which states that:

Every one is protected from criminal responsibility for performing a surgical operation upon any person for the benefit of that person if

(a) the operation is performed with reasonable care and skill, and

(b) it is reasonable to perform the operation, having regard to the state of health of the person at the time the operation is performed and to all the circumstances of the case.

The section makes no reference to consent, and it may be argued that refusal of consent is a decisive circumstance of the case (28). A general common law defence, not limited to surgical intervention, is available, however, when action is taken which is necessary to save human life; it operates on an objective assessment of the circumstances perceived by the actor (29). The necessity defence, directed to the saving of a person's life, applies in both criminal and civil proceedings. This is consistent with the outcomes of the *Bouvia* case and the *Astaforoff* incident, (30), where both persons subject to involuntary treatment were mentally competent but were not permitted to decline ordinary care. The former case may be the more significant, because United States courts have recognized a fundamental constitutionally protected right of individual privacy (31). This is the right to be left alone and to be free in personal decision-making from state supervision and answerability (32). In the *Quinlan* case it was recognized, however, that this right, although substantial, is not necessarily absolute. The court found that the right of privacy may be subject to 'interests of the State in ... the preservation and sanctity of human life and defense of the right of the physician to administer medical treatment according to his best judgment' (33).

The value of human life has been confirmed in the general refusal of civil courts to admit claims for so-called 'wrongful life.' Those actions tend to be brought on behalf of seriously handicapped newborn children whose complaint is that, but for the negligence of the defendants, they would not have been conceived, or, having been conceived, they would not have been born (34). Defendants are alleged to have given negligent genetic advice or, for instance, to have conducted prenatal diagnosis negligently, causing women to start or continue pregnancies of children irreparably doomed to lives of severe handicap and pain. Courts have invoked the language used by the New Jersey Supreme Court in 1967 to reject these claims:

> The ... plaintiff would have us measure the difference between his life with defects against the utter void of nonexistence, but it is impossible to make such a determination. This Court cannot weigh the value of life with impairments against the nonexistence of life itself (35).

A number of more recent decisions have allowed the claim (36) on the basis that the wrong of 'wrongful life' is not the life itself, but the plaintiff's foreseeable pain and suffering. So long as the claim is generally rejected, however, a patient whose life was sustained because of treatment the patient opposed may be unable to recover damages. Even the assault on the patient, which may in principle justify a damage award in the absence of calculable loss, may be defensible under the principle of necessity to save life.

The imperative to preserve human life is of reduced importance where terminal patients are concerned. In the face of the unfavorable prognosis, artificial or mechanical care will be at best death-postponing, and therefore extraordinary; it may legally be refused or terminated by the patient. Its administration is governed in principle by the patient's wishes. While this may appear self-evident, the health professional frequently has been trained instead to identify and to serve the patient's best interests. Ideally, wishes and interests coincide; most patients want their best interests to be served. The function of giving information is to review treatment options in light of their likely effects upon patients' interests. The patient, however, is the one in control of the commanding heights of the decision; any discretion the physician has to choose means of treatment is predicated upon the implicit belief that the physician and the patient have the same treatment goals. In the event of a conflict between the patient's wishes and the patient's best interests as perceived by a health professional, the patient's wishes prevail.

Accordingly, when a terminal patient wishes to refuse or terminate a life-support program, which because of the prognosis constitutes extraordinary care, that wish must be given effect. The terminal patient has the right to a natural death and the right to decline a postponement of death sought by use of artificial or mechanical means. While the patient whose wishes are ignored may find difficulty succeeding in an action for wrongful life, the assault on the patient is not defensible by the claim of necessity to save life, because the terminal patient's life, by definition, cannot be saved.

While the patient's autonomy to decline extraordinary treatment must be respected, the patient has no right to demand that such treatment be rendered or continued. Extraordinary care is mutually discretionary, and a patient cannot legally demand of a physician or health facility that disproportionate resources or means of treatment which, in the attending physician's clinical judgment, will not assist the patient, be allocated to his or her care. In this regard, the patient's wishes will not prevail. This principle is reinforced by the perception that the expensive or scarce resource that will not assist a terminal patient will be

ordinary, and perhaps mandatory, for another patient whom that resource appears likely to assist. The terminal patient cannot demand that such resources be applied to his or her care, even if they were initiated before the other patient became eligible for them. The patient does not accumulate additional claims to extraordinary care simply by virtue of having received it already. It will be different, of course, if the patient's prognosis improves. In that case the treatment may be found to assist the patient; if so, it will become ordinary care, to which the patient has a right.

How effectively a patient expresses the wish that extraordinary means not be used when his or her condition becomes terminal has been a matter of recent concern. The so-called 'living will' expresses such a wish, and its presence may legally justify a medical decision not to render artificial or mechanical care. It is not clear, however, that it compels that decision; there may be contrary but equally reliable evidence of the patient's wishes. Further, the 'living will' may have been executed some time beforehand and in quite different circumstances of the patient's life.

This 'living will' is no more than an informal written statement of the patient's wish. An unwritten statement made to a physician or other reliable person, such as a clergyman or hospital chaplain, can be equally effective. The patient's statement should be recorded on the medical chart, however, because it is an important element in determination of the patient's care. The patient may be advised to ensure that a statement is so noted. If the patient is in a terminal condition when stating a duly recorded intention to refuse or terminate a life-support program, the statement may be given prompt effect. If the statement is made in anticipation of entering a terminal condition, it may be similarly effective, except perhaps when that condition arises a considerable time later, or in circumstances materially different from those in which it was made. While a statement exists on the record, however, and no reliable contrary evidence is available regarding the terminal patient's wishes, it may legally justify a decision to withhold or withdraw extraordinary care.

A number of jurisdictions in the United States have natural death statutes, which provide a patient with a form of statutory declaration declining use of artificial or mechanical care on entering a terminal condition (37). This declaration has legal effect, and disregard by a person who knows of it is legally penalized. A declaration usually has legal force only within the jurisdiction under whose law the declaration was made, but some jurisdictions may recognize a declaration legally made elsewhere. Even when a declaration is not strictly enforceable, however, awareness of it will justify a decision to refuse or terminate extraordinary care.

Less effective than a declaration under a Natural Death Act is a declaration under a 'durable' Power of Attorney Act (38). Unlike ordinary power of attorney authorizations, which cease to apply when the persons appointing attorneys lose legal competence, the 'durable' power of attorney permits competent persons to

anticipate their own future incompetence and to make provisions which will be effective at that time. These arrangements may not specify what choices attorneys are then to make, but they do make clear the identity of attorneys who are empowered to exercise choice on patient's behalves. Traditionally the power of attorney was limited to control and disposal of property, however, and not all durable power of attorney legislation clearly applies in addition to medical and comparable management of the persons who have executed powers.

Living wills, Natural Death Act declarations and durable powers of attorney may permit patients to make provisions for their future medical management with which their family members cannot interfere. A power of attorney, for instance, will displace a next-of-kin family member in favor of a person specifically approved by the patient. This may relieve family members of responsibility for decision-making, limit family conflict about provisions for the incompetent patient, and preclude the patient from coming under the influence of a family member whose judgment the patient distrusts or disapproves. In the absence of such a clear arrangement, however, the role of the family of the incompetent patient becomes an issue where life-sustaining care is concerned.

THE ROLE OF THE FAMILY

Patients' autonomous rights to be governed by their wishes do not cease simply because the patients become incompetent, even when incompetence will be permanent. They do not become subject to others' perceptions of their best interests at the expense of their own demonstrable wishes; even less do they become liable to others' wishes. The primary role of the family members of incompetent patients is to assist and perhaps be instrumental in establishing what the patients' wishes are. They may be suited to this task because of their close, prolonged familiarity with patients' conversations, dispositions, attitudes and preferences. If their relationships to patients are merely legal or genetic and lack an intimate personal quality, however, evidence may be sought from other sources, such as close and caring friends, to establish patients' wishes.

Patients' adequately demonstrated wishes are not subject to veto by their families. This is obviously true of Natural Death Act declarations and exercises of a durable power of attorney; it is intended also to be the case regarding living wills. The same is true in principle, however, regarding wishes reliably identified by other means, such as, for instance, statements made to friends and colleagues (39), or to hospital personnel for notation on patients' medical records. It is recognized that establishing adequate evidence of patients' wishes may be difficult, not least when patients have disclosed wishes only to family members who do not agree with the preference expressed. The quest for an authentic expression of patients' wishes, to find the words they would want spoken on their behalves, is further confounded by the fact that patients may not

have addressed in specific detail or clear language the issue of acceptance, refusal or withdrawal of extraordinary medical care when in a terminal condition. Their wishes may have to be distilled, interpreted or interpolated from knowledge of their personalities and dispositions. That is why evidence should be sought from others whose relationships with them have had an intimate quality. Those with only nominal ties, such as long separated and perhaps estranged spouses, children or sibs, are not credible as sources of evidence of patients' subjective preferences (40). A reliable nurse's note made at the time of an apparently competent patient's observations will have greater evidentiary weight.

In a number of cases it will be impossible reliably to find an adequate expression or interpretation of a patient's wish. There may be no one, or no one accessible, to whom the patient disclosed preferences; close family members, for instance, may simply not know what the patient would wish, and may not be able in good faith to apply the patient's personality credibly to the choice at hand. In such a case the patient does not become liable to the personal preference of a family member, a health professional or other person. When the patient cannot be managed in accordance with his or her subjective wish, he or she is to be managed on the objective basis of his or her best interests; the patient does not fall under the influence or disposal of another person's subjective wish. Second persons cannot do as they wish with the patient's life.

Accordingly, when the patient is incompetent and his or her wishes cannot be reliably established, the attending physician's perception of the patient's best interests prevails. This may be a perception independently reached, but it is likely to be influenced by some knowledge of the patient's personality and lifestyle and of family members' concerns. It may also be influenced by discussions with an institutional ethics committee (41). Family members legally cannot insist upon treatment the attending physician determines to be valueless to the patient's welfare (that so, extraordinary treatment); neither can they legally deny treatment the physician considers to be in the patient's best interests (42). The patient's implied consent to such care, which is credible where no evidence exists that the patient would oppose it, may prevail over family members' insistence that they do not want it used. Their claims that the patient would not wish it to be used have to be clearly established, since the presumption is that patients wish to receive treatment which is medically assessed to be in their best interests. As the U.S. President's Commission observed, '[h]ealth care professionals serve patients best by maintaining a presumption in favor of sustaining life...' (43) where life appears sustainable.

Family members sometimes urge their preferences by threatening or initiating legal proceedings. Evidence indicates that some physicians and health facilities accede in those circumstances. In doing so, however, they risk disadvantaging or denying benefit to their patients and losing charge of their own professional practices and health facility administration. The former risk is perhaps the greater, but the latter is of no small account. Indeed, in the *Quinlan* case the

court found that even the patient's interest in privacy may be subordinated to 'the right of the physician to administer medical treatment according to his best judgment' (44). To maintain the integrity of medical practice, particularly (though not exclusively) regarding incompetent patients, physicians should not be governed by the threat of being taken to court, but by the danger of being legally liable, whether sued or not.

For the reduction of doubt, physicians and health facilities may apply the legal equivalent of defensive medicine, namely defensive litigation. In the event of disagreement between health professionals' assessments and the preferences of patients' family members, professionals or facilities may initiate appropriate court proceedings, for instance for declarations favoring their treatment proposals. Alternatively, professionals or facilities may require family members to obtain judicial approval of their preferences, particularly when family members want treatment withheld or withdrawn. This has been the origin of many important cases, including the *Quinlan* and *Bouvia* cases discussed above. A further option may be to require those family members who disagree with physicians' or health facilities' treatment proposals to receive discharge of the patients, perhaps with a view to their transfer to other facilities offering care the family members approve. This option may not be available in all cases, however; the patient might be very sick or transfer might be psychologically traumatic. The latter is sometimes the case with geriatric patients who may be physically removable.

Family members may misunderstand their role in decision-making, and may misconstrue their responsibilities, when they are uninformed of the basis upon which medical treatments are proposed. Particularly difficult are the situations in which competent patients have made Natural Death Act declarations, powers of attorney, living wills or other informal expressions of their wishes, but do not want family members to be informed. Patients should be asked whether information of their wishes may be so communicated, but their confidentiality has to be respected if they refuse. They may prefer not to burden a family member, such as an elderly spouse, with responsibility for a life-or-death decision; on the other hand, they may want to escape what they perceive as the oppression of dependency on or subordination to the choices others may make, without having family members so informed.

Litigation by family members may compel production of data disclosing the basis of medical choices; patients' privacy will not necessarily prevail over the public's interest in the due administration of justice. In the absence of judicial orders to produce documents showing patients' private expressions of their wishes, however, physicians and health facilities will have to cope as comfortably as they can with the anger or bewilderment of family members who cannot understand why treatment of an apparently dying loved one is maintained, or especially why a loved one is being permitted to die when artificial means of sustaining life are available. After death, disclosure may be made to relatives,

both to ease their grief and sense of bereavement and because control of patients' medical data may have passed to certain of them. While the patient lives, however, respect is due to his or her wishes regarding both refusal of extraordinary care and maintenance of confidentiality.

NOTES

1. 'Negligence' and 'malpractice' are often treated as synonymous, but even when the latter includes the former, it also includes battery, breach of contract and, for instance, breach of fiduciary duty.
2. See the statement of Pope Pius XII in 1957: The Pope Speaks: Prolongation of Life (1957) 4 Osservatore Romano 393-8.
3. [U.S.] President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Deciding to Forgo Life-Sustaining Treatment: Ethical, Medical, and Legal Issues in Treatment Decisions* (1983), at 88. A brief review of the report appears in B.M. Dickens, 'The Final Freedom: Deciding to Forgo Life-Sustaining Treatment' [1984] *Public Law*, 34-43.
4. See note 2 above.
5. See the discussion in *Helling v. Carey* (1974), 519 P. 2d 981 (Wash. S.C.) and *Wyatt v. Stickney* (1972), 344 F. Supp. 373 (M.D., Ala.)
6. *In the Matter of Karen Quinlan* (1976), 355 A.2d 647 (N.J.S.C.).
7. *Ibid.*, at 667-8.
8. See *Re Superintendent of Family and Child Service and Dawson* (1983), 145 D.L.R. (3d) 610 (B.C.S.C.), discussed in B.M. Dickens, Comment (1984) 62 *Can. Bar Rev.* 196-210.
9. See *R. v. Arthur, The Times (London)*, November 6, 1981 (Leicester Crown Court), discussed *Ibid.*
10. *In the Matter of Robert Quackenbush* (1978), 283 A. 2d 785 (N.J. Co. Ct., Probate Division).
11. Cal. Stats. 1976, c. 1439, constituting c. 3.9 of the *Health and Safety Code.*
12. *Ibid.* S 7187 (f).
13. *Ibid.* S 7187 (c).
14. M.T. Rabkin, G. Gillerman and N.R. Rize, 'Orders Not to Resuscitate' (1976), 295 *New England J. Med.* 364-366 at 365.
15. See *Whitehouse v. Jordan*, [1981] 1 All E.R. 267 (H.L.) and *Maynard v. West Midlands Regional Health Authority*, [1985] 1 All E.R. 635 (H.L.).
16. See note 6 above, at 669.
17. On the interaction of pain and suffering, see M.A. Somerville, 'Pain and Suffering at Interfaces of Medicine and Law' (1984), 10 *Jus Medicum* 133-142.
18. *In re B (A Minor) (Wardship: Medical Treatment)*, [1981] 1 W.L.R. 1421 (C.A.).
19. *Ibid.*, at 1424; this observation was repeated in the *Dawson* case, note 8 above, at 623.
20. R.S.C. 1970, c. C-34.
21. *R. v. Brooks* (1902), 5 c.c.c. 372 (B.C.S.C.).
22. Criminal Code, note 20 above, s. 197 (1) (c).
23. *Ibid.*, s. 197 (2) (b).
24. See below on the patient's limited right to natural death.
25. See *Bouvia v. County of Riverside*, No. 159780, Sup.Ct., Riverside Co., Cal., Dec. 16, 1983, Tr. 1238-1250, unreported to date but critically discussed in G.J. Annas, 'When Suicide Prevention Becomes Brutality: The Case of Elizabeth Bouvia' (1984), *Hastings Center Report* 20-21, 46.
26. *Re Attorney-General of British Columbia and Astaforoff* (1983), 6 C.C.C. (3d) 798 (B.C.C.A.).
27. See the discussion in *Rogers v. Okin* (1980), 634 F.2d 650 (1st Cir.).

28. See B. Starkman, 'A Defence to Criminal Responsibility for Performing Surgical Operations: Section 45 of the Criminal Code' (1981), 26 *McGill L.J.* 1048-1055.
29. See *Morgentaler v. The Queen* (1975), 53 D.L.R. (3d) 161 (S.C.C.), and *Perka v. The Queen* (1984), 14 C.C.C. (3d) 385 (S.C.C.).
30. See notes 25 and 26 above.
31. Both United States and Canadian constitutional law recognize a fundamental right to be safe from cruel and unusual treatment; this may provide a basis for future challenges to imposed medical treatment. Indeed, the lower court judge in the *Dawson* case (see note 8 above) held that imposing treatment would violate this right; see *Re S.D.* (1983), 42 B.C. L.R. 153 at 172 (B.C. Prov. Ct.).
32. *Roe v. Wade* (1973), 93 S. Ct. 705.
33. Note 6 above, at 663.
34. See generally W.H. Winborne (ed), *Handling Pregnancy and Birth Cases* (Family Law Series), Colorado Springs: Shepards's/McGraw- Hill, 1983, at 393-419.
35. *Gleitman v. Cosgrove* (1967), 227 A.2d 689, at 692.
36. Beginning with *Curlender v. Big-Science Laboratories* (1980), 165 Cal. Rptr. 477 (Cal.C.A.); see W.H. Winborne, note 34 above.
37. California's Natural Death Act, note 11 above, provides a widely used model. The statute also appears in the President's Commission's report, note 3 above, at 324-329. The report presents Acts of 15 jurisdictions at 318-387.
38. See *ibid.*, at 391-437.
39. See *Eichner v. Dillon* (1980), 426 N.Y.S.2d 517 (N.Y. App. Div.) (The 'Brother Fox' case).
40. See the distinction between 'bonded guardians' and 'non-bonded guardians' drawn by R.M. Veatch in 'Limits of Guardian Treatment Refusal: A Reasonableness Standard' (1984), 9 *Amer. J. Law and Medicine* 427-468.
41. See R.E. Cranford and A.E. Doudera, 'The Emergence of Institutional Ethics Committees' (1984), 12 *Law, Medicine and Health Care* 13-20, and R.A. McCormick, 'Ethics Committees: Promise or Peril?' *ibid.*, at 150-155.
42. Compare parents' responsibilities for children's medical care, shown in the *Dawson* case, note 8 above.
43. See note 3 above, at 3. The commission's conclusion continued: '...while recognizing that competent patients are entitled to choose to forgo any treatments, including those that sustain life' but this ethical conclusion is necessarily legally compellable.
44. See note 33 above, and text.

22. UREMIA IN THE AGED: CAN WE AFFORD TO TREAT EVERYONE?

ELI A. FRIEDMAN, M.D., D. SCI., (HON)

INTRODUCTION

Kidney failure occurs at all ages. Older patients may develop uremia due to renal manifestations of a systemic disorder after years of diabetes, hypertension, and nephrosclerosis. Intrinsic renal diseases such as poststreptococcal glomerulonephritis and lupus nephritis may begin as late as the eighth decade of life. Malignancy occurs with progressively higher incidence as age advances, causing renal impairment either by direct invasion of the kidney or obstruction of urine flow to or from the bladder. Thus, geriatric nephrology is concerned with a variety of renal syndromes, a number of which culminate in renal failure. As is true for all illness in old age, expectations for therapy ought to be free of illusions but, permitting a 90-year-old dialysis patient to attend her grandchild's wedding is sufficient reward for the tribulations of establishing a vascular access and dealing with hypotension after dialysis.

The inclusion of geriatric patients in a program of universal uremia therapy, however, requires an alteration of prevalent prejudices and misconceptions about the outcome of dialysis and kidney transplantation in the aged. There is no doubt that advancing age is a substantive risk factor for survival on maintenance hemodialysis (1), kidney transplantation (2), or peritoneal dialysis (3). Reports over the last few years, however, indicate that one can attain a surprising prolongation of life even in uremic patients in their ninth decade.

For example, Ost *et al* reported that, of 34 recipients of cadaveric renal transplants who were 60 years or older, 49% lived for at least two years (4). While complications, especially serious infections, heart disease, and steroid diabetes were more prevalent in older recipients, the authors were sufficiently satisfied with the outcome to conclude that 'we intend to offer renal transplantation to patients of 60 years and above.' In an analysis of 242 patients over age 60 (180 on hemodialysis and 62 on hemofiltration), Schaefer *et al* advised that 'this group of patients when suffering from primary renal disease has a very good chance of surviving many years (5).' Furthermore, an astounding

50% five-year survival rate was observed in patients 75 years or older.

In the United States the mean age of dialysis patients is increasing rapidly. About 25% of all patients are 70 years or older. Employing the Cox proportional hazards model of risk analysis, Westlie *et al* found that,in Minnesota, the 1,3, and 5-year survival rates in these geriatric patients was 78%, 47%, and 22% (6). In the United Kingdom where age is used as an exclusion criterion (7), careful evaluation of the fate of the few accepted geriatric patients confirms the impression that often dialysis achieves a useful extension of life. For instance, Taube *et al*, who rated the quality of life and prognosis in 84 British patients over the age of 55 who had irreversible uremia, reported a five-year survival of 62%; 78.1% of the survivors 'either having successful transplants or caring for themselves using home haemodialysis or CAPD' (8).

Why then, if a substantial subset of older uremic patients respond well to dialysis and transplantation, is their access to uremia therapy limited and why the current debate over their treatment? The answer, though complex, is based on intertwined economic and political realities; there is a brisk competition for health-care dollars and in this the elderly may be defeated (Table I).

CHANGES IN THE 1980'S

One quarter century has passed since Scribner's epochal introduction in 1960 of the external arteriovenous shunt, which allowed maintenance hemodialysis and thereby preempting certain death from uremia. At first, social misfits, unmarrieds, the unemployed, and those over age 45 were excluded from dialysis. During the 1970's, legislation provided funding and program development for the treatment of uremia in the elderly in the United States and much of Western Europe. However, there was little improvement in prognosis, either with hemodialysis or kidney transplantation. In the first one-half of the 1980's there have been two major improvements: 1. continuous ambulatory peritoneal dialysis (CAPD) has been used widely particularly in old age, and 2. the increasing use of cyclosporine for immunosuppression in kidney transplants of all ages.

PRAGMATIC REALITIES

Uremia therapy for undeveloped and developing nations lags far behind the level applied in the United States, Canada, Japan, Israel, and Western European nations. Health resources are allocated by a process open to the pressures of politics, economics, religious, and ethical concerns. While the United States debates the morality of dialyzing patients with cancer, AIDS (acquired immune deficiency syndrome), or psychosis, most of the rest of the world struggles to

treat uncomplicated young adults in primary renal failure. As is true for most aspects of health care, America and Western Europe do not represent what can be accomplished for most of the world's population. For example, while Switzerland, Israel and the United States each sustain more than 200 dialysis and transplant patients per million population, fewer than one in five people now living have any hope of receiving uremia therapy should their kidneys fail. All of the 1 billion Chinese, 700 million Indians, 90 million Nigerians, and nearly all South Americans combined have a smaller number of patients on dialysis than the Northeastern United States. Kidney transplantation is virtually absent in Communist block nations (9). When confronted with pressures of malnutrition, perinatal mortality, malaria, trachoma, and diarrheal illness, health planners in low-income nations must dismiss uremia therapy as an unattainable luxury.

Careful medical economic analysis of the growth of dialysis and transplantation shows a linear correlation between *per-capita* gross national product and the number per million treated with dialysis or kidney transplant (10). In 1981, three-quarters of the world's population had a *per-capita* gross national product below $2700 - the lower level at which nations are able to sustain uremia therapy. Current, mid-decade starvation in Ethiopia, Chad, and other regions of Africa precludes expensive kidney programs for these nations. Who shall be treated then becomes a question of triage (11), wherever poverty forces ranking of health priorities. Seedat *et al* in Durban, South Africa, state the problem well: 'There are searching questions about whether developing countries can afford a chronic renal failure programme' (12). Not surprisingly, the elderly are ranked below the young and vigorous whenever a society must practice life-or-death selection.

POLITICAL CONSIDERATIONS

When dealing with allocation of health care funding to meet a seemingly limitless demand nations make different choices; The United States, for example, determined early in the 1980's that, with the exception of a single research facility, heart transplantation would not be supported by Medicare. As a consequence, patients primarily in the middle and geriatric age range, who might have gained useful life extension with a replacement heart, are permitted to die. Only those accepted by a proprietary hospital network seeking to gain favorable publicity will be considered for artificial heart implants in 1986. Further to this point, Great Britain excludes *de facto* diabetics and those over age 50 from dialysis or kidney transplantation. For that nation, the geopolitics of retaining the Falkland Islands was viewed as more important than building additional dialysis facilities.

RACIAL BIAS

Although blacks have a distinctly greater risk of developing uremia than do whites or orientals, they are treated at a lower rate than are whites in South Africa (13) and other countries. Blacks are deselected for home hemodialysis and kidney transplantation. Diabetic nephropathy and malignant hypertension are more common in blacks than whites but blacks are less likely than whites to receive a kidney transplant for these disorders (14). Assignment by race to a specific uremia therapy - CAPD, hemodialysis, or kidney transplantation - reflects other variables than antipathy to color. In the United States, blacks are poorer, more frequently come from broken homes, and have had less education than whites. Intensive training for home hemodialysis may be withheld from blacks in the belief that their homes or ability to learn are inadequate. However, Delano *et al* found that, with home dialysis, inner-city blacks had as good an outcome as middle class whites (15). Reluctance to offer a cadaver kidney to a black uremic may be based on reports of inferior patient and graft survival in black recipients (16).

AGE BIAS

Infants and very small children rarely survive maintenance hemodialysis or peritoneal dialysis for more than a year. However, Najarian *et al* reported that kidney transplantation is more likely to achieve a longer survival in this age group; 10 of 12 recipients, whose mean age was 25 months at the time of transplantation, were alive after a mean age of 68 months (17). At the other extreme, mean age of treated uremic patients in the United States increased to 52 years in 1982 (18); approximately 54% of new hemodialysis patients are older than 55 years. While some reports in the 1970's expressed enthusiasm for the performance of kidney transplants in the geriatric population, (*vide supra*), such operations are now rare. Now CAPD and hemodialysis are uniformly applied to patients older than 70, and offered as the preferred treatment to nearly all over age 60. One year survival after beginning uremia therapy is age-related. When comparing outcomes in several series, it is essential to select equivalent ages in patient groups. This point is illustrated by contrasting survival up to age 60 with that of older patients; in this context, it is pertinent to note that in the United States Medicare series (10), only 70% of men between 65 and 74 years of age lived one year contrasted with 89% of those aged 25 to 34 years.

The foregoing data suggest that we recommend a renal transplant for uremic infants and children, while, with selective exceptions, geriatric patients are best managed by hemodialysis or CAPD. Individualization of assignment to uremia therapy requires a mixture of art and science. In terms of the risk to life imposed by a kidney transplant, a 55-year-old, Type I diabetic may be medically 'older' than a 65-year-old polycystic disease patient.

WORLD PLANNING

As an initial step toward planning renal failure programs, developing Third World countries might analyze exactly how high on their 'must' list kidney failure ranks. There is little point in considering a kidney tranplant program in the midst of overt starvation, high perinatal mortality, or the crushing need for population control. Delaying the need for dialysis by dietary protein restriction is an interim step in implementing universal uremia therapy. Until intestinal dialysis or oral sorbents improve to the point where their use gives protracted survival there is little likelihood that treatment for uremia can be extended to underdeveloped nations. Geriatric patients *de facto* will continue to be excluded from uremia therapy in all but the affluent nations for the remainder of this century.

SUMMARY

Uremia in the elderly responds to standard therapy of dialysis and kidney transplantation. Pressures imposed by economic realities limits uremia therapy to only a minority of people now living. For the foreseeable future, it is unlikely that developing nations will be able to devise treatment strategies for the geriatric population with failed kidneys.

REFERENCES

1. Degoulet P, Reach I, Rioux P, Jacobs C, Legrain M: Risk factors in chronic haemodialysis. Proc Eur Dial Transplant Assoc 17:149- 54, 1980.
2. Lundgren G, Fehrman I, Gunnarsson R, Lindholm B, Tillegard A, Ost L, Groth CG: Cadaveric renal transplantation in patients over 55 years of age with special emphasis on immunosuppressive therapy. Transplant Proc 14:601-4, 1982.
3. Nicholls AJ, Waldek S, Platts MM, Moorhead PJ, Brown CB: Impact of continuous ambulatory peritoneal dialysis on treatment of renal failure in patients aged over 60. Br Med J (Clin Res) 2888:18-9, 1984.
4. Ost L, Groth CG, Lindholm B, Lundgren G, Magnusson G, Tillegard E: Cadaveric renal transplantation in patients of 60 years and above. Transplantation 30:339-40, 1980.
5. Schaefer K, Asmus G, Quellhorst E, Pauls A, von-Herrath D, Jahnke J: Optimum dialysis treatment for patients over 60 years with primary renal disease. Survival data and clinical results from 242 patients treated either by haemodialysis or haemofiltration. Proc Eur Dial Transplant Assoc Eur Renal Assoc 21:510-23, 1985.
6. Westlie L, Umen A, Nestrud S, Kjellstrand CM: Mortality, morbidity, and life satisfaction in the very old dialysis patient. Trans Amer Soc Artif Intern Organs 30:21-30, 1984.
7. Berlyne GM: Over 50 and uremic-death; the failure of the British National Health Service to provide adequate dialysis facilities. Nephron 31:181-190, 1982.
8. Taube DH, Winder EA, Ogg CS, Bewick M, Cameron JS, Rudge CJ, Williams DSG: Successful treatment of middle aged and elderly patients with end stage renal disease. Br Med J (Clin Res) 286:2018-20, 1983.

9. Valek A, Wing AJ: Development of dialysis and transplant activity in the world during the seventies of the 20th century. Z Exp Chir Transplant Kunstlich Organs 17:69-78, 1984.
10. Jacobs C, Broyer M, Brunner FP, Brynger H, Donckerwolcke RA, Kramer P, Selwood NH, Wing AJ, Blake PH: Combined reports on regular dialysis and transplantation in Europe, XI, 1980. Proc Eur Dial Transplant Assoc 18:4-58, 1981.
11. Ethics and the nephrologist: Editorial. Lancet 1:594-596, 1981.
12. Seedat YK, Naicker S, Rawat R, Parsoo I: Racial differences in the causes of end-stage renal failure in Natal. S Afr Med J 65:956-8, 1984.
13. Fuman KI, Du-Toit ED: Facilities for treatment and patients on renal replacement therapy in South Africa. A report on the 1982 registration. S Afr Med J 63:407-8, 1983.
14. Gold CH, Isaacson C, Levin L: The pathological basis of end-stage renal disease in blacks. S Afr Med J 61:263-5, 1982.
15. Delano BG, Lundin AP, Friedman EA: Successful home hemodialysis in purportedly unacceptable patients. Nephron 31:191-3, 1982.
16. Oriol R, Le-Pendu J, Chun C: Influence of the original disease, race, and center on the outcome of kidney transplantation. Transplantation 33:22-6, 1982.
17. Miller LC, Bock GH, Lum CT, Najarian JS, mauer SM: Transplantation of the adult kidney into the very small child: Long-term outcome. J Pediatr 100:675-680, 1982.
18. Hull AR, Warren E, Prati RC, Long DL, Parker TF III, Rinner S, White MG, Vergne-Marini P, Emmett M, Stephens M, Silverstein R, Lerman M, Nesser D: Dialysis: A ten year review. Seminars in Nephrology 2:90-98, 1982.
19. End-Stage Renal Disease Second Annual Report to Congress FY 1980. Department of Health and Human Services. Health Care Financing Administration, 1981.

23. CAN WE AFFORD TO TREAT EVERYBODY? THE UK VIEW

ANTONY J. WING.

INTRODUCTION

The number of patients treated for end-stage renal failure (ESRF) correlates roughly with the economic productivity of different countries (1). The higher the gross nation product (GNP) the more a country has to spend per head on health and the larger the number on treatment. Put in another way, the patient's expectation of being accepted for treatment is higher in a wealthy country than in a poor one and is almost non-existent in the developing Third World. High-cost renal-replacement therapy (RRT) has underscored the wide differences in the implicit value of human life in different countries.

The Registry organised by the European Dialysis and Transplant Association - European Renal Association (EDTA - ERA) has collected data on RRT since 1965, and has documented the achievements of European countries since the earliest days of dialysis and transplantation (2). Eighteen hundred centres in 31 countries with a total population of 574 million collaborate and individual patients are tracked as they change from one therapy to another and move between centres. This registry data base illustrates the varied approaches to ESRF adopted by countries with different levels of economic development and at different stages in the provision of high technological care.

International comparisons (3) have drawn attention to the fact that the United Kingdom (UK), although prompt to make the advance of dialysis and transplantation available through its National Health Service (NHS) in the 1960's and early 1970's, subsequently has limited deployment of these treatments. The number of patients treated has not kept pace with the growth in programs in other Western European countries.

Berlyne has been scornful of this limitation of life-saving therapy (4). Others, aware that cost containment is an inevitable accompaniment of high technology opportunities in medical care, have analysed the NHS approach to rationing hospital care (5). This article will review recent investigations (6,7) of the mechanisms of rationing and will add some personal insights into the social structures and traditions which lie behind these constraints.

INTERNATIONAL COMPARISONS

Tables I, II, and III are international 'league tables' derived from records of the EDTA - ERA Registry in 1983. Coverage was comprehensive and replies were received from over 90% of known centres in 21 countries and 85% of centres overall. These tables, which are derived from replies to the centre questionnaires, summarise the activity of each centre (3) and present the most up-to-date information available.

Table I shows the total 'stock' of patients on Dec. 31, 1983 in 30 countries reporting to the Registry. It gives the numbers on hospital hemodialysis, home

Table I. Stock of patients (pmp) alive on Dec. 31, 1983, according to country and methods of treatment.

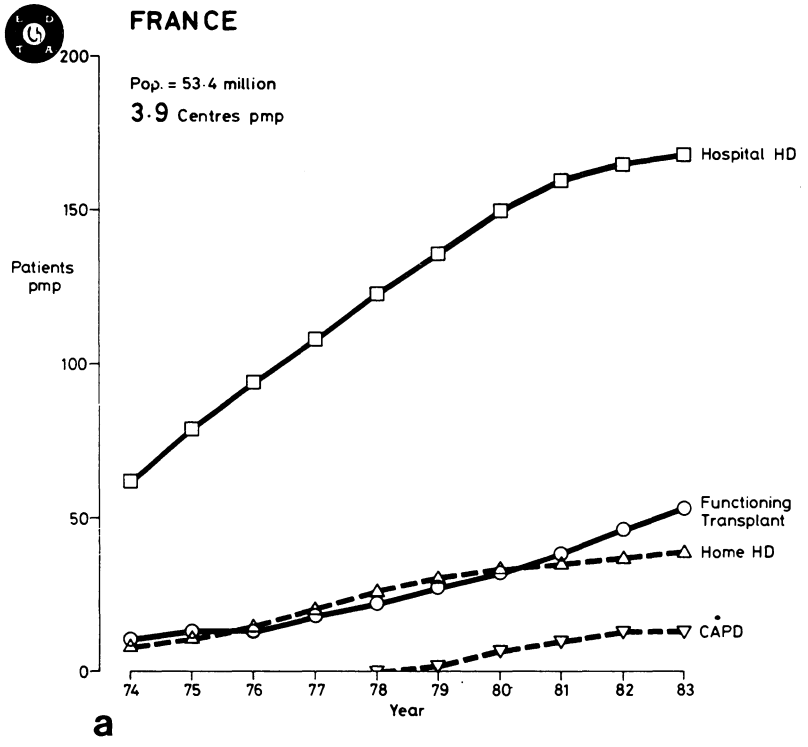
Country	Hosp. HD	Home HD	PD	Graft	Total
Belgium	201.4	11.2	16.7	127.0	356.3
Israel	231.3	16.8	27.9	34.5	310.5
Italy	256.5	16.9	21.6	15.2	310.2
Fed. Re. Germany	210.0	29.8	6.5	33.3	279.6
Switzerland	146.6	29.7	32.9	68.5	277.7
Spain	201.3	10.1	17.4	32.5	261.3
France	158.4	43.7	17.1	36.6	255.8
Luxembourg	217.5	7.5	0	12.5	237.5
Norway	53.7	1.5	5.6	161.0	221.8
Finland	47.7	0.6	34.2	135.6	218.1
Denmark	85.1	19.4	35.1	74.7	214.3
Netherlands	132.1	10.8	16.7	44.6	204.2
Austria	115.6	6.5	2.5	56.0	180.6
Sweden	78.0	13.7	28.3	58.9	178.9
Portugal	145.7	9.2	5.4	8.3	168.6
United Kingdom	27.6	39.2	27.8	68.2	162.8
Cyprus	158.3	0	0	0	158.3
Ireland	42.4	10.0	14.5	72.4	139.3
Greece	91.7	0	9.8	16.6	118.1
Yugoslavia	97.1	3.2	3.2	6.9	110.4
German Dem. Rep.	75.9	0	0.4	22.1	98.4
Bulgaria	78.0	2.6	0	0	80.6
Czechoslovakia	45.8	0.1	1.0	14.9	61.8
Iceland	60.0	0	0	0	60.0
Tunisia	33.1	0	3.1	0	36.2
Hungary	21.0	0	2.4	11.0	34.4
Poland	18.9	0.5	1.6	0.5	21.5
Egypt	11.6	0	1.3	0.7	13.6
Turkey	4.5	0.1	0.4	0	1.8
Algeria	1.3	0.1	0.4	0	1.8
Total Registry	108.2	15.2	11.4	28.7	163.5

hemodialysis, peritoneal dialysis and alive with a functioning transplant. The numbers are given per million population so that one can make comparisions. The 'stock' which is the accumulated number on treatment at one specific time, reflects the rate of new-patient acquisition and the death rate of those on treatment. National programs differ in the timing of their expansion because new centres were not opened synchronously across Europe, and, indeed, development is barely beginning in some large countries, such as Algeria, Egypt and Turkey and countries of the Eastern bloc.

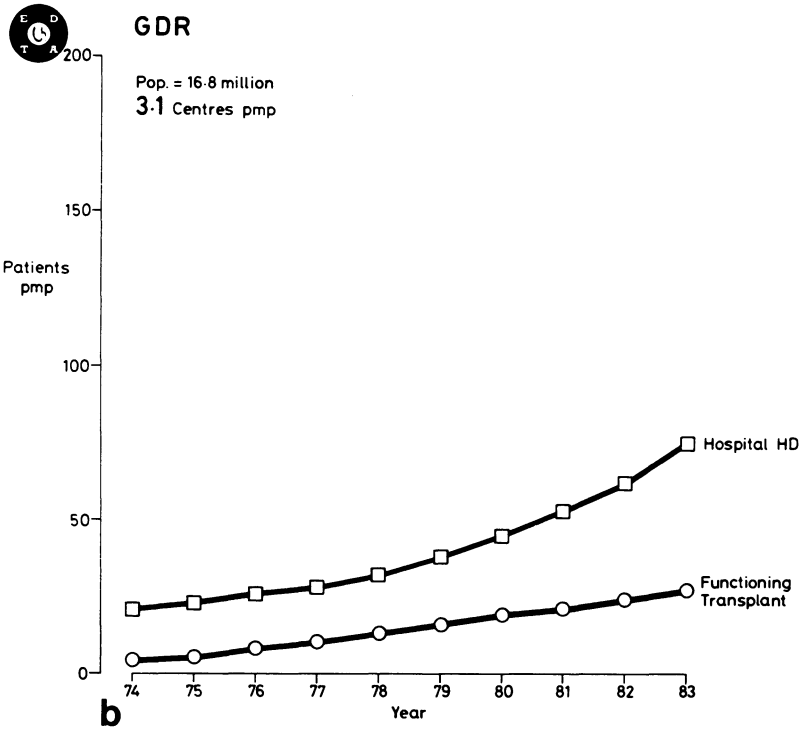
Table II which shows the number of new patients accepted in 1983, allows the

Table II. Number of new patients accepted for renal replacement therapy during 1983.

Country	Number	PMP
Luxembourg	29	72.5
Israel	254	66.8
Sweden	510	61.4
Spain	2.267	61.3
Belgium	598	61.0
Fed. Rep. Germany	3.416	55.8
Switzerland	358	55.1
Norway	222	54.1
Austria	402	53.6
Finland	220	45.8
Netherlands	640	45.7
Italy	2.586	45.5
France	2.366	44.3
Greece	379	40.8
Portugal	399	40.7
Denmark	206	40.4
Wales	98	35.0
Scotland	175	33.7
England	1.534	33.0
Yugoslavia	708	32.0
Cyprus	19	31.7
Bulgaria	254	28.2
German Dem. Rep.	466	27.7
N. Ireland	39	26.0
Eire	80	24.2
Czechoslovakia	315	20.7
Hungary	128	12.0
Tunisia	50	8.1
Poland	285	8.1
Egypt	301	7.7
Turkey	319	7.2
Iceland	1	5.0
Algeria	25	1.4


FRANCE
Pop. = 53·4 million
3·9 Centres pmp
Patients pmp
200
150
100
50
0
Hospital HD
Functioning Transplant
Home HD
CAPD
74
75
76
77
78
79
80
81
82
83
Year

a


GDR
Pop. = 16·8 million
3·1 Centres pmp
Patients pmp
200
150
100
50
0
Hospital HD
Functioning Transplant
74
75
76
77
78
79
80
81
82
83
Year

b

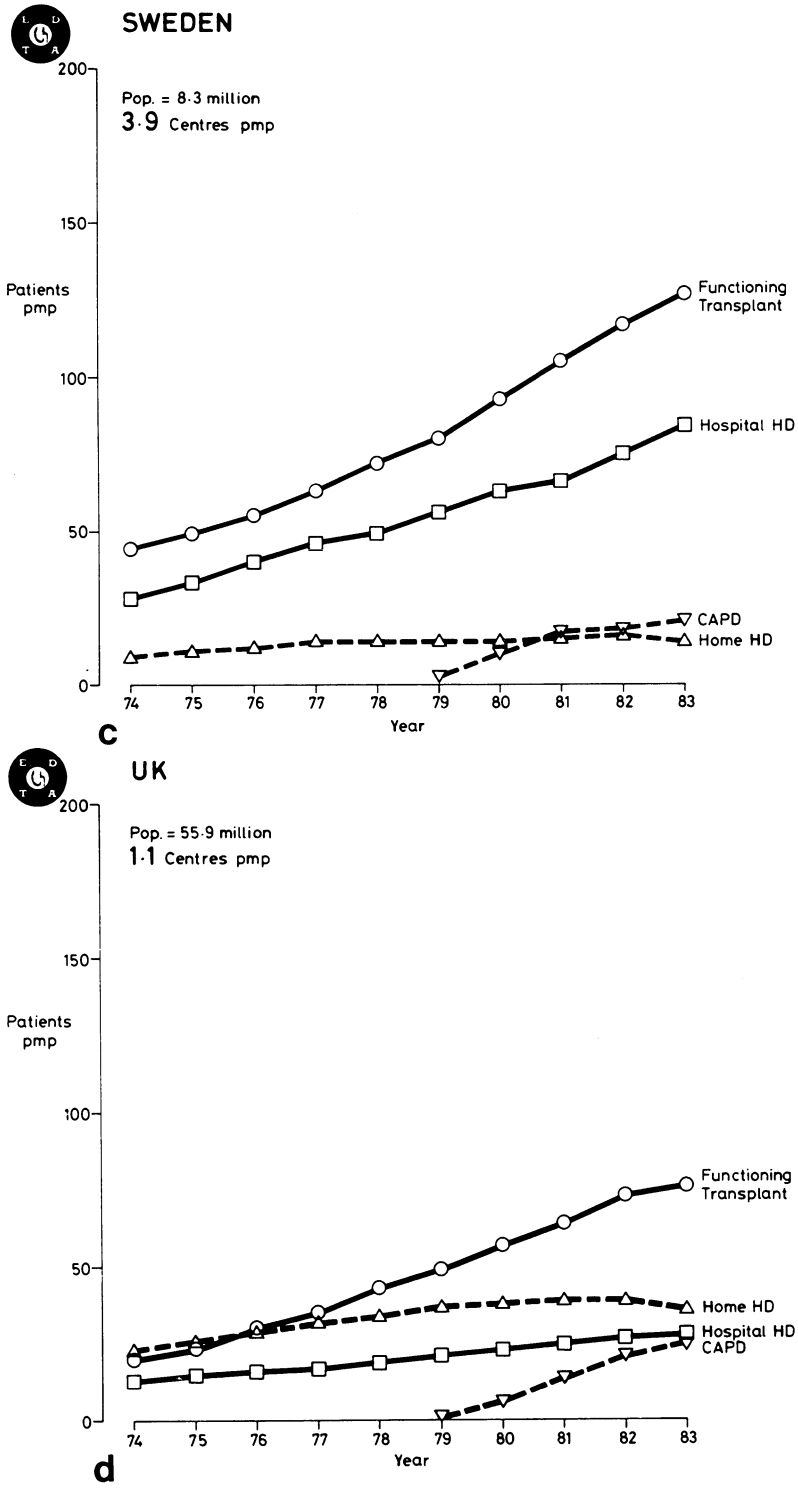


Fig. 1. Cumulative stock of patients according to mode of therapy in four European countries with contrasting styles of national programs. (France, GDR, Sweden, UK).

reader to estimate the chances of a new patient obtaining treatment. Five countries accepted over 60 patients per million population (pmp) and seven accepted less than 20. The four countries which comprise the UK accepted between 26 and 35 pmp.

In Europe, transplantation activity varies (Table III), Scandinavian countries and Switzerland - the richest country per capita in Europe - setting the pace. The UK has performed more transplants than any other European country.

Figure 1, which selects four countries, illustrates different styles of European programs. It shows the year-by-year growth in stocks of patients per million population (pmp) according to method of treatment. France is typical of other large Western European countries; it has an active hospital hemodialysis program whose rate of growth has been curtailed in the last three years. Associated with this is a low level of activity in home hemodialysis and CAPD,

Table III. Number of renal transplant operations performed in 1983, according to source of donor and country.

Country	CAD Grafts	LD Grafts	ALL Grafts	pmp
Norway	97	44	141	34.4
Sweden	202	76	278	33.5
Netherlands	350	13	363	25.9
Switzerland	165	2	167	25.7
UNITED KINGDOM	1.212	117	1.329	23.8
Belgium	198	31	229	23.4
Denmark	111	5	116	22.8
Austria	154	0	156	20.5
Israel	58	20	78	20.5
Finland	89	6	95	19.8
Spain	665	61	726	19.6
France	958	33	991	18.6
Fed. Repl. Germany	983	35	1.019	16.6
IRELAND	38	11	49	14.9
Czechoslovakia	133	1	134	8.8
Italy	410	25	435	7.7
Portugal	73	3	76	7.7
Luxembourg	3	0	3	7.5
German Dem. Rep.	102	1	103	6.1
Hungary	49	3	52	4.9
Turkey	107	40	147	3.3
Greece	5	25	30	3.2
Poland	94	5	99	2.8
Yugoslavia	0	14	14	0.4
Total Registry	6.272	597	6.869	12.0

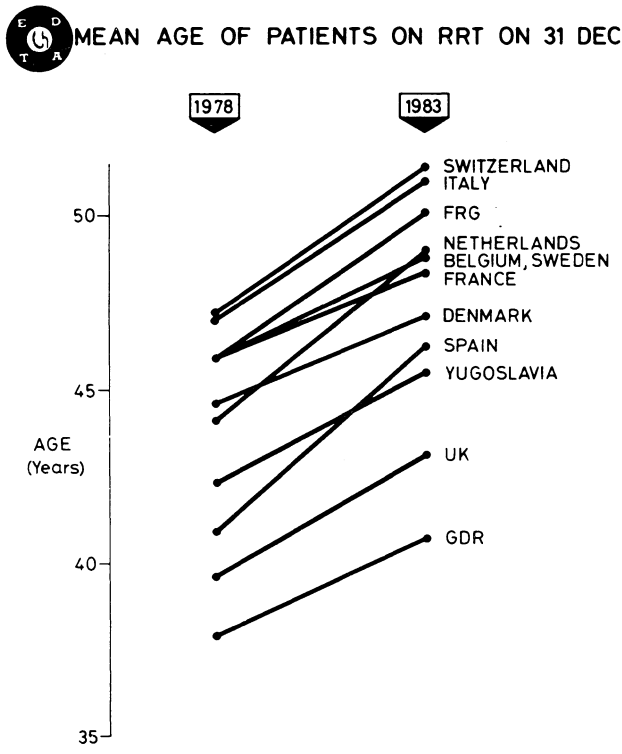


Fig. 2. Mean age of patients alive on RRT in 12 selected countries.

and an accelerating transplant program. The German Democratic Republic (GDR) represents the programs seen in Eastern Europe; here hospital hemodialysis and transplantation appear to be linked in the absence of home hemodialysis and with negligle CAPD. For the last decade in Sweden, and in other Scandinavian countries, transplantation has been the single most important contributing therapy. The UK program contrasts with the other three styles. Because of limited hospital hemodialysis, twice as many patients have been treated by home hemodialysis, although, in the last five years, with the advent of CAPD, there appears to be a decline in the number of patients treating themselves by home hemodialysis. Now all three methods of dialysis have plateaued, sustaining almost equal numbers of patients while the program has relied on transplantation for its growth.

The mean age of patients on RRT has been rising in all countries. Figure 2 shows the ages of patients in 1978 and 1983 in 12 countries. As the age of the population being treated successfully has risen it has become impossible to deny treatment to older patients. However, there is still a wide variation (Fig. 3) in the rate of acceptance of geriatric patients (aged over 65). Sweden treated over 14 geriatric patients pmp in 1983 while GDR managed only one. The UK put only

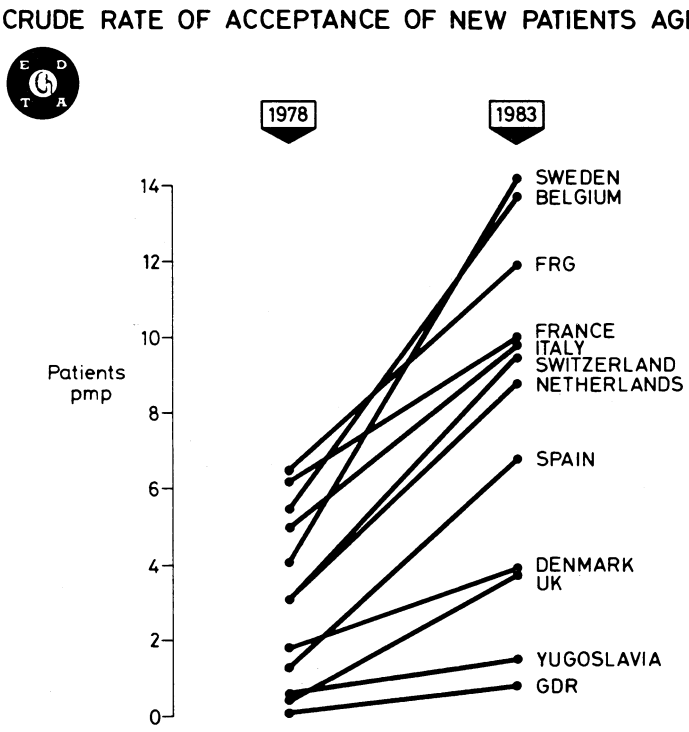


Fig. 3. Crude rate of acceptance of new patients age over 65 in 1978 and 1983 in 12 selected countries.

four geriatric patients pmp onto treatment, France and Italy almost 10 and Federal Republic of Germany (FRG) approximately 12. Figure 4 shows the crude rate of acceptance of new patients in these large four Western European countries. During the last three years, when growth began to be constrained, the rate of acceptance has remained stable in accordance with the patterns developed in each country. There is no reason to suspect that clinical need differs in these countries. Treatment rates appear to be governed by the availability of facilities and by the resources committed, notably the number of specialists.

Data from the four countries, whose different styles were illustrated in Fig. 1, have been analysed to show the patterns adopted for geriatric RRT (Fig. 5). Transplantation has been successful in this age group in Sweden and UK. Peritoneal dialysis has made an important contribution in all except for GDR and home hemodialysis has played a part in France and UK. However, the major contribution to geriatric RRT is hospital hemodialysis. It is chiefly because the program of geriatric hospital hemodialysis is so limited in GDR and UK that these countries do not offer treatment to many patients over 65 years old.

CRUDE RATE OF ACCEPTANCE OF NEW PATIENTS 1981-1983

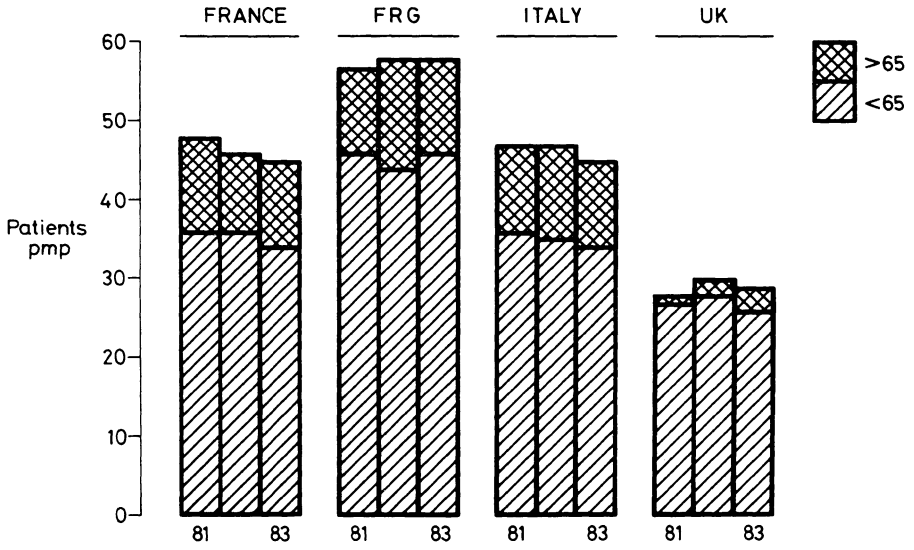


Fig. 4. Crude rate of acceptance of new patients aged under and over 65, in four large Western Europeans countries, 1981 - 1983.

METHOD OF TREATMENT OF PATIENTS AGED >65 ON 31 DEC. 1983

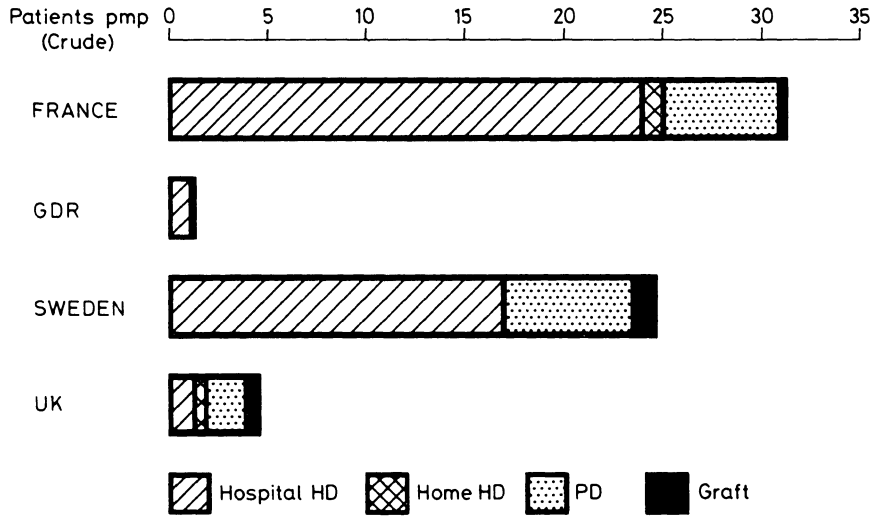


Fig. 5. Method of treatment for patients aged over 65 on Dec. 31, 1983 in four European countries with contrasting styles of national programs.

RATIONING OF RRT IN UK

The limited hospital hemodialysis program available for ESRF patients in UK has forced clinicians to choose outpatient therapies as much as possible. Patients suitable only for hospital hemodialysis would block this program. Therefore, before CAPD became available, only patients for whom transplantation or home hemodialysis were potential options were accepted. In particular, this excluded elderly patients and diabetics (8). CAPD has altered the picture, because it provides a mode of therapy that is suitable for geriatric patients and moves patients quickly to outpatient self-care. Some fear that many patients accepted for CAPD will have to be transferred to hospital hemodialysis, either temporarily or permanently, but successful transplanation in elderly patients (9) offers hope to hard pressed hospital renal units.

British renal units are large; the average centre treats nearly 200 patients on integrated therapies, but these centres are sparsely distributed at 1.1 pmp compared to 6.4 in Italy, 5.0 in Spain, 4.9 in FRG and 3.9 in France (3). Even Eastern European countries have more centres - 3.4 in Yugoslavia and 3.1 in GDR.

In 1982 there were the equivalent of 87 whole-time career posts in nephrology in UK (7). This works out at 1.5 specialists pmp, far fewer than most Western countries, which have an estimate of 10 pmp. With a small number of centres and of specialists, it seems likely that a limited number of nurses are working in nephrology. The emphasis on outpatient therapies and self-treatment based on a small number of centres seems to have produced a cost-effective solution to the problem of providing RRT in UK.

The outside observer would expect to find that UK nephrologists are turning away many patients from their units. However, most nephrologists claim that they are treating almost all the patients referred to them. Therefore it was suggested that selection was being made by non-specialist physicians who were acting as 'gatekeepers' to the system. To test this hypothesis, Challah et al (6) devised a questionnaire containing 16 brief case histories exemplifying medical and social problems which would militate against successful therapy; then they asked a random selection of doctors whether they considered these patients suitable for treatment. UK nephrologists rejected 4.7% $\pm$ 0.3 of the 16 patients, UK general practitioners 6.9 $\pm$ 0.3 and UK consultant physicians 7.4 $\pm$ 0.2. North American doctors rejected 0.3, Western European colleagues 3.6, and Eastern Europeans 7.5 of the 16 cases. The results emphasized the difference between selection practices in UK and other countries, particularly in North America. They also show that referring physicians are out of step with the opinions of British nephrologists. In the UK referral is controlled not by the specialists but by the generalists and therefore the latter control entry of patients to programs such as those for ESRF.

The patient cannot refer himself to a specialist under the British NHS. The

consultant advises this only when he is asked to do so by the primary care physician who retains responsibility for the patient. The British general practitioner is the backbone of the NHS and his role is crucial in the rationing of hospital care. Many of his clinical decisions relate to whether his patients need further investigation or referral for specialist advice. At his best he is supremely professional, protecting his patient from unnecessary tests and time-consuming hospital visits, reserving scarce facilities for those who are in most need of them. At his worst, he may seem paternalistic and his professional pride may make him appear resentful of any request for a second opinion. His role in our society may owe something to his historic inheritance from the country squires and colonial administrators of bygone years. He never gets sued.

NHS consultants, both nephrologists and transplant surgeons, are salaried employees. There is no financial incentive for them to treat more patients. The funding of their units is based on an overall budget and some now operate clinical budgets, which enable them to take their own management decisions such as switching resources from hemodialysis machines to CAPD fluid, to implement dialyser re-use and to weigh the high cost of cyclosporin against that of azathioprin. In the present economic climate it is very difficult to increase the funding of a program. We are coerced into doing the best we can for as many as possible with a finite sum of money.

THE ETHICS OF FINANCIAL CONSTRAINT

Health care resources are not infinite. The exercise of clinical and professional freedom is constrained by financial reality (10). This makes an ethical impact on doctors who must respond by showing responsibility for the quantum of resources apportioned to them by the societies in which they work. If they do this, there remains some prospect that they can retain the confidence of their societies and avoid increasingly rigorous external control (11).

How powerfully should the nephrologists press the claims of patients with ESRF? The dilemma for society arises because of the success of treatment. The treatment of geriatric patients with ESRF produces satisfactory outcomes. Inevitably more will be treated in wealthy societies than in the poorer (1). The UK spends approximately £350 per capita annually on medical care. The FRG spends two and one-half times and USA three and one-half as much. Salaries of doctors and nurses are lower in UK but the cost of dialysis hardware is linked to the dollar. Tragic choices are forced upon us (12). In the UK these appear particularly stark because of traditional expectations. Our program for ESRF probably is cost effective but we are forced to inquire whether it is humane (8).

Agonising over the patients we cannot treat makes us more determined to refine present methods to a less expensive package. One answer could be found in cheaper methods of blood purification. Another, ready to hand, lies in more

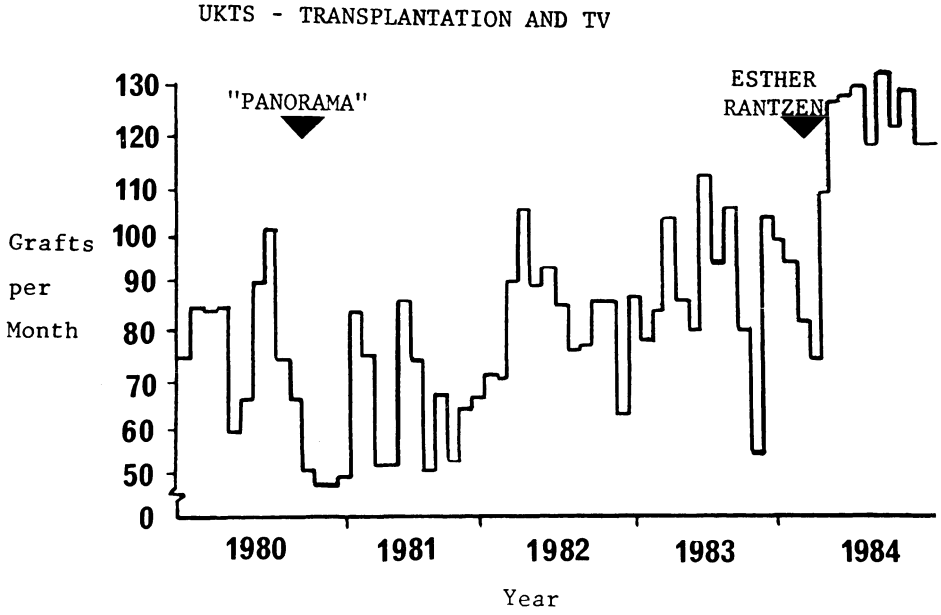


Fig. 6. Monthly number of cadaver transplants performed in UK in 1980 - 1984 to show the impact of BBC Panorama Program in 1980 and of Esther Rantzen's publicity in 1984 (UKTS data).

efficient co-ordination of integrated therapies. Transplantation is the least costly alternative and the more a national program incorporates transplantation, the more cost-effective it will become. The prospect of an enhanced quality of life attracts most patients to transplantation. Modern immunosuppressive regimes carry less risk even to older patients. The cadaver organ, therefore, becomes a part of a nation's resources, and we begin to feel an ethical compulsion that this resource should not be wasted. In the UK there is deep professional resistance to non-related, live-organ donation.

Modern high-technology medicine commands great media interest. The media also are highly influential in determining attitudes to organ donation. TV programs have made both an adverse and a favourable impact on renal transplantation in UK. An infamous BBC Panorama (a current affairs non-scientific show) program on brain death halved the rate of cadaver transplantation. A TV campaign by interviewer Esther Rantzen, seeking a liver graft for a small boy, had the effect of doubling kidney transplantation (Fig. 6). Such a caring response of the society which we serve is a profound encouragement to us all.

ACKNOWLEDGEMENTS

The EDTA - ERA Registry depends totally on voluntary collaboration of the staff of centres throughout Europe. Their hard work in completing returns is acknowledged. Tables I - III and Fig. 6 are reproduced with the permission of Dr. B. Bradley, UK Transplant Service.

REFERENCES

1. Wing AJ. Treatment of renal failure in the light of increasingly limited resources. Contr Nephrol 1985; *44*: 260-275.
2. Wing AJ, D'Amaro J, Lamm LU, Selwood NH. Evolving Methodologies in Computerised European Registries. Kid Int 1983; *24*: 507-515.
3. Kramer P, Broyer M, Brunner FP et al. Combined Report on Regular Dialysis and Transplantation in Europe, XIV, 1983. Proc EDTA - ERA 1984; *21*: 2-68.
4. Berlyne GM. Over 50 and uremic = death. Nephron 1982; *32*: 189-190.
5. Schwartz WB, Aaron HJ. Rationing hospital care: Lessons from Britain. New Engl J Med 1984; *310*: 52.
6. Challah S, Wing AJ, Bauer R et al. Negative selection of patients for dialysis and transplantation in the United Kingdom. Br Med J 1984; *288*: 1119.
7. Jones NF, Goodwin FJ, Roberts AH. Manpower and workload in renal medicine in the United Kingdom, 1975-1982. Br Med J 1984: *288*: 992-994.
8. Wing AJ. Why don't the British treat more patients with kidney failure? Br Med J 1983; *287*: 1157.
9. Taube DH, Winder EA, Ogg CS et al. Successful treatment of middle aged and elderly patients with end stage renal disease. Br Med J 1983; *286*: 2018-2020.
10. Owen D. Clinical freedom and professional freedom. Lancet 1976; *1*: 1006.
11. Wing AJ. The impact of financial constraint in Decision Making in Medicine. Ed CG Scorer and AJ Wing. Arnold, London 1979; 151-164.
12. Calebrese G, Bobbit P. Tragic Choices. Norton, New York 1978.

24. IT IS HAPPENING HERE

THEODORE R. REIFF, M.D.

INTRODUCTION

A previous paper (1) described some suggestions (2) for cost containment made by the administrator of the Health Care Financing Administration - the U.S. Federal Government agency, which controls Medicare, Medicaid, and the Professional Review Organizations. As a 'cost-saving initiative', the Health Care Financing Administrator proposed to encourage life termination of older persons covered by Medicare. The method entitled 'Encourage Adoption of Living Wills' would have encouraged older persons to sign documents that would preclude life-sustaining medical care. According to this proposal 'the cost savings from a nationwide push toward living wills is likely to be enormous. Over one-fifth of Medicare expenditures are for persons in their last year of life. Thus in FY (fiscal year) 1978, $4.9 billion will be spent for such persons and if just one-quarter of these expenditures were avoided through adoption of 'living wills', the savings under Medicare alone would amount to $1.2 billion. Additional federal savings would accrue to Medicare, the VA and Defense Department health programs'.

The government's Advisory Council on Social Security has endorsed the concept of living wills, has recommended that people should be offered an opportunity to draw up such a document when registering for Medicare, and said that information on the wills could be supplied at local social security offices. The advisory council said it 'encourages' the 36 states that do not recognize living wills to recognize them (3). The method of 'encouragement' recommended by the HCFA administrator was 'withholding Federal funds' from those states which did not pass living-will legislation.

Although most would agree that elderly human beings should have the right to refuse radical or inappropriate heroic life sustaining procedures, the hazard is that what starts out as a right, may soon become an obligation, namely to forego expensive life sustaining care.

A former social security commissioner said: 'We must ask, how much money do we want to spend on cases where death is more or less inevitable in a short

period of time'? A congressman picked this up and stated that the government 'can literally go broke trying to keep folks in this society alive'. Another stated 'the cost of these things requires a line to be drawn, but no one wants to talk about it now'.

In an interview in the August 1982 issue of *Science*, the Journal of the American Association for the Advancement of Science, Dr. Robert Butler, founding director of the National Institute on Aging, saw 'great danger' in the current trend and recalled that a white paper had been circulated in the Department of Health and Human Services urging support of right to die legislation because it could cut health costs.

Since the living-will suggestion was made, I know of numerous instances where elderly patients have been denied adequate diagnostic and therapeutic medical care because of 'cost containment' pressures on hospital and physicians. These pressures also have resulted in denial of hospitalization and inappropriate shortening of hospitalizations of some elderly patients, who, for similar illnesses, may require longer periods of treatment than do younger persons.

The Advisory Council on Social Security also has recommended that the eligibility age of Medicare be 'advanced' from 65 to 67 - a move that would deprive persons 65 and 66 years old of Medicare coverage. HCFA's cost-containment memorandum contained an additional example of policies that tend to decrease Federal expenditures, at the expense of elderly persons. In 1973 Congress fixed the Medicare Part B Deductible at $60 per calendar year. The suggestion, euphemistically entitled 'Dynamic Part B Deductible', recommended increasing the deductible amount in future years, calculating that a $15 increase would reduced Medicare outlays by about $200 million. The administrator noted that there would be no system-wide savings, only a transfer of expenditures from the Federal budget to the private sector. The term 'private sector' meant (but did not say) that older persons would pay more. The HCFA administrator noted 'this proposal would undoubtedly be strongly resisted by senior citizen groups such as the American Association of Retired Persons and the National Council for Senior Citizens, since it would increase beneficiary out-of-pocket expense'.

In addition to increasing the amount older persons have to pay for their health care, the Health Care Financing administrator recommended rescinding of previous Federal law, which required states to reimburse skilled and intermediate-care facilities (ICF) on a reasonable, cost-related basis. This change it was said would 'reduce state reimbursement to SNF's and ICF's which, in turn, would lower the amount of Federal matching'. The administrator noted 'there would probably be considerable opposition to the proposal' and that 'some consumer groups would oppose it on the grounds that state rates would be too low to provide the quality of care that Medicaid patients need'. What HCFA recommended was to reduce reimbursement for nursing home care below what HCFA itself felt to be reasonable costs. This type of policy has contributed to the increased morbidity and mortality seen in nursing-home patients deprived of good care.

In 1982, the Health Care Financing Administration solicited research proposals, which would reduce costs of long-term institutional care for elderly persons. When the then-administrator of HCFA was asked whether her agency was interested in proposals, which would improve the quality of long-term care of elderly persons without increasing or decreasing costs, the negative reply was received that the focus of that agency was to reduce program costs (4).

U.S. Government policy to contain cost 'at all cost' namely Medicare regulations, which determine reimburseable amounts for medical care, act as a disincentive to physicians to provide good medical care to older persons. Medicare reimburses for general medical care, x-ray and other radiographic procedures, laboratory tests, electrocardiographic procedures, etc. at 80% of 'usual, customary, and reasonable' fees without any yearly dollar limit. For psychiatric outpatient evaluation and care, Medicare now reimburses at 62.5% of 'usual, customary, and reasonable' fees with a maximum payment of $312.50 per year. These days $312.50 will pay for hardly more than a consultation and few follow-up visits. As a result, older persons with emotional disorders, many of which have been shown to respond well to psychotherapy, are treated almost exclusively with psychopharmacologic agents (5).

Of course, these may be important therapeutic adjuncts, but they should not necessarily constitute the main form of treatment. Because older persons are more prone to side effects, idiosyncratic reactions, toxicity, etc., from psychopharmacological agents, inappropriate management of emotional disorders in the elderly can increase morbidity and mortality considerably. This is an immense problem because hundreds of thousands of older persons are being treated inappropriately. In effect our government is telling us it is not worth spending money on appropriate care of older persons.

Another example of cost containment is the Federal Government policy toward reimbursement for physician attendance on nursing-home patients (6). Initially, in order to set minimum standards of physician attendance, this policy stated that nursing home patients covered by Medicare must be seen by physicians, at least once a month. When fiscal constraints came to determine this policy, the government and their third-party carriers distorted the provision so that Medicare would provide for only one physician visit per month. This perversion of intent has encouraged some members of the medical profession to neglect the institutionalized elderly. The U.S. Senate Special Committee on Aging described the plight of nursing home patients by entitling its report, (7) 'Doctors in Nursing Homes: The Shunned Responsibility'. This title and the report are stinging indictments of our attitudes and practice toward the dependent institutionalized elderly.

In 1980, to thousands of 'health care providers' - hospitals, nursing homes, clinics, physicians, pharmacists, etc. - in an area covering several states a Blue Cross/Blue Shield Medicare intermediary, acting under authority of the Health Care Financing Administration, sent (8) a notice identifying by name, and

without his permission, a patient who it said was overutilizing emergency room services. The notice warned the health care-providers about the individual, who was identified by name and social security number, and labelled him as a 'professional patient'. Aside from violating his privacy by disseminating confidential information, such a notice may deny care to a patient who may have a real need. After I expressed concern over this matter to a member of the U.S. Senate Special Committee on Aging, the senator wrote (9) the administrator of the Health Care Financing Administration saying that this seemed to be not only an invasion of privacy but to run the risk of denying care to people who might need it.

The concept of cost containment is sweeping the U.S.A., and often is supported by labor interests, and by industry and business groups that operate under no mandated cost containment. Several states have passed legislation limiting the development and growth of health care services. It is said that we are spending over 10% of our gross national product on health care services and that this is too much. Perhaps, if we spent more on life-sustaining and valued activities and education, we would spend less on more destructive activities.

Physicians and the public exhibit much fear and defensiveness concerning the high cost of medical and health care. Our goal should be efficiency, avoidance of waste, and appropriate use of health services. Good medical and health care is and will continue to be expensive, nevertheless, this does not mean we should tolerate a lower fiscal priority for good health care.

'Cost containment' actually results in reduced service to patients and suppression of improvements and advances in medical care and technology. We are seeing evidence that the public now resents expenditures for health care of the elderly and others in our society who 'do not contribute to the economy'.

Although it was of a different order of magnitude, during the early days of World War II, Germany's National Socialist Government initiated a 'cost containment' program under which medical personnel put senescent institutionalized and other 'non-productive' Germans to death by gassing and lethal injection. The German people were prepared for the philosophical acceptance of this 'pragmatic' practice by techniques most of which were based upon socioeconomic arguments (10) that resemble some of those emanating from governmental and health-care administrators in the U.S.A.* Under this 'euthanasia' program over one-quarter of a million Germans, mostly the elderly, emotionally ill, and mentally retarded were put to death.

American-Medical-News, the weekly newspaper of the American Medical Association reported that the Health Care Financing Administrator had questioned the right of every American to health care stating, 'underlying that mortality is the assumption that (the right to health care) is an unlimited right. In no other area have we made this kind of decision'. He went on 'The right to

*Refer to Appendix.

housing does not mean a mansion, and the right to food does not necessarily mean a feast'. In an editorial, the *American Medical News* welcomed the author of that statement to what it called 'the world of reality'.

When he was questioning expenditures for mental health hospitals in Germany during the 1930's before the institution of the 'euthanasia program', Dr. Joseph Goebbels', said 'palaces for the insane and hovels for the workers are things of the past'. Only afterwards did they apply the technique developed for the euthanasia program, on a larger scale for the genocide program. The reader should not draw too close an analogy between current cost containment efforts in the U.S.A. and the enormity of the Nazi experience, but the memory of that period should make us pause and reflect during the current period of fiscal pressures.

Recently I have attended hospital meetings where discussion was held regarding the setting up of committees, which would decide in which high-cost patients with poor prognoses therapeutic measures could be terminated as a cost-saving mechanism. At times, because of cost containment pressures, elderly patients are denied diagnostic procedures such as C-T scans, which in some instances could have detected treatable disease at a stage when it could be treated.

The October 21, 1983 issue of American Medical News reported that the president of Blue Shield of Massachusetts referred to public reaction to the unwillingness of his company to pay for a liver transplant as 'a virtual frenzy in the media'. He thought it was 'outrageous' that candidates for transplant procedures and health care professionals would go to the media for support in getting the procedure funded. Perhaps the real 'outrage' is that human beings in our society have to go to the media because our institutions and government have failed to provide resources for life-sustaining medical care.

At the present time Federal and State Governments are providing 'disincentives' to encourage hospitals and physicians not to treat high-cost patients'. The prospective method of payment and caps on hospital payment by Medicare are yielding profits based upon reduced service and curtailment of care to high cost patients.

On March 27, 1984, in a speech to the Colorado Health Lawyers Association, the Governor of the State of Colorado was reported to have said that terminally ill old people have 'a duty to die and get out of the way'. While there would be little argument that individuals should have the right to reject recommended treatment, the danger is that what may be a right could soon become, by societal pressure, an obligation to die. To paraphrase the words of Santayana, 'Those who do not learn from the past may be condemned to repeat it'. It appears that, if current policy and practice is not reversed, it may, for reasons of fiscal expediency, lead to 'gerocide'. Thus I make a plea for the health professions, especially the medical profession, to stand fast as advocates for optimal care based upon the best interest of the patient. In so doing, I urge the government to consider that excess profit containment is a more ethical method to conserve scare health care dollars than is cost containment.

REFERENCES

1. Reiff TR. It can happen here. JAMA 1978;30:2761-2.
2. Additional cost-saving initiatives-action. Health Care Financing Administration, June 4, 1977.
3. Rosenblatt R. Boston Sunday Globe 1983, Dec 18:
4. Communication with administrator, Health Care Financing Administration, 1982.
5. Reiff TR. A close look at the care of the elderly. Hosp Prac 1982; (Feb):15-6.
6. Reiff TR. We're doing a third-rate job for the aged. Medical care of the aged: a national scandal. Prism 1973; (Dec): 23-8.
7. Nursing home care in the United States: failure in public policy, Supporting Paper no. 3. Doctors in nursing homes: the shunned responsibility. Subcommittee on aging, United States Senate, February 1975.
8. Medicare Part B Communication No. 132, RE: HIC No.-- A, February 26, 1980.
9. Letter from Senator Quentin Burdick to the administrator of the Health Care Financing Administration, May 23, 1980.
10. Aziz P. Doctors of death. In Aziz P. Operation gentle death. Geneva: Ferni Publishers, 1976:20-3.

APPENDIX

STATEMENTS EMANATING FROM THE THIRD REICH 1930's-1940's

'The economic burden represented by people suffering from hereditary diseases is a danger for the state and for society. In all it is necessary to spend 301 million reichsmarks per year for treatment, without counting the expenditures for 200,000 drunkards and about 400,000 psychopaths'.

'The maintenance and care of the mentally deficient, feeble-minded and of psychopaths gobble up considerable sums of money which must be paid for by active people and which affect their standard of living. Simply imagine the miserable housing which could be improved with this money'.

'Let us take the case of a life span of fifty years. It is simple to calculate the enormous capital in the form of food, clothing and heating which is subtracted from the national wealth for an underproductive objective. A nursing staff of several thousand people is necessary for this totally unproductive task. It is painful to note that all these generations of nurses grow old alongside these empty human envelopes'.

Changes were made in the arithmetic textbooks. Old arithmetic problems were eliminated and in their place appeared:

'A mental patient costs 4 RM each day. A crippled person costs 3.50 RM per day. In many cases, a civil servant earns only 4 RM a day, an office worker barely 3.50 RM, an illiterate worker less than 3 RM per family head.

A. Analyze these figures on the basis of the fact that in Germany there are 300,000 mental patients in the institutions.

B. On the basis of 4 RM each per day, what is their total cost each year?

C. How many marriage loans of 1000 RM each could be obtained each year with this money?'

'Iron has always made a country strong; butter and lard have, at most, made people fat'.

Herman Goering
(In a speech in Hamburg referring to the rationale for the government's rearmament program during a decline in the nation's standard of living)

DISCUSSIONS

DISCUSSION AFTER PRESENTATION BY DR. ROSEMARY H.M. MEIER

DR. FISHER: It is important to have a clearer definition of 'aging' and to agree about who the elderly are. Dr. Meier, you made some reference to the 'young-old' and the 'old-old'. Could you expand on that?

DR. MEIER: Until recently, the aged were lumped together as if they were a homogeneous group. Aging is defined arbitrarily rather than biologically as beginning at age 65, so we are looking at people who may be between 65 and 100 *plus* - a long period of time. Men's lives tend to be marked by vocational or occupational landmarks and women's by biological events. For example, at least one-third of a woman's life is lived after the menopause. The span - three score years and ten no longer has the significance it had in Biblical times, even though we have perpetuated it as a marker. People may live 15 to 20 years beyond that. The young-old, a group who are around 70 and are healthy are biologically, medically and socially much different from those between, 75 and 85, the old-old, and we now have an increasingly large group of the frail elderly, who are 85 *plus*.

DR. OREOPOULOS: I have a question about acceptance of death. If we go through life not having accepted death, how can we, at the end, switch and accept death? Is acceptance something that will come by itself?

Can a doctor, who has not accepted death, tell his patient to accept death?

DR. MEIER: This question brings in two associations: That of the older persons and the professional looking after them and, the particular view of life and death that each holds. I hope, by emphasizing the sense of development and sense of continuity of the self, to show that acceptance of death and making oneself ready to die will take its place as part of that continuum.

The concept of developmental stages contains many dimensions and psychological, psychosocial and, often unconscious, mechanisms. The idea of 'subception', though it does not constitute denial helps us understand how somebody for example, may, seem to the staff to understand the patient's condition and to know that theyre dying. To their closest relatives they may seem to have a different view and, to an intimate companion, to have yet a different

view of their impending death. The concept of developmental maturing includes the idea of one's place in the life cycle and also the place of death in life.

Those are highly individual developments, which should occur during every life, but they are not things one can have imposed on one, or even try to impose on another our context of their person's our philosophy or beliefs.

DISCUSSION AFTER PRESENTATION BY DR. GRYFE

DR. REIFF: Your slide of detriments in organ system function showed that the detriments lie within a spectrum of decreasing functions depending upon degrees of atrophy that are superimposed on physiologic aging.

The maximum line, the 100 per cent, falls in the third decade of life, from about age 30 function keeps decreasing. Theoretically, with proper hypertrophy and exercise and stimulus, one should be able to increase to the maximum line.

Do you know any data, which shows the maximum degree of hypertrophy of which human beings are capable with proper stimuli? Is it possible to surpass that 100% line during the aging process?

DR. GRYFE: I don't know of any specific studies. Cross-sectional studies upon which these curves are based show individuals in their 7th, 8th, and 9th decades, who perform at a level of poorer individuals in their 2nd, 3rd and 4th decades.

I have no idea what they represent, because they are examined only in a cross-sectional way. I don't know if they would show an 'exultation' - a term coined by Mateef to describe that kind of rejuvenation.

DR.REIFF: Some data have just been released that contradict our belief that the glomerular filtration rate decreases about one-half of one per cent per year after age 30.

A group has been identified who seem to show an increment in renal function with age, and a group also that does not show a decrement or an increment. Thus it is possible that some individuals have the capacity to exceed the 100% line.

K. MONCKTON: We have seen an extraordinary increase in average life expectancy in this century. What about life span? This is important because if, by the year 2050, we expect people to live to 150 years, we are going to have to make great changes in our views. Does man have a finite upper limit of life expectancy?

DR.GRYFE: Do you wish me to be speculative or be factual?

K. MONCKTON: Either.

DR. GRYFE: As far as I know, the longest documented human survival is 113 years, and that in a Canadian. Population data show a phenomenon referred to as 'squaring' the population curve. Mortality rates at given ages of any given cohort show that more and more people are surviving into the 7th, 8th and even 9th decades. The individuals surviving past the 8th, 9th and into the 10th decade are a very small proportion and, as a percentage of those who get to 60, probably

no more than 100 years ago. We are not observing any real increase in life span, biologically. We have an increase in life expectancy, particularly life expectancy at birth.

In other words people reaching the age of 65 today have only a slightly better chance of reaching the age of 85 than their counterparts of a century ago. We can only claim to be shifting that expectation further to the right - and to be influencing life span, if we show that the curve, instead of sloping downward from about age 70, moves out towards 80 or 85 or 90, before steeply sloping downward.

I know of no data, that have demonstrated that. Currently some believe that some shifting is taking place at the very tail end of the curve; in other words, proportionately, more people are surviving through the 8th, 9th and 10th decades than previously.

DR. SCHREINER: For over 10 years now, a colleague of mine has been studying the renal 'compensatory hypertrophy factor' - a substance which is organ specific and is able to stimulate the renal cell. We don't know what it is yet, but we know a lot about it. It appears that the kidney elaborates an inhibitor to this substance which opens up the possibility that there is proportionate decline in the inhibitor to the tropic substance. The end result - compensatory hypertrophy - may go either way because there are two separate systems in the feed-back group.

DR. REIFF: That information is important to other areas beside nephrology, because cells have a limited number of replications - they are not immortal. This gives us the idea that the life span ultimately may be limited by our cellular replication potential. Connective tissue cells are capable of replications dependent upon age of the organism; fetal fibroblast cells are capable of about 50 replications; normal adult fibroblast cells about 30 replications, and senescent adult fibroblast cells about 20 replications. If one extrapolates that line of decreasing number of replications, you reach zero replication somewhere beyond 125 to 150 years.

People who have limited life span - those with progeria - at age 10 have only perhaps five to seven replications instead of a normal child's 40 replications.

However, substances, which seem to be neurohumoral substances, are capable of enhancing cell replication potential *in vitro*. By adding some of these neurohumoral substances, you can increase the cell replication potential, by about 50%. Studies on kidney tissue could make it possible to demonstrate that that finding is universal, as Dr. Shreiner mentioned. One should also be looking for inhibitor substances because for every biological process capable of being stimulated and enhanced, usually there is an inhibitory process.

DR. GRYFE: I was handed this question: 'If we are programed to age, can we deprogram the system in our genes, and how irreversible is its course?'

DR. REIFF: Work in cell biology indicates that perhaps this program can be altered. In fact, many neurobiologists looking at cell replication potential may challenge our concept of limited replication potential of neurons.

In fact, all cells are theoretically totipotential and probably their replication is limited by some type of inhibition, which might be capable of reversal.

DR. FISHER: Dr. Gryfe, concerning the controversy of the squaring of the curve, we have, on one hand, the optimistic viewpoint that older people are going to live longer, healthier lives, and on the other hand, the sudden onset of disability. Are we going to have more and more older people with greater and greater disabilities, renal failure, etc? Can you comment?

DR. GRYFE: As clinicians, we take the position that we are not manipulating physiology, we are practicing nephrology. Whether we can reduce morbidity remains to be seen.

We are trying to minimize disease and deterioration, and to improve the quality of function in advanced years.

DR. FISHER: A major issue with the public and within the profession is the loss of mental function with aging. With regard to mental function, what range of physiological changes is normal?

DR. GRYFE: It is important to emphasize that the stereotype of the older person as 'senile', that is having lost mental capacity, reflects only the prevalence of disease and not normal aging. We have no reason to believe that normal ageing alone produces sufficient deterioration of brain function to render the old person incompetent.

In the clinical setting, when we are confronted with an older person whose mental capacity has declined, we are obligated to look for an underlying desease rather than to remain passive, attributing the decline to the inherent ageing process.

This attitude has borne fruit, e.g. in our increased understanding of the most common disease-producing dementia, namely, Alzheimer's disease.

QUESTIONS TO DR. OGILVIE

DR. KASSOFF: Dr. Ogilvie, what is your experience with the effect of psychotropic drugs on the elderly depressed patient?

DR. OGILVIE: All CNS-active drugs tend to produce a greater response in the elderly than in the younger population. For example, the antidepressants - all the psychotropics, have lower dose requirements and adverse effects are more frequent.

The use of psychotropic drugs in the elderly is quite difficult and frequently the doses required are extremely small. When possible they should be avoided but, if they are used, they should be used with extreme care.

DR. REIFF: Digoxin dosage has an interesting historical background. During the 1950's the dictum was that patients had to be digitalized completely. In New York, a distinguished pharmacologist used to tell us that we should digitalize to toxicity to obtain maximal therapeutic efffect and then back off slowly. When

our patients, especially older patients, developed arrhythmias and died, we would rationalize, saying that 'Their cardiac condition was so severe that they could not reach a balance between the therapeutic and toxic effect, and, they would have died of their heart disease anyway.'

Later, during the late '60's and early '70's, a group at the University of Arkansas, studied digoxin handling in older people and pointed out some of the factors in distribution and in muscle mass changes and recommended that older people receive much smaller digoxin doses than younger people. Their studies also brought to light the knowledge that you dont have to digitalize people to toxicity and, in fact, that partial digitalization has some therapeutic effect. These unfortunate experiences with older persons helped us to understand the principles of digitalis utilization - a benefit which has since been applied to all people. Similar phenomenon probably apply to other medications that we have not yet identified.

DR. FISHER: Dr. Ogilvie, would you comment on hypertension in the elderly?

DR. OGILVIE: Hypertension in the elderly has not been defined clearly although we know that the morbidity and mortality of elevated blood pressure, systolic or diastolic, continues in the aged as in younger persons. It is not clear whether reduction of these pressures to 'normal' would reduce morbidity or mortality from cardiovascular disease or stroke. In summary, we don't know whether we should be reducing blood pressure and, secondly, we don't know how to do it.

If we decide that an arterial pressure of 180 over 100 is abnormal in older patients and we begin to treat them, we often put them in jeopardy, especially if we choose a diuretic that has a long duration of action and can produce a profound change in circulating blood volume and serum potassium. Also we may make them miserable with possible hypotension, reduced renal function and altered cardiac function. Of course we urge everyone not to overtreat, and recommend a small dose perhaps 25 mg of hydrochlorothiazide a day or even every second day to 'take the edge off' high blood pressure. One would not go to other agents unless it was determined that the patient had damage to target organs, because you want to preserve the remaining function of the heart or the kidneys.

DR. OREOPOULOS: Your advice to use drugs only when necessary and for as short a period as possible is easier said than done, especially in the end stage renal patient on dialysis, who has several other conditions. When I review the long list of medication that these patients are on, I am shocked. In our efforts to treat all of their complications, we may administer 10 or 12 medications. I don't know how they remember to take them all!

DR. OGILVIE: They don't, fortunately they don't.

DR. OREOPOULOS: What option do we have - to forget about all these other complications and not treat them?

DR. OGILVIE: It is important to define our therapeutic and other goals at the

outset and, if we are administering a drug, it should be used for a specific period. We should decide these things in advance and say we are going to stop it when a certain event occurs or time has passed. Often we initiate therapy that continues 'forever' without even specifying our therapeutic goal. Did we want to modify a symptom? Did we want to prevent some complications or did we want to change some aspect of organ function for a period? Could the patient manage without that change later on?

We have to specify these goals in writing because our minds play tricks on us. We should write down the therapeutic objective before starting therapy and try to adhere to it. The purpose of treatment by objective criteria will do much to reduce the number of drugs that we are prescribing in the chronically ill patient.

DR. REIFF: I tell the house staff not to memorize about drugs in a pharmacology course; I do so because there's so much to learn. With a superficial knowledge they delude themselves into thinking that they know all about the use and properties of the various medications. I tell them that the only way to learn about a medication is to take the AMA or the PDR drug reference, and every time they are going to order something, to look it up and read the one to two pages. By doing that, probably they will not order 50% of the drugs they might otherwise order. No one, not even the pharmacologist, knows everything about all of the drugs we are using. The safe way is to have the book open before you as you write the prescription.

DR. SCHREINER: The most important drug which nephrologists use is cyclosporin. You would predict perhaps that its dose will be age related, but the transplant surgeons use it with set dosage protocols and monitor peak and trough blood levels, which may have nothing to do with tissue levels.

DR. OGILVIE: Cyclosporin is an important example. It points out the general need for knowledge of methods that are specific and reproducible and a protocol approach to the monitoring of the drug. I predict, that significant changes will be made in our dosing schedules in the near future.

DR. SCHREINER: Your slide about old age being hereditary reminds me of Dr. I.Q. Someone asked him whether children were hereditary, and he answered, 'Of course, if your mother and father didn't have any, neither will you!'

DR. FISHER: May I make a comment concerning compliance. A British geriatrician said that the most common error made by elderly patients was that of omission (of prescribed drugs), and that they lived a long time because of this protective mechanism.

DR. OGILVIE: One is asking for trouble if one treats' drug concentration rather than the patient. Always go back to the patient and find out whether that drug is required and what its effects are in that patient.

QUESTIONS TO DRS. RICHARDSON AND REIFF

DR. LAMEIRE: Dr. Richardson, one of the mechanisms of hyponatremia which is very important to the nephrologist is potassium wasting due to diuretics. Could you comment?
DR. RICHARDSON: Some patients who have a severe potassium depletion also have hyponatremia. My clinical impression is that many patients on diuretics who get hyponatremia don't have severe hypokalemia. I don't think there is a good correlation between the two.
DR. LAMEIRE: There is a shift of sodium going into the cells.
DR. RICHARDSON: One might expect anti-diuretic hormonal levels to fall to compensate for that.
DR. LAMEIRE: Angiotensin II is a strong stimulus for thirst. During water deprivation in elderly people with reduced thirst, is there any evidence that they show less response to plasma angiotensin II?
DR. RICHARDSON: Certainly in the elderly in general, angiotensin II levels are lower. Its role is debatable and the mechanism for the thirst defect is still unknown.
QUESTION FROM THE FLOOR: 'Is natriuretic hormone an important regulator of sodium?'
DR. RICHARDSON: Evidence is accumulating that it is.
DR. GRYFE: Concerning 'hypertension', general statements can be extremely misleading. We can be reasonably accurate if we are talking about data that apply to patients up to age 70. Above age 75 *plus*, we are in no mans land; the definition of hypertension in this group is very inprecise.

Concerning Dr. Reiff's issue of management of water balance in the elderly it is often very difficult to get a 24-hour urine. We have relied on precise weighing of the patient and, of course, on measures of intake and output. Central to this is a clear understanding of the net insensible loss and how this changes with age. Do you have any good data which would allow us to predict for any given age the insensible water loss?
DR. REIFF: I know of no such data. I agree that one should measure not only intake and output, but weight and 24-hour urine osmolality. I made a spot check of the admission of elderly patients to acute hospitals and found that less than 50% are weighed on admission, despite hospital regulations for the nursing staff to do so.

Many of the things we have to do for older people are difficult and require more time. When the staff cut corners we do not get the data we need to manage older people properly.
QUESTION FROM THE FLOOR: Dr. Reiff, specific heat is important in heat and cold exposure and renal patients seem to be quite sensitive to heat and cold exposure. Does any of the available data relate this to intercellular water?
DR. REIFF: Undoubtedly some of these changes are related to changes in total

water volume or mass, and many are related to central nervous system regulation. Abnormalities in thermoregulation in older people is a multifactorial phenomenon.

QUESTION FROM THE FLOOR: Please explain the differences between oncotic pressure and osmotic pressure.

DR.REIFF: Oncotic pressure refers to colloid osmotic pressure exerted by macromolecules within or outside the cell. Normally it is only about 1% of the total osmotic pressure of the plasma. We can't talk about colloid osmotic pressure within the cell because we haven't measured it. We need a direct measurement of colloid osmotic pressure and total osmolality within cells.

DR. KOPPLE: We know that protein mass is reduced in elderly people and that the percentage body fat has to increase. On this basis, can you estimate the true reduction in intracellular water by relating it to the intracellular protein mass rather than as a per cent of body water?

DR. REIFF: We don't know. All previous estimates of intracellular water have been made by subtracting intracellular water from total body water. That doesn't 'give us a handle' on what intracellular water is. We haven't defined it. Steen and I, who were at the World Health Organization meeting in Washington last month, came to the conclusion that we have to start from scratch in our understanding of what's happening to water in the body with aging.

DR. KOPPLE : How accurate are the measures of intracellular and extracellular water in the elderly? Nephrologists confront enormous difficulties because markers of extracellular fluid are different in the uremic and the non-uremic individual. Has it been shown that these markers in the non-uremic elderly are the same as in the non-uremic young individual?

DR. REIFF: No, it has not. All these measurements are based on the assumption that what we call the extracellular volume is what's being measured by bromide, inulin, thiocyanate, or sulfate. In a sense, it is best to take the phenomenologic approach. Instead of talking about extracellular volume, perhaps we should say the volume of distribution of inulin, or of sulfate, or of thiocyante.

DR. SCHREINER: How do Eskimos do it? They have high body fats and therefore might have low body water and also they are in a hostile hypothermic environment.

DR. REIFF: I had never thought of that, and I don't know of anybody who's studied it.

QUESTIONS TO DR. ANDERSON

DR. FENTON: Do you have any information about changes in protein intake in the elderly? Does the dietary protein intake decrease spontaneously?

DR. ANDERSON: It probably does. Dr. Kopple is going to speak on this subject.

DR. KOPPLE: Dietary protein intake does decline somewhat with ageing. Some people have suggested that protein requirements may increase slightly in the elderly but, on the average, the protein intake falls slightly. It depends in part, of course, upon the underlying diseases.

DR. OREOPOULOS: I want to stress what you said that serum creatinine does not increase with age, at a time that kidney function declines; Is this, 'normal' decrease in kidney function similar to the decrease secondary to various kidney disease? Do elderly persons with low kidney function have the same degree of secondary hyperparathyroidism, for example, as another patient in whom kidney function has declined after a glomerular disease?

DR. ANDERSON: I'm not sure that anybody has looked at that. In the aging kidney there is a wide range in the degree of decline in renal function and a wide range in the number of sclerotic glomeruli you would find by biopsy.

DR. REIFF: You have indicated that hyperfunction leads to renal damage. Is there any evidence that the hypertrophy after unilateral nephrectomy also results in increasing glomerular sclerosis? Your paper suggested that older people should get enough fluid intake to keep their urine iso-osmolar. Your data seems to strengthen the argument that, by reducing the workload - at least the osmotic workload - you would protect against further damage. Would you comment on both of these possibilities?

DR. ANDERSON: For years the donor was told that a unilateral nephrectomy was never a problem and he was told, 'You don't ever have to see a doctor again.' However, recent studies suggest that the prognosis may not always be that good. After five or even 10 years, you may not find even microscopic proteinuria but, if you look further out, perhaps in 20 years, the donors have a significantly higher incidence of hypertension and proteinuria. Admittedly, a little hypertension and a little proteinuria may not reflect serious injury, but this evidence suggests that the kidney of the donor is not doing as well as it was before.

Renal failure with glomerular sclerosis has been reported in donors, but we're not sure what these cases mean. It is potentially alarming, but the numbers are so small that one cannot be certain that it represents pure hyperfiltration. However, it does appear that the remaining kidney in the donor is not completely normal; what this is going to mean evenutally depends on how long the donor is going to live. There is much less concern when we take a kidney from a 40-year old donor than if we take one from a 12-year old child. Presumably the child is going to live another 60 years or so making his sole kidney hyperfilter over a long time on our protein-rich diet.

I agree with your recommendations concerning treatment of the elderly. The risk is of too much and too little of everything: too little fluid, too much fluid, too much hyperfiltration, particularly when these patients have severe vascular disease.

DR. REIFF: If that's the case, then dehydration in the elderly is much more

hazardous than we had thought previously. The hypothesis that increased intracellular aggregation of macromolecules is deleterious suggests that dehydration would lead to some degree of irreversible change even after the patient is rehydrated. Clinically, we recognize that dehydration in an older person is a hazardous state that is associated with a great deal of morbidity and mortality. Thus, a healthy 80-year old with a serum creatinine of 1 mg and a GFR of 60 ml/min, which is one-half of what mine is, does not have a great deal of reserve. Adding dehydration, nephrotoxins, and other hazards increases the risk further.

DR. FENTON: In terms of declining GFR stimulating hyperfiltration of the remaining nephrons, does that not suggest that, as the nephron population declines, that the rate of deterioration should accelerate in a linear fashion? Can one presume that, as you get older, your decline should increase linearly?

DR. ANDERSON: That would be a logical deduction. GFR does decline in a linear fashion or possibly a little faster than linear after about age 40. We don't have comparable data on the number of sclerotic glomeruli. The work from Gallo shows a wide scatter, but the main conclusion is that there isn't much decline before age 40, and that more patients are likely to have a greater decline afterwards.

DR. FENTON: I thought the evidence was not reliable in terms of rate of change with age. In other words, the scatter in the ageing population is large in terms of preservation of GFR, leading one to suspect that other factors may be operating in addition to hyperfiltration.

DR. ANDERSON: You are correct. There is a great deal of scatter and some patients maintain their GFR even into the older years and others go down more precipitously. The difference may be due to other factors such as hypertension. Uncontrolled hypertension contributes to the natural decline in GFR. A recent paper by Lindeman, et al., suggested that uncontrolled hypertension was a risk factor and that these patients would have a steeper decline. Vascular disease contributes too.

DR. GRYFE: There are two slopes of deterioration one in the GFR and one in the slope of renal plasma flow. The latter decline appears to be steeper than that in the glomerular filtration rate.

DR. ANDERSON: I'm not sure that we can demonstrate that the two are interdependent. Dr. Hollenberg and others, in a well-known study 10 years ago, showed that the volume of renal plasma flow per unit kidney mass declines with age, and GFR, to a certain degree, is plasma flow dependent in humans as well as in animals. The difficulties of these studies are compounded by the higher incidence of vascular disease in the aging population.

QUESTIONS TO DR. SCHREINER

DR. LAMEIRE: I would like to ask about the incidence of papillary necrosis. I come from Belgium where in some dialysis units, up to 50% of the patients are suffereing from analgesic nephropathy. As you know, the American incidence is a great deal lower than ours.

My question is this: are they truly much lower or are these lesions are not correctly diagnosed in America?

DR. SCHREINER: If you look at the *per capita* consumption of analgesics by country, those countries which reported the highest prevalence, like Australia, South Africa, and to some extent in the early days in Canada, the consumption of analgesics was considerably higher than per capita consumption in the United States. Australia and Denmark were the highest in the world. We did a survey in response to the allegation by the group at the University of Pennsylvania, that 20% of ESRD patients were due to analgesics. A research nurse administered a questionnaire to some 300 dialysis patients. Psychiatrists had reviewed the questions to ensure that it was understood by the patient, and was corrected by computer so that no human bias was involved. The absolute maximum was 2.7% and several of those patients had other diseases, like diabetes. The true figure was about 1.7% of our dialysis population who could have had analgesic nephropathy. It varies all the way to 30% in the literature in certain countries. In Australia, up until a few years ago, Dr. Kincaid Smith was saying that, even though they banned and had taken phenacetin out of mixed analgesic tablets, the incidence remained the same. Is that true?

DR. LAMEIRE: Yes, that's true.

DR. SCHREINER: Thus we don't know the whole answer concerning the high incidence of analgesic nephropathy in Australia. Another factor is that the population is moderately dehydrated most of the time. It is one of the few places where Caucasian men work in the tropical sun and do heavy labor for a long time. Thus, there is an inordinate prevalence of skin cancer, lupus, or other possible actinie related diseases. Also, some other factors as yet undefined may have been involved.

DR. OREOPOULOS: Can you state briefly your views about the role of control of blood sugar in elderly diabetics.

DR. SCHREINER: There is much evidence that controlling blood sugar does prevent some of the sequellae of diabetes. The Polynesian dialysis patients, who have a high percentage of diabetics and a low incidence of hypertension, are roughly 10 years older than diabetics on dialysis in Metropolitan Washington or in New York City. Over ninety per cent of the diabetics in Dr. Friedman's unit have hypertension. To me that means that the acceleration of vascular disease probably is due more to the hypertension than to the diabetes. We have some isolated Native American Indian populations in the United States of whom over two-thirds are diabetic, and where few have hypertension. Thus, I believe that

the principal factor in accelerating the vascular disease is high blood pressure, albeit on a diabetic base.

If the two diseases - diabetes and hypertension occur together, it is worse than either alone. There is a summation of the effects of uncontrolled diabetes and hypertension. Overnight studies need to be done. Perhaps diabetic hypertensives get less sleep relief in their blood pressure.

QUESTION FROM THE FLOOR: In regard to angiographic procedures in the elderly, at what point do you begin your protocol for a saline infusion? At what point would you recommend against an angiogram?

DR. SCHREINER: If there is any sign of dehydration and the individual has any significant impairment of kidney function, we start the protocol because thereby you reduce contrast nephrotoxicity.

One bizarre thing is that in hospitals, when they do a renal work-up, they run a maximum concentrating ability or maximum UP ratio by dehydrating the patient overnight. They get the morning urine and send the patient down for an x-ray. The patient couldn't be in a worse physiologic situation at that point.

If you're pressed for time in a hospital, don't do your UP ratio that way. If you have to do them on the first day, give the patient ADH and keep him well hydrated so that at least his plasma fluids are up. You can test the kidney and the capacity to respond to exogenous ADH without dehydrating him. Since ADH has a functional half life of about 30 minutes, a short interval is sufficient between the concentration test and the contrast administration. I would suggest 4 to 6 hours.

QUESTIONS TO DR. LAMEIRE

DR. SCHLEIFER: Your results are impressive. Did you have elderly patients whom you chose not to treat?

DR. LAMEIRE: No.

DR. SCHLEIFER: Did you treat everybody?

DR. LAMEIRE: Once they come in and have evidence of acute renal failure, no matter the age, they are treated. There's no selection.

DR. SCHLIEFER: No matter what type of illness? Did you treat people with carcinoma?

DR. LAMEIRE: If it is a postrenal - acute renal failure in a patient with carcinoma, we treat him.

DR. SCHLEIFER: Do you do follow-up after discharge from hospital? Do you have any data about the prognosis in elderly patients once they leave hospital?

DR. LAMEIRE: Many of them are followed in the outpatient department. So far they don't seem to differ from the younger ones, but some, of course, are lost to follow-up. In surviving patients and in those with sufficient follow-up, allowing these measurements, we define recovery by a creatinine clearance that

is at least normal again or back to the pre-acute renal failure level.
DR. SCHREINER: I don't think you can presume, because they come back, that they're going to stay that way. Dr. Freeman, in our group, reviewed all the patients over 10 years with acute renal failure, and identified several who recovered normal function and then deteriorated.
DR. LAMEIRE: We stopped this study in '84, hence we do not have a 10-year follow-up of these patients.
DR. WING: Further to these seriously ill patients with multisystem failure, can you point to a group of patients with multisystem involvement or complicating side effects which you would not dialyze but would treat only by supportive measures.
DR. LAMEIRE: I know of no single variable, which is able to predict which patient is hopeless and has only a slight chance to recover. If you have a patient who, after 48 hours, has more than four or five complications, the overall mortality will be extremely high, but even here age is not a discriminating factor.
FROM THE FLOOR: How did you define mortality or , let us say survival? Was it survival until renal function recovered or until the patient left the hospital?
DR. LAMEIRE: Mortality, in my view, is when the patient is dead. Survival is when they leave the hospital alive.
FROM THE FLOOR: Your failure to show any response to amino acid therapy may indicate that there is no effect on survival, but it also may reflect the possibility that, because you did not randomize your patients, it was those, who were unable to eat and had a large number of complications, who received amino acids.
DR. LAMEIRE: Exactly. I would not conclude that amino acids are not necessary or even not useful in acute renal failure. Our results reflect the fact that the nephrologist, when there were no complications and when the patient was able to eat, did not prescribe amino acids and, indeed, prescribed them only for patients who really could not eat or showed more than two or three complications.
FROM THE FLOOR: Regarding your finding that peritoneal dialysis seems to have a poorer outcome in the elderly than hemodialysis, were you able to show that peritoneal dialysis was chosen for the poorer patient on cardiovascular grounds? Also, do you consider continuous hemofiltration an alternative for those patients who are cardiovascularly unstable and therefore do not tolerate hemodialysis?
DR. LAMEIRE: I have limited experience with continuous hemofiltration. In our hands the maximum duration of one filter is not more than 24 hours, especially in unstable, slightly hypotensive patients, so I cannot comment on that. It is true that peritoneal dialysis was chosen in the patients who were hemodynamically unstable and therefore those who have the worst prognosis.

QUESTIONS TO DR. BLAGG

DR. SCHREINER: In anticipation of the meeting, we analyzed our 83 CAPD patients by age, and the people over 55 came out well. The catheter failure rate was 6.9 per thousand in the over 55, and 8.5 per thousand in the under 55 group. Thus the catheter failure rate was better. Perhaps they were less vigorous in work/play or just more careful. Similarly the older group had a greater incidence of hypertension - 75% *versus* 42%; the older group had a higher number of chronic diseases when compared to the younger - 1.56 *versus* 0.97.

We found no difference in the incidence of peritonitis, transfusion requirement, or number of hospitalizations; no difference in actuarial survival at any time - 83% in the over 55, and 77% in the under 55 at two years. The likelihood of being free from morbid events did not differ - 51% at two years in the over 55 *versus* 54% in the under 55. Thus the elderly do well on CAPD despite allegations to the contrary.

DR. BLAGG: Our experience with those selected for home hemodialysis, is that some of our best home hemodialysis patients are in their 60s and 70s; if they have family support and are capable of doing it. It is not true to say that elderly patients can't care for themselves when they are provided with appropriate support.

FROM THE FLOOR: I am a bit surprised that the quality of life scores were not able to discriminate between one group and the other. There are three interpretations of that; that they are all doing well, that the general population is in deep trouble, and finally that these scores are not a good tool for discrimination. Recently we looked at what dialysis patients are doing when theyre not on dialysis. We were surprised and disappointed to find that most sit around and watch television. As a group, they're markedly inactive.

From your experience, can you determine what these different groups of patients are doing? At what level are we able to rehabilitate the elderly patient on dialysis?

DR. BLAGG: When we separate out the over 65s from the under 65s, we found that dialysis patients demonstrate a lot of denial and adjust to their problems to a surprising degree. Our paper was published in the *New England Journal* about two months ago. About six months before, another paper in the same journal about patients with CAPD and heart problems, showed a similar phenomenon; patients saw their quality of life as very good.

We can discriminate between the different modalities. On the other hand, these are not a nation-wide, randomly selected group of patients. They were picked from 10 centres because HCFA would not provide funds to select patients nationally. So, in that sense, they are a selected population.

DR. WING: I want to make a comment concerning the types of primary renal disease, which produce end stage renal failure in the elderly. We know the distribution of the causes of end-stage renal failure in patients in Europe going

into treatment for the first time in 1983; we divided these patients into those aged under 65 and those aged over 65. There is less glomerulonephritis in older patients and more of them have reno-vascular disease. The most intriguing finding is that both the males and females show an increased proportion of patients who are classified as having 'chronic renal failure, etiology uncertain'. The data from Seattle are similar. This challenges all of us to understand better the causes in this large portion - one in five of all older patients. Among them may be some preventable causes. Are these patients whose kidneys have reached 'the end of the road' because of hyperperfusion?

DR. BLAGG: I believe at least some of these cases represent patients with multiple etiologies that the physician has not sorted out.

DR. SCHREINER: Dr. Wing, you once pointed out that if you take it country by country, a close association is seen between the number of patients with acute renal failure and the number with chronic renal failure in each country.

DR. WING: That's correct. We found almost the same number of patients under treatment for acute renal failure per million of population as we found with chronic renal failure. However we gained access to that data through the renal centres - through people who normally present data on chronic renal failure - so it was not comprehensive and did not include the intensive care areas where many patients with acute failure probably are treated.

DR. SCHREINER: I suspect you don't get answers to these unknowns (a) how many were rejected for biopsy or other diagnostic techniques because they were elderly or (b) what illness or other trauma did these people suffer earlier in their lives, because the longer you go on, the more likely you are to collect all of the chronic processes for example, acute renal failure that is forgotten about 10 years or 15 years later. I remember a patient who came in 30 years after mercury poisoning; he had interstitial fibrosis and had forgotten about the incident 30 years earlier. It was recorded only because we remembered him. You will find chronic drug poisoning, chronic evolution of acute renal failures, and many diseases that just ran their course because they had the time to do it.

DR. WING: Then we should take greater care of the patients who have had some previous renal insult that would have reduced the number of nephrons available to serve through the years ahead?

DR. SCHREINER: I'm not sure that nephron loss is a function of hyperfiltration. It may be the progression of fibrosis; for example, it takes three and one-half to four years for cyclosporin A to kill an occasional epithelial cell, and then later the fibrosis appears. The same thing happens with CIS-platinum, lead and so on. These insults appear to initiate a very slow process, which slowly runs its course toward a general process we call TIN - Tubuler interstitial disease with some specific variations that may be related to the particular etiology.

FROM THE FLOOR: Life satisfaction among older people generally is below-average. Is it possible that older dialysis patients have a higher life satisfaction because coming to a treatment centre alleviates their loneliness?

DR. BLAGG: That's one factor but another is that, if you have a fatal disease and then are snatched from the jaws of death, you are likely to be more grateful for life.
DR. SCHREINER: You reported a slightly higher satisfaction index on CAPD than on hemodialysis. We did the same kind of a study and also found that CAPD patients gave considerably higher ratings than those on hemodialysis.
DR. BLAGG: That is true for centre hemodialysis, but our home hemodialysis patients did better than our CAPD and our centre hemodialysis patients. However, that may not be an accurate reflection of the present situation because our study was done in the early days of CAPD, and management of patients has improved since that time.

I showed that, not so much to compare the different modalities, but to show that elderly patients, if they do well on dialysis, have a good quality of life.
DR. SCHREINER: Dr. Anderson, if you believe that hyperfiltration leads to progressive damage, why isn't this happening? Or is it happening? Have you studied renal function in every uninephrectomized patient since transplants began?
DR. ANDERSON: We are starting to study that. In the past most of us felt a sense of security about transplant donors as well as recipients.
DR. SCHREINER: I'm talking about recipients.
DR. ANDERSON: Recipients are another population entirely. The more you think about them, the stickier it gets. Most of them are on steroids, and we know that these agents raise GFR. Focal sclerosis has been reported in transplant patients, but there aren't enough to draw firm conclusions. I don't think that we can always determine what is due to hyperfiltration, or 'idiopathic' focal sclerosis, or is some sort of slow form of chronic rejection.

We know that for a while, renal function is initially well maintained in both donor and recipient. However, the recipient's rejection and treatment cloud the issue. It might be reasonable to recommend that the recipients lower their dietary protein intake.
DR. LAMEIRE: Is it true that in the recipients who develop focal sclerosis after transplantation, many were suffering from sclerosis before operation? Does that not suggest to immunological aggression of the transplant rather than hemodynamically mediated hyperfiltration?
DR. ANDERSON: The patients who had a diagnosis of focal sclerosis before renal failure, probably had recurrent disease. The interesting question is, 'What about the patients who had an entirely different disease before transplantation? We just don't know.
FROM THE FLOOR: Do you consider that non-steroidal anti-inflammatory agents are a cause of chronic interstitial nephritis? Is there a hazard in their use? Old people are taking a great deal of them.
DR. SCHREINER: Many drugs produce allergic interstitial nephritis or lipoid nephrosis. So far we have identified only a few drugs that produce the

combination of a lipoid nephrosis and allergic interstitial nephritis. This combination has been associated with non-steroidal anti-inflammatory agents and also with cyclosporin A, *cis* platinum and possibly pencillamine.

DR. LAMEIRE: Lithium?

DR. SCHREINER: Yes, lithium as well; we have collected in the neighbourhood of 12 to 15 cases with this combination. There may be a potential for chronic interstitial fibrosis with other drugs as well.

FROM THE FLOOR: Calcium channel blockers, converting enzyme inhibitors, and non-steroidal drugs all have been shown to cause acute renal failure in the elderly, and one of the explanations is disturbances in renal autoregulation. What do we know about renal autorregulation in the aging person and what degree of renal insufficiency might predispose the elderly to acute renal failure from these types of drugs?

DR. SCHREINER: Autoregulation seems to be a combination of intrarenal effects - or a balance between intrarenal effects of agents like renin and angiotensin, and something like prostaglandins. Of course, plasma renin levels decline with age, and this is also the mechanism whereby these drugs interrupt the cyclo-oxygenase pathway. I saw a patient who had been hypertensive for several years; when he took one or two tablets of indomethacin his diastolic blood pressure dropped by 30 mm HG.

Usually these are acute effects. Our poison centre at Georgetown has reported only one day's hospitalization as a result of taking a non-steroidal anti-inflammatory drug; so they are safer than salicylates and acetaminophen with respect to suicides and overdoses, and with exposure to the general population.

DR. KARANICOLAS: We have found CAPD useful in patients with acute renal failure. Dr. Lameire, would you comment on the kind of dialysis you use?

DR. LAMEIRE: For the peritoneally dialyzed patients, we use the old classic acute peritoneal dialysis, let's say, one hour or one and one-half hour exchanges. We never have used CAPD in acute renal failure but several centres have used it with apparently good success. One advantage would be that the patient would receive part of his alimentation across the peritoneum instead of having to infuse all the calories intravenously.

DR. FENTON: Dr. Anderson, will you comment further on the finding in follow-up of hypertension and minimal proteinuria in renal transplant donors.

A Mayo Clinic group found a significant incidence of occult renal disease in the families of people with end stage renal disease, when they worked them up for kidney donation. Does this represent a long-term manifestation of occult renal disease in a family who are more predisposed to develop related renal disease?

DR. ANDERSON: I suspect some of them are. One of the real advantages of having the donors as a study group is that they are screened carefully before donation. For this reason, donor studies are much more reliable than the studies in the 30s and the 40s where a general surgeon would say, 'I have done 16

nephrectomies and all my patients are doing fine.' In those days nephrectomies were done for such indications as tuberculosis and a variety of other diseases. There was no way to rule out bilateral disease.

The point is that a kidney donor has undergone extensive evaluation and if something is lurking in the other kidney it will be much more likely to be discovered than in patients who have a uninephrectomy for trauma, tumor or other causes. Some donors may have a lesion that was there before, and the studies all separate them out. Some patients later develop diabetes or other diseases, which clearly can contribute to hypertension and proteinuria. In any event the best studies which match donors with age and sex-matched controls are beginning to show a higher incidence of proteinuria and hypertension in the donors. However, that is not a unanimous finding. The various studies differ widely in terms of the care with which they matched controls and patients, and in the length of follow-up. However, you cannot rule out completely the possibility, that donors come from a group that are predisposed to renal disease.

DR. SCHREINER: You have to be careful to exclude all the things that might appear in familial clusterings, such as hypertension. The Framingham study has shown that family members or parents, who are on a track, remain on that track. For example, if the parents are in the upper 20th percentile in absolute blood pressure, there's a high probability that other members of the family will be in the upper 20th percentile for their blood pressures; so you can expect some familial cluster with all the complications of hypertension and also a higher familial incidence of diabetes, polycystic disease and Alport's syndrome and probably focal sclerosis, and other lesions. You have to take all those things out before you ask 'Do families have a higher incidence than some other well-screened population?' I believe the general population contains a great deal of occult renal disease that is not diagnosed.

FROM THE FLOOR: What are the chances of finding more than one preventable cause of acute or chronic renal failure in the same patient?

DR. SCHREINER: Very good. Both my data for the elderly and Dr. Blagg's data show that the number of associated conditions was over one. Right away you can say that, not only are the chances very good, but almost certainly more than one cause will be contributing in these individuals and, of course, there are clusters or syndromes; the slightly obese, hypertensive, hyperuricemic, diabetic business executive is an example. In my practice, this is almost a syndrome.

FROM THE FLOOR: Frequently, is it necessary to treat elderly patients for acute heart failure precipitated by infection? The combination of cephaloridine and furosemide has been blamed for precipitating acute renal failure in such patients. Is there any evidence that the later generation of cephalosporins in combination with furosemide are less nephrotoxic?

DR. SCHREINER: I don' think data is available on the more recent generation of cephalosporins, such as cyclosporine G which is less nephrotoxic in early trials. Any synthetic penicillin can produce acute allergic interstitial nephritis.

DR. REIFF: What is the relationship, if any, between the age of a donor and the degree of hypertrophy his remaining unilateral kidney may undergo?
DR. ANDERSON: This data exists, both in humans and in animals. Generally speaking, the older donor - person or rat - will show less hypertrophy by size and function afterwards, than is seen in the younger animal. In modern studies the radiologists have looked at it using ultrasound but older studies used IVPs. One human study that I know of measured functional response and showed that the older kidney increased its GFR in response to uninephrectomy but not as much as the younger.
DR. OREOPOULOS: Dr. Lameire, I was struck by the high mortality rate in postoperative acute renal failures. What preventive measures would you recommend to improve these results? Dr. Blagg, since there are more elderly women around, why did you see more men with renal failure? Does any particular disease account for this predominance of males in the older group?
DR. LAMEIRE: Concerning the high mortality in postsurgical acute renal failure, the literature shows a universally bad prognosis in this condition. Of course, it depends also on the type of operation; for example, aortic aneurysm surgery has by far the worst prognosis - a mortality of over 80% in a recent report.

There are many reasons for this: First, most of the patients are elderly; Secondly, they have serious cardiovascular handicaps; Thirdly, the surgeon's lack of appreciation of the basic fluid and electrolyte disturbances in their patients; There is the trauma of the operation and the type and duration of anaesthesia.

Good hydration is, of course, of primary importance; giving mannitol during operation could prevent postoperative deterioration of renal function. Only part of the post-operative acute renal failure can be attributed to the surgical aggression, some is due to the infections, which occur after the operation. The prevention of these infections would reduce dramatically the incidence of ARF.
DR. GOLDSTEIN: We have just completed a study of acute renal failure in the post-aneurysm patient; 100% of them, when clinically assessed by nephrologists before the surgical procedure, had contracted ECF volumes.

Extracellular volume depletion is preventable through good clinical assessment before operation. These patients miss meals; they are undergoing various procedures; and they get salt-depleted before operation. In our study, we did saline expansion during the operation. We could demonstrate no additional benefit of mannitol and dopamine over ECF volume expansion with saline alone.

DR. WING: The difference between males and females which Dr. Oreopoulos inquired about, is due to glomerular nephritis and vascular disease which affects the males particularly.
FROM THE FLOOR: Since there is the possibility of increased renal complications in the donor, should we continue to encourage live-related donor transplants?

DR. SCHREINER: Sharon, what is your policy at the Brigham?
DR. ANDERSON: I believe in living-related donor transplants, and the Brigham does quite a few of them. For many reasons we will continue to demand stringent donor work-ups before transplant. For example, you don't want to transplant a kidney that has disease in it. You're not doing a favor to the donor or to the recipient. I don't know anybody who believes we should discontinue the living-related transplant donation.

We tell the donor that the chances are very good that nothing important is ever going to happen, but they should be seen by a doctor on a regular basis. They should have their blood pressure and their serum creatinine checked once in a while and their urine checked for protein. Some nephrologists recommend that the donor go on a low-protein diet at the time of nephrectomy. The data is not yet available to prove that a low protein diet will benefit every kidney donor. However, it would be imperative to do so at the first sign of rising creatinine or a similar abnormality.
DR. SCHREINER: With respect to elderly people, serum creatinine is not a good yardstick because creatinine generation rates are considerably lower in older people. As has been pointed out, you can get a decline in function with a normal serum creatinine. An elevated creatinine in an elderly patient probably means disease - probably means an inordinate reduction in clearance. However, in assessing older people, clearances are a lot more important than our screening tests using the serum creatinine Scr or its reductional, 1/Scr.
FROM THE FLOOR: Do any of the panel members use protein restricted diets in chronic renal failure patients to prevent or delay the need for dialysis? If so, when do you start protein restriction and what level of protein restriction do you use in relation to the level of creatinine clearance? Does anybody believe this is simply planned starvation, and that they should just let the people eat?
DR. LAMEIRE: We have started a prospective study in patients with creatinine clearance of around 50 ml per minute, using ketoanalogues instead of the full protein diet.

Twenty years ago when patients came for dialysis, who had been followed for several years on 'conservative' treatment - with extremely strict protein restriction, they were all malnourished; anemic and in bad shape. The renewed interest in protein restriction should not go in that direction. There is a danger that if you enforce it too strictly, you may end up with a malnourished patient when you start dialysis.
DR. ANDERSON: I would add that, since the 'rediscovery' of the low protein diet, investigators in many countries are looking at the effect of the low-protein diet on the rate of decline of renal function. Some of the best studies show that you can reduce the intake of dietary protein to a level, which still allows positive or at least neutral nitrogen balance, and still help the kidney. In other words, you don't have to go into negative nitrogen balance. A ball park figure would be about .6 g protein per kg. of body weight a day, or even lower levels if you

supplement it with keto-acids or essential amino acids. Dr. William Mitch, at the Brigham, in conjunction with Dr. Walzer and some other doctors, recently reported their results in the *New England Journal of Medicine*. We don't have to starve them. We can reduce the protein to a level that's tolerable physiologically, and still see beneficial effects.

DR. BLAGG: A national (U.S.A.) study soon will be undertaken involving the Brigham and various other centers, to answer these questions in a controlled prospective study. In addition, many studies suggest that a low protein diet is safe and beneficial.

DISCUSSION ON DR. KOPPLE'S PAPER

DR. FRIEDMAN: You said that elderly patients are frustrated and depressed more easily than younger. How do you know? Is it possible that they resist frustration and depression better and that you are just projecting on them what you think it might be like to be old. In studies of traffic accidents, for example, there is evidence that older persons are more patient and less likely to jump out of line and cause an accident.

DR. KOPPLE: You are correct. I don't know. However, this has been described among the non-uremic elderly as a cause of poor nutrient intake and of poor compliance.

DR. FRIEDMAN: Concerning your study of the causes of ESRD in 18 patients and 18 controls. In our program in Brooklyn, no diagnosis was made in about 60% of all patients with kidney failure. We did not know and so decided not to use confusing terms like 'golmerulonephritis' when we didn't know the true pathogenesis. Did you have patients in whom you could not make a diagnosis?

DR. KOPPLE: Yes, two in one group and four in the other. For the purposes of the study, we selected patients from two teaching hospitals; these patients had been 'worked up', and both institutions seemed ready to make a specific diagnosis.

DR. MORGENTHAL: What daily protein intake do you recommend for an average 30 or 40-year old, expressed in g per kg?

DR. KOPPLE: For a dialysis patient?

DR. MORGENTHAL: No, non-dialysis. Just a healthy, normal person.

DR. KOPPLE: The current recommendation for a non-pregnant, non-lactating adult, is 0.8 g per kg b.w./day. I understand that the new Recommended Daily Allowance (RDA), which probably will be published this summer, has been raised to 0.9 g per kg. This refers to a mixed quality protein.

DR. MORGENTHAL: If we follow Brenner's hypothesis concerning hyperfiltration and put our pre-dialysis patients on 0.8 g of protein per kg b.w./day, and when they start dialysis, we will increase the intake to 1.2 g/kg/day. Why do they require so much more protein? Obviously dialysis involves amino-acid losses, but why so much more?

DR. KOPPLE: First, I would not prescribe 0.8 g of protein/kg b.w. for a patient with substantial renal insufficiency, but would less than that because the evidence suggests that in some people a low protein intake retards the rate of progression of renal failure.

I don't know why the requirement increases when people go on dialysis, but there is ample evidence that it does. We can maintain almost everybody in nitrogen balance on 0.55 to 0.6 g protein/kg/day if one-half the protein is of high biological value. Over the last 15 years I've done 30 studies in different classes of patients. In contrast, we cannot maintain a positive nitrogen balance in the hemodialysis patient. There's evidence that even on a protein intake of 0.75 g/kg/day they will be slightly protein depleted.

Part of the reason is that during dialysis they lose some amino acids- about 6 to 8 grams. They also lose some peptides, maybe 3 grams, with each dialysis. Some protein is lost in the area of the membrane but I dont know exactly how much, and some blood is sequestered. Also, there may be other reasons.

DR. KAYE: I understand that the average phosphate intake of your patients was 1000 mg per day. Since you increased their protein intake and their pre-dialysis phosphate values were normal, it must mean that you are giving them a great deal of phosphate binder. By increasing their protein intake, you are increasing their phosphate intake, which means you are going to give them more aluminum salts, and thus you are poisoning them even more.

I believe this is moving in the wrong direction. Will you comment on how we can keep the phosphate intake lower?

DR.KOPPLE: I don't think you can. That's the point. I don't believe I'm recommending an increased phosphorus intake. If you give somebody a 60 or 70 g protein diet, you are not going to get their phosphorus below 1000 mg per day. To try to do so only makes the patient miserable. I am a strong advocate of dietary compliance. The average phosphorus intake of non-uremic New Yorkers is about 1600 mg per day. The intake depends in part upon how much dairy products and how many soft drinks they ingest. Thus, 1000mg/day is a substantial phosphorus restriction. On a 40- g protein diet, it is difficult for a patient to maintain a phosphorus intake below 900 mg/day. Often you can get it below 800 or 700 mg, but it's tough. I don't think you can lower it further.

DR. KAYE: In the National Cooperative Dialysis Study it was lower than your figures. I believe it was 800 mg/day.

DR. KOPPLE: They may report that, but I do not believe their patients maintain that level. We have struggled with this for many years and right now are designing diets for a co-operative study of the effect of a low protein diet in patients with renal failure. The limit in this study is 900 mg of phosphorus/day for a 40- gram protein diet.

DR. GERALD: Some studies have looked at zinc deficiency and 'hypogeusia' or poor appetite; have you noticed whether appetite improves with zinc supplementation?

DR. KOPPLE: I don't know. Some impressive studies do show that zinc can improve appetite and also you can improve sexual function slightly. On the other hand, there is unpublished data which refutes this. My personal preference is not to give zinc supplements unless the patient presents clear evidence of anorexia.
DR. FRIEDMAN: Dr. Kopple, is it true that while the zinc plasma levels are low, the total body, or red cell zinc levels, may be high?
DR. KOPPLE: The red cell zinc is high probably because, in a uremic population, the red cells are younger. In young red cells, the concentration of many enzyme is increased and in the uremic red cell carbonic anhydrase activity, and hence carbonic anhydrase enzyme already is increased. This enzyme carries zinc into the red cell, so the increased red cell zinc could represent nothing more than the increased level of this enzyme in a youthful cell population.
DR. BLACK: In new patients, do you notice any significant nutritional difference in the elderly *versus* non-elderly? Are there more elderly malnourished patients starting dialysis?
DR. KOPPLE: I have no data on that. However, to me, they don't look any different after they have been on dialysis for several months or a year than on the day they start. If they are small, they tend to stay small. We made an intriguing observation: About a year ago, we reviewed data from two studies, one pediatric, and the other in adults patients. In both after a three-year follow-up, we found that the nutritional status at the onset of dialysis was a strong predictor of the subsequent nutritional status. If the patient is malnourished when he starts dialysis, generally he will be so two or three years later. The most important way to prevent malnutrition, is to correct it before the patient starts dialysis.
QUESTION FROM THE FLOOR: Do you prefer 25 hydroxy or 1,25 dihydroxy cholecalciferol?
DR. KOPPLE: I prefer 1,25, in part, because that is the agent I have had the most experience with. It has a more rapid onset of action and more rapid disappearance. Clearly the 25 - hydroxy vitamin has less activity. One ßin vitroß study, which never was repeated, and hence never confirmed or refuted, indicates that, in rat muscle, 25 hydroxy has a more potent stimulating effect upon muscle protein synthesis than 1,25 (OH)2 Vit. D. In fact, 1,25 has no effect while 25 has a potent effect. Despite this, several of our patients with profound myopathy had a dramatic improvement after treatment with 1,25; on this basis, we have continued to use 1,25.
QUESTION FROM THE FLOOR: What diet, especially protein, would you prescribe for a 28-year old diabetic patient, who has a creatinine clearance of 145 ml/min and four-g per day proteinuria?
DR.KOPPLE: Probably I would not restrict protein but before I made this recommendation I would discuss it with the patient and obtain informed consent. When you prescribe diets for patients, one of two things will happen: The patient will follow the diet and become uncomfortable, or the patient will not follow the

diet and will feel guilty. Thus, if you are going to intervene, you have to get the patient's consent. Probably I would put the patient on about 0.7, or 0.8 g of protein/kg/day and watch for signs of malnutrition. I don't think it will occur at that level, but you need to watch for it.

QUESTIONS AFTER DR. KJELLSTRAND'S PAPER

DR. FRIEDMAN: At the age of 20, if not on dialysis, your chance of dying in the next five years, is less than 1%. If you're on dialysis for renal failure, it rises to 20%; your risk of dying because of uremia has increased ten-fold. At 75 and with good renal function, your chance of dying in the next five years is 40%, if you have ESRD, it may be up to three times as high. Correct?

DR. KJELLSTRAND: No, the risk of dying is only doubled. In the United States, if you're aged 70, the chance of reaching 75 is 65%. In our renal patients, that survival drops to approximately 35%; i.e. you've doubled the chance of dying from about 30% up to 60%.

DR. SCHREINER: Do any nursing homes in your area have dialysis facilities?

DR. KJELLSTRAND: No, they do not. At a given moment about 10 of our patients live in a nursing home. We have a transportation service that goes to the nursing home, brings the patients to the dialysis unit and returns them to the home afterwards.

DR. SCHREINER: With such small numbers, there is always the risk that you are measuring not choice, but availability or opportunity. In the greater Washington area, you can go all the way from Wilmington to the Chesapeake Bay and not find a single nursing home with a dialysis facility. On the MedicAid program alone, the government spends $150,000 a year transporting people long distances from little nursing homes to dialysis units. One group with a beautiful nursing home has been trying to get a certificate of need (for a dialysis unit) and after two years they have just completed the first stage of the paperwork. It has been rejected four times on the basis that they had too many dialysis stations in the Washington area.

I wonder whether you are selecting out patients who chiefly need nursing home care. It is difficult and wearisome to leave a nursing home and travel across town three times a week. Would you not do better if you gave them the choice and made dialysis availabile at the nursing home.

DR. KJELLSTRAND: I believe you are correct, although I suspect the economics of the thing would defeat us. We have only a small number of patients in nursing homes, and dialysis may be expensive to set up there. On the other hand, we would save the trasnportation costs, and the patient would have much greater convenience.

DR. SCHREINER: We have nursing homes of 300 and 400 beds where all dialysis patients who required nursing care could be concentrated in one place. Actually it is cheaper in the long run.

DR.KJELLSTRAND: I agree, but Washington is much bigger than the Twin Cities. We have only a million and a one-half people; the rest are scattered all over the state.

DR. GRYFE: As a geriatrician who is not a nephrologist, I was greatly heartened by your strong advocacy of an aggressive and optimistic approach to the treatment of the elderly.

However, in the patients you presented, you may be pointing to factors, which determine the success of dialysis generally. You have shown us some remarkable individuals, who are not only remarkable in their old age, but probably have been all their lives. All through their lives they have selected themselves for survival. This will to live, to enjoy and take advantage of every aspect of life may be the ultimate selector.

Will the rest of the program provide any opportunity to talk about patient selection on the basis of personality characteristics?

DR. FRIEDMAN: Dr. Gryfe, are you saying that Dr. Kjellstrand overrated the emotional status of his elderly patients and that the outlook is more dismal than he has presented?

DR. GRYFE: Not at all, only that he has maximized that which we who have a special interest in the care of the elderly, have recognized all along.

DR. FRIEDMAN: Do you agree with his analysis?

DR. GRYFE: Yes, I do.

DR. FRIEDMAN: Your point then is that his analysis revealed those features of being old which are necessary for survival, and, in your judgment, most elderly patients on dialysis should do well.

DR. GRYFE: One other point. He also raised the practical question of treating patients who are based in long-term care facilities. This group introduces a new range of practical problems. This subject alone would occupy a major part of a separate symposium.

DR. KJELLSTRAND: First, it was hinted that these patients were the product of a heavy selection. We are extremely liberal in our acceptance of patients; the mean age of those coming to dialysis is now 63, 20% are 70 years and older. We're also liberal in discontinuing dialysis, and that is, I believe, a sensible and humane philosophy.

My statements were harsh about what is done in England. I did not attack either Dr. Isaacs or Dr. Wing. I feel sorry for those who work in a society that seems indifferent to the care of patients who suffer from mortal illnesses. What philosophy should one follow when selecting patients when you cannot treat them. My answer is that our first priority should be developing techniques to save lives, then proceed with attempts to restore function and decrease pain; at the bottom of the list would be the 'cosmetic considerations' of medicine.

QUESTION FROM THE FLOOR: Does difficult vascular access increase the risk of death in the elderly on hemodialysis?

DR. KJELLSTRAND: No, I don't think so. I have no data that vascular access

is more difficult in old patients. Like everybody else, we try to prepare a fistula six months before we think dialysis will be required, and, of course, we have all the problems of clotting, infection, septicemia, etc...
DR. FRIEDMAN: Generally it is accepted that an old patient takes longer to develop a fistula ---- That's not true?
DR. KJELLSTRAND: I don't think so, but I have no data.
QUESTION FROM THE FLOOR: Is there not a discrepancy when you say that most patients are happy but many stop dialysis? Can we predict who will quit?
DR. KJELLSTRAND: Two factors increase the likelihood of stopping dialysis; diabetes and old age. Other factors we looked at did not stand up. For example, we tried to measure the effect of a new systemic disease; many of these patients who were on dialysis developed cancer, heart attacks and so forth, and these, one can speculate, would have made them stop dialysis. We have comparable data only for amputations and blindness. These were not more common in the patient who stopped dialysis. One third of those who discontinued dialysis simply said, 'I am tired of it' and quit. The other two thirds did have serious medical complications, but I do not know how to weigh the impact of these because they were common also in those who continued dialysis. In my experience it is the incompetent patient who is the one who suffers most on dialysis. They scream and they yell in fear and pain. You tie them in bed. You knock them out. You have the technicians sitting on them. They take all that pain and still do not understand what we are trying to do. It is in these patients that we stop dialysis after consultation with the family.
DR. FRIEDMAN: Does faith or willpower derived from religious training alter the outcome in the elderly?
DR. KJELLSTRAND: I cannot tell you. We have not looked at that factor in our patients. Two years ago, we interviewed 80 patients and put on an 'enjoyability of life' scale. We hope to determine whether this scale, over two years, will help us predict death or withdrawal from dialysis. However, I have no data on the patient's religious convictions.
DR. WING: I come from the little island (Britain) which has been labelled a 'socialist gangster' society.
DR. KJELLSTRAND: Dr. Wing. Dr. Wing. Not you! It is the society you live in that seems to have gone wrong.
DR. WING: Obviously, I have to rise and join in this particular discussion. Dr. Kjellstrand's powerful comments will help me as I try to do something for our patients with renal failure in Britain. For the record, I have some patients over 70. I have two.
DR. FRIEDMAN: You are hiding them from the police?
DR. WING: No. On one occasion I introduced one of them to our Secretary of State, who was most pleased to meet him. They are both doing well. That just makes our present situation more difficult. All our societies - yours included, are going to have to face hard questions about priorities in this area of medicine and

in all areas of expenditure. You have just told us of people whose lives you extended by an average of three years and who, after all that hard work and public and private expense, turn to their doctors and say, 'No thank you, doctor, that's enough. I'm getting out.' If you put a price tag on what you have done, that small gain in human life probably has cost $100,000. Can we go to Parliament or to the Senate and insist on the claims of these patients against those for whom you may do much more at much less costs?

DR. KJELLSTRAND: Obvisously I think it is worthwhile to treat these patients. When these patients quit dialysis, usually they have strokes, they become incompetent, they develop dementia, but it doesnt drag on. Most of those patients are either dead or doing well on dialysis

Dr. Wing, I regard you very highly. I wish you the best of luck as you fight for your patients. I'm sure there's no division between us. You will fight for your patients; I will fight for mine. But I'm not going to stop because someone else says he needs the money for other purposes.

In the United States we are spending our money in a way I find obscene. In the last budget, 30 billion was taken away from the old patients and I believe there were over 10 billion in tax relief returned to those who already have too much. 20 billion, I understand, went to defense. Clearly, it is more important for the people in charge to kill whoever they perceive as their enemy than to save their own people.

I hope Dr. Wing will excuse me if I 'rattle his cage', but I believe he and I have no disagreement, but that we should stand up for our patients. That is the physician's duty. Presently, it seems harder to do so in Britain, but if the present trend in reorganizing priorities in the United States continue, we will soon be in the same boat.

DISCUSSION AFTER DR. NISSENSON'S PAPER

DR. FRIEDMAN: Dr. Nissenson, if I recall correctly, you had 12.8% diabetics, yet the National CAPD Registry says that 48% of new patients are diabetics and the prevalence study throughout the United States says that 30% are diabetic. Where have you hidden your diabetics?

DR. NISSENSON: That data is a bit skewed because 20% of our CAPD population is made up of infants or children many of whom have congenital urologic abnormalities. If we take out that group and look at patients over 20 years our figures for adult diabetics on chronic peritoneal dialysis is closer to 20%. This is less than but similar to the overall NCC $\pm$ 4 figures of 25% for diabetics on all forms of dialysis.

DR. FRIEDMAN: What proportion of your group are geriatric diabetics?

DR. NISSENSON: The overall figure in all age groups for diabetics on CAPD is 16%, while that for the geriatric patients is about 13%.

DR. FRIEDMAN: As they get older, the proportion of diabetics falls?
DR. NISSENSON: Yes, the proportion of diabetics we start on CAPD falls. My report presents data from 40 different dialysis centers, hence you might argue that nephrologists are showing a bias against placing the elderly diabetic on CAPD.
DR. WING: CAPD has been a great help to us. We are able to get patients out of hospital and into their homes very quickly and that is a great advantage when you are treating the elderly. The presence of CAPD raises the question of how this mode of treatment is integrated into other methods of renal replacement. My question is this: How did you calculate your survival on CAPD? How did you count the patients who transferred to hemodialysis; were they still included or were they regarded as lost to observation?
DR. NISSENSON: The actuarial data relate only to the period when the patient is still on CAPD and prior to or one month following a change of modality to or from CAPD. We start the survival clock when the patient starts CAPD as the initial form of renal replacement and use a one month overlap time is patients have changed modalities. There is a mix of new patients and those who have been switched from hemodialysis to CAPD in our data. We havent looked at patients over their entire period of kidney replacement therapy, so one month after they change therapy is arbitrarilly used.
DR. FRIEDMAN: Based on your extensive experience with the EDTA registry Dr. Wing, what course would you recommend?
DR. WING: I would not want to make any recommendations. I would suggest that when anybody reports results, they should spell out the assumptions on which their calculations rest. Then the rest of us will know what they are doing and how they made their calculations.

These treatments should be viewed as complementary. We are treating people by integrated therapy and, as we further incorporate these various methods, survival on renal replacement therapy - the whole package becomes the important thing. Some programs employ more transplantation and have an overall survival as good as those which are with transplantation in their package. In addition, this information allows you to make some important economic points as well.
DR. FRIEDMAN: What method do you use in the EDTA Registry?
DR. WING: We have used all these methods and we have calculated results in all these different ways to illustrate how changing the assumptions changes the results. Currently we are interested in looking at renal replacement as a whole package. Later this year, we shall compare the results achieved by different patterns of programs in different countries.
DR. FENTON: Concerning your survival curves, when you compared the elderly with persons under age 61, did you match these patients for common morbidity risk factors. Even though Dr. Kjellstrand has said that risk factors are not important in the elderly, it still seems probable that cardiac disease, for example,

may have an important influence when one compares the young and the old.
DR. FRIEDMAN: Are you referring to the Cox Proportional Hazard model?
DR. FENTON: Yes, I suggest that the morbidity risk factors were the same in the young as in the elderly.
DR. NISSENSON: We don't know that. This is registry data which has all of the pitfalls of that type of information. We do not have adequate co-morbidity data to do a Cox analysis.
DR. FRIEDMAN: In your judgment, should not all survival figures applied to therapies for renal failure now be reported as a 'proportional hazard' analysis? Is anything less acceptable for comparison between states or countries or networks?
DR. NISSENSON: I agree if modalities and groups are being compared. If a 'snapshot' of the modality in a given area is desired, as with our data, this type of analysis is not critical.
DR. WING: I believe you are right. Proportional hazard is a better way of expressing survival, but we must, as you pointed out earlier, be careful when comparing two different modalities.

The patient mix is different. Our use of CAPD and perhaps yours tends towards older and also high-risk patients so we must be careful not to use these methods to compare one treatment modality against another. The only way to do that would be to undertake a random-mix, prospective controlled trial but I don't think anybody is going to do that.
DR. FRIEDMAN: Is there another method besides the Cox proportional hazard we should be aware of or is that the definitive method?
DR. WING: All these methods are based on actuarial methods; there are different methods of doing these things, such as the Caplan-Meier method and different ways of looking at the time intervals when you project these curves.
DR. FRIEDMAN: That is just life table analysis!
DR. WING: Yes, but with a shorter time interval looking at each event.
DR. HEINZ: Over the past 10 years we have treated over 200 patients with IPD on automatic dialysis machines. Many of them were elderly - 60 and older, up to the age of 80; in our experience, they do well with even 30 hours of dialysis in the hospital. We have no financial interest in the outcome and the government still has a lot of compassion left. I would suggest that an excellent alternative is to set up an intermittent peritoneal dialysis program for some of these patients.
DR. FRIEDMAN: What about technique survival at two years?
DR. HEINZ: It was over 50% in elderly patients.
DR. FRIEDMAN: This is better than any of the results reported from the CAPD Registry.
DR. SCHREINER: We have 75%-two year-survival on CAPD.
DR. FRIEDMAN: In elderly patients, Dr. Schreiner?
DR. SCHREINER: It is no different. In 83 patients, our technique survival was no different over 55 than under 55.

Would you comment on catheter survival? We were surprised that it was not worse, but in fact was slightly better, in those over 55 than in younger patients.
DR. NISSENSON: In our group it was approximately 80% after three years. It was substantially better than in the younger patients.
DR. SCHREINER: You listed diverticulosis as a complication. In our early CAPD series, this condition was highly correlated with morbidity and mortality, and almost all of our mixed-flora infections were associated with diverticulitis. We consider diverticualr diseases to be a contraindication to CAPD and hence I was surprised to see it listed there. We have done partial colectomies in some patients to qualify them for CAPD. Do you not consider this a contraindication?

DR. NISSENSON: We don't do formal screening for diverticulosis, and have seen only one patient out of about 200 who developed the sort of syndrome you are describing. Our practice is not to screen patients routinely because we know the incidence of diverticulosis is going to be high; we have not been willing to exclude those patients on the basis of having diverticuli, and, in any event, it has not emerged as a limiting problem.
DR. KARANICOLAS: You concentrated on CAPD patients but I would have thought that there is still a group of elderly patients who would do better on IPD. Is that where your diabetics were? Have you made any comparisons between IPD and CAPD?
DR. NISSENSON: We had only 33 patients on IPD as of December 31, 1983, but this was less than 7% of the entire home dialysis population. It is not a popular form of therapy.
DR. KOPPLE: May I comment on the term 'elderly' to persons as young as 50 and up to 64 or 65, and with our methods of analyzing this group. A patient who is 60 years of age may be as different from one who is 85 as he is from one who is 20. As we continue to work in this field, should we not add another category, perhaps 60 to 70 and 70 to older, or 60 to 75 years of age. Also some of our best results may be due to the fact that we are calling the middle-aged, 'elderly'; perhaps most of our so-called 'elderly' are under 70 or 75 and that those who are older than that will respond in a dramatically different manner.
DR. FRIEDMAN: Dr. Kopple's point is superb. We must use the Cox proportional hazard approach in which age is a factor.
DR.KOPPLE: It is hard to do this once one gets away from survival data, and of course, much of what we are studying is not survival. With other parameters it would be difficult to do, but it needs to be done.

Another difficult issue is that we tend to define 'elderly' in terms of a chronological age. Social security begins at a certain time. Retirement begins at 65. The government categorizes people that way but, it is clear that there is a remarkable variability with respect to how rapidly people age. Because we are characterizing people as 'elderly' and not 'elderly', we should start now to see if we can identify other kinds of parameters by which we can categorize them.

DR. NISSENSON: In our part of the United States, CAPD, at least in the elderly patient is increasing dramatically; and we believe that this modality not only is successful in the elderly but for many, is the treatment of choice.

PRESENTATION BY DR. SOMMER

PRESENTATION BY DR. CARDELLA

DR. FENTON: Many urge us to transplant the elderly, but, in Toronto, for a person of blood type O, the waiting time for a type O kidney is in the order of two years. If we are going to start transplanting the elderly, the waiting list is going to increase considerably. What are your thoughts on that?
DR. CARDELLA: Transplantation should not be withheld on age alone.
DR. FENTON: Do you have any comments on the practical obstacle that if you put blood-group-O patients, of all ages, on the transplant list, the list will be five years long?
DR. CARDELLA: We should address the shortage of kidneys and not attempt to plan selection for transplantation on waiting time.

I understand your point: any O patient may have to wait two or three years for a transplant and some patients will have to wait longer if older patients are placed on the transplant list. We should do everything we can to shorten the waiting time for both younger and older patients, but not try to shorten the waiting time by excluding people from transplantation on the basis of age alone.
DR. SOMMER: For ABO blood group O patients, the average waiting time is one year. Over the past two years we have increased the number of transplants performed to about 150 transplants a year by educating nurses, dialysis doctors and neurosurgeons, and involving these members of the health team in donor identification. The number of renal transplants performed will only be increased by finding more donors.
DR. FENTON: I agree that if there was an unlimited supply of kidneys we would have no concern about the allocation of resources.
DR. CARDELLA: We should not discriminate the type of therapy by age alone. If an active 30-year-old or an active 60-year-old waits to be transplanted, each will have an equal opportunity to receive a kidney. theyll get the kidney.
DR. WING: May I ask a question on behalf of our nurses concerning the length of previous dialysis before transplantation.

Do these patients go on dialysis with a view to transplantation as soon as possible, or are these people who have struggled with dialysis for years and years and then, almost as a last resort, have come to transplantation. I ask this because data now emerging from the UK Transplant Service shows a notable dialysis effect - the longer a patient has been on dialysis before transplantation, the better his results appear to be. We thought this was an indirect way of looking at the

effect of blood transfusion, but it appears to be separate. Can you tell us about your comparisons between older and younger patients, expecially with respect to the length of previous dialysis.
DR. CARDELLA: We have not looked at that.
DR. SOMMER: One of the main criteria we use in deciding whether to accept a patient for transplantation is whether they have tolerated hemodialysis. If a potential recipient is 70 years old and has no cardiovascular problems on hemodialysis, he or she can be transplanted, and will usually do very well. I believe hemodialysis constitutes a great selection process. The patients with cardiovascular instability are usually weeded out on hemodialysis. We will transplant patients with cardiovascular instabilities; however, one must be aware that cardiovascular disasters may occur in the post operative period.
DR. SCHREINER: Has anybody used a transplanted kidney sequentially in two patients; that is when one patient dies, the kidney is put into a second patient?
DR. CARDELLA: No, I have not.
DR. SOMMER: We have thought about it; howver, problems would arise in obtaining a final cross match since donor cells would be unavailable and the kidney harvest would be an extremely difficult operation.

QUESTIONS TO DR. KLINE

FROM THE FLOOR: My older dialysis patients, as a group, seem to do better perhaps because they could look back over a life of 70 or 75 years and be philosophical about the whole thing. It's hard for somebody who is 35 to be philosophical about a life on dialysis. Why do we call this 'denial', what is it they are denying?
DR. KLINE: Denial is a poorly understood mechanism, it varies all the way from a mild, coping mechanism to a psychotic defence. In this instance, we are talking about a coping capacity as opposed to a major defensive capacity. Life tasks do appear simpler looking back on them than when looking ahead to them, but I believe the implications of treatment and what it means to individuals as they deteriorate, is similar across age groups. It means as much to older people to live well as it means to younger persons. The implications of a blunted future are not quite so severe to the elderly, but nonetheless they also use denial.
FROM THE FLOOR: It is not that they deny that they have a serious illness; that is not what we are talking about?
DR. KLINE: Yes, it is denial of the long-range implications of dialysis because this helps them to accept the procedures.
FROM THE FLOOR: The elderly can look back and see more reasons to be thankful than younger people can.
DR. KLINE: That's possible but it is not just that they are thankful, but the elderly also have fewer life tasks to accomplish. Much of what they've had to do

is done, but they still want the same quality of day-to-day life and they still utilize denial in a manner which is seemingly more effective than their younger cohorts.

QUESTIONS TO DR. DICKENS

DR. KJELLSTRAND: Two technical questions: First, in Canada, how binding is a decision in one province on another one? In the United States each state is sovereign and therefore decisions may differ in between California, New Jersey, Massachusetts, New York and so forth. Second, has Canada decided whether fluid and food are extraordinary, or an ordinary treatment that must be given? In the United States three bitter lawsuits have evolved around this issue.

DR. DICKENS: One province, as such, does not bind another, although one would expect one province to be influenced by others. The provincial Courts of Appeal treat each others decisions with a good deal of respect. A decision of the Supreme Court of Canada, however, will be binding upon all of the provinces, with one exception. The province of Quebec is not in the Common law tradition. This province, like Louisiana, operates in the civil law tradition, and therefore civil (as opposed to animal) decisions of the Supreme Court don't necessarily have the same effect in Quebec, if they concern cases appealed from other provinces. Equally, Supreme Court decisions in Quebec cases are not so influential in Common law provinces.

Regarding whether fluids and food are ordinary and hence mandatory, the Canadian courts have not addressed this. Arguments in the *Steven Dawson* case cited United States and English cases, and it was recognized in the *Arthur* decision of the English Crown Court that the withholding of food may have been a proper decision, based upon the credibility of the prognosis. In Canada, I believe that the determination of whether fluids or food are ordinary or extraordinary would be determined by the prognosis of whether they would help the patient.

DR. FRIEDMAN: The United States, being a more litigious society, does not take things as calmly and may decide less rationally than you suggest. I would like to continue Dr. Kjellstrand's point about the technique of discontinuing 'extraordinary' therapy. Antibiotics have been considered extraordinary therapy by some. The Catholic Church categorizes intravenous fluids administration as extraordinary therapy. With respect to hemodialysis, I don't think an American court would permit a physician to stop hemodialysis as an extraordinary therapy because he no longer believed it appropriate or likely to produce rehabilitation. Has there been such a case in Canada?

DR. DICKENS: In Canada, no. Here, the courts are reluctant to 'second guess' a physician's clinical judgment. In a number of cases in England, for example, which Canadian courts would be disposed to follow, medical decisions have been made on the basis of clinical prognoses, which were judicially accepted. The

highest court, The House of Lords, considered, in the case of *Whitehouse* v. *Jordan* (1981) that a decision was lawful and not negligent because the clinical assessment was competently reached by appropriate knowledge and sensitivity. If that prognosis was that continuation of a particular treatment would be of no avail, its termination would not be judicially faulted.

The American courts have at times gone further: in the case of *Wyatt* v. *Stickney*, for example, the courts didn't quite get into the practice of medicine, but they got into the field of hospital administration. American courts may exhibit a greater tendency to 'get into the action'. This, I believe, is a product of their great receptiveness to expert medical evidence; that is, when given expert data, they will accept it and apply it in considerable detail.

I'm not certain that the position in any of the United States in fact is far removed from the outline that I've given. Indeed, the outline is very much based upon the American case law. That law does not address treatments in themselves, but treats them in the context of individual patients, as the *Quinlan* and related cases show.

DR. MORGENTHAL: I have enjoyed your discussion, but at times the distinction between ordinary and extraordinary care is somewhat more difficult than you suggest. There is no doubt that dialysis, if given to an elderly patient with acute renal failure, who also has adult respiratory distress syndrome and is in septic shock, would keep him from dying from hyperkalemia within the next 24 hours. However, will dialysis offered to a patient who has a less than 10% chance of survival really help him? When the prognosis is uncertain, and the patient clearly has less than a 50-50 chance of survival, how can we distinguish between 'ordinary and extraordinary' care?

DR. DICKENS: Clearly we can do so only with great difficulty! Underlying many legal decisions is a vision of a patient's quality of future life, influenced by the patient's mental awareness and capacity to feel pain (although courts may deny this). However, the courts must give weight to the ethic of medical practice. In the *Bouvia* case, the court concluded that treatment is a matter which physicians must be able to resolve in accordance with their ethical sensitivities. If physicians demonstrated a greater degree of certainty about what the physical and neurological prognosis is in a variety of different circumstances, and what the clinical responses should be, I doubt the courts would 'second guess' that. On occasion, the American courts have said that a practitioner has little defense if the standard of care he or she provides falls short of the standard of ordinary practice. The question, I believe, is essentially procedural: How is the clinical prognosis made? Is it only individual, or does it reflect a body of reputable medical opinion? If one takes other clinical opinions, or can locate appropriate conclusions in the medical literature, a court would be unlikely to fault the decision made. As the 1974 case of *Helling* v. *Carey* showed, however, the courts are final arbiters of patients' legal rights to an appropriate standard of care, and determine *ex post facto* whether it was met.

DR. PORT: You have separated 'extraordinary' from 'ordinary' care. Will you comment on the 'living will', which doesn't address that issue but rather states: 'I don't want a respirator. I don't want an artificial kidney.' What if the patient states in legal document: 'I don't want this kind of machine'?
DR. DICKENS: Again, you have to base your assessment on the clinical facts - is the treatment so prohibited ordinary or extraordinary? If it is extraordinary, it can be withheld or terminated. If in your assessment it is ordinary, you can ask the patient to accept the treatment or to agree to be your patient no longer. If the patient insists on remaining in your care, or must so remain, you may do what the physicians did in the *Bouvia* case, and seek a judicial ruling.
DR. SHIMIZU: Could you comment on the following scenario: A 90-year old man wishes dialysis but he has heart and some other diseases and the physicians refuse him. Can he seek the protection of Section 15 of the Charter of Rights and Freedoms, which guarantees against discrimination on account of age and mental and physical disability?
DR. DICKENS: If the institution has a rule that it will not dialyze anyone over, let us say, 85, that is discrimination on grounds of age and can be a source of legal trouble. Once it is decided that the patient can sustain 'a life of human experience' and can continue for a time in some degree of mental alertness, dialysis probably is legally required, when means to apply it are available.
DR. SHIMIZU: If the family says they want him dialyzed or he says, I want to be dialyzed, what then?
DR. DICKENS: If he and the family both want the treatment, it remains for you to determine whether it will help him. If he is a 'healthy' 90-year-old, that will give him the right to dialysis.
DR. SHIMIZU: Does not Section 15 limit the doctor's freedom of action? His position is not as clear cut as it was before the Charter of Rights was introduced.
DR. DICKENS: There is less legal freedom to be arbitrary. If you refuse treatment, it should not be because the patient is 90, but only because, in your clinical assessment, it won't help the patient to live a life of human experience, measured by a test of modest mental functioning (the *Quinlan* court required active treatment if a 'cognitive, sapient life' could be preserved).

DISCUSSION AFTER THE PANEL

DR. OREOPOULOS: Dr. Wing, I had a patient - an active surgeon who had a mild elevation in his serum creatinine. He said to his wife, 'If I ever develop renal failure, don't ever let me go on dialysis.' He kept repeating that; eventually he did develop end-stage renal disease. His wife said, 'Instead of asking me to make the decision, make it yourself.' When he was faced with the dilemma, he decided to go on dialysis and he spent five years on dialysis before he died.
Dr. Reiff emphasized that we are advocates for our patients, and that our

responsibility to society and the public purse is secondary to our responsibility towards our patients. I understand the situation in Great Britain has changed recently, and that the Government has decided to increase the number of ESRD patients who will be treated. I believe this change of heart is the result of the efforts of many nephrologists and those of that admirable lady, Elizabeth Ward. However, I gathered from your presentation that we should accept the situation and adjust to the pressures of the Government.

DR. WING: Regarding your senior physician, my own reaction is to wait and see what happens when he develops renal failure. Attitudes change remarkably when the issue is real rather than theoretical.

Regarding the need for us to be advocates, I am well known as an advocate for patients with renal failure and use my data and comparisons to press their case more strongly. However, at the end of the day I see that we get what we can for our patients but we won't ever get everything we could spend as doctors. In the United Kingdom in response to our pressure, the Government has announced a target of 40 patients per million of population. Currently we accept only 33 per million; 40 per million is now the target. They haven't given us a date for reaching it. The next stage will be: If that is the target, then we need so many facilities. The battle lines are drawn. We go on with our campaign.

DR. HALLORAN: The challenge seems to be: How can we contain costs? Can we discover more cost-effective ways of treating all the people who need it? Should we not direct some research towards cost containment?

DR. WING: I agree. If we could reduce the cost of dialysis, we could make it available to more people. The lower the cost per individual, the more patients I can treat. Also, your cost is determined by the type of program you have, for example transplantation is the cheapest alternative. The more of your patients who are alive with functioning transplants, the lower your individual costs. Thus we should look not only at individual methods but at the entire renal replacement program.

DR. SCHREINER: Dr. Reiff pointed to a fundamental flaw in society's approach to chronic illness. Once you place a price on human life or on spiritual values, the corruption is not in a technique but in the fact that you have decided that the patient is for sale at a price. The chief economic error is in saying that because your budget is limited that your health dollar must also be proportionately limited. Society should have choices within a limited budget and free society should have the freedom to change or rearrange its priorities as the environment changes.

If we view the conquest of ESRD as a race, is it even ethical to quit the race? In the British system it appears that someone has decided that now is the time to quit the race.

DR. WING: We live in a democracy. Our elected leaders make the decisions. I have to do the best I can for my patients with what my elected leaders give me.

DR. FRIEDMAN: We need to distinguish three degrees of triage in uremia therapy:

Firstly, underdeveloped nations must decide: Do we provide uremia therapy or malaria control? Uremia therapy or nutrition for underfed mothers and children?

Secondly, industrialized but economically depressed nations like Great Britain need to choose between transplants with expensive cyclosporin, dialysis, or not treatment and pass the burden on to underfunded nephrologists.

Thirdly, in the United States, Israel and Japan, we are very quick to say that any attempt to cut back on money for nephrology care translates into excluding the elderly, diabetics, and demented patients.

Many defects in renal care under the American Medicare program were due to misdirection of funds by nephrologists. I am in favor of legitimate cost accounting, auditing and restrictions forcing the use of all dollars directed for renal failure therapy to the renal patient.

DR. REIFF: Dr. Schreiner raised an important issue: money has no value except as a symbol. There's no shortage of money. The government prints as much as it wants when it wants to. We do have certain material shortages but those have not been the limiting factors. The limiting factor is the will of our society to do what needs to be done.

I also think that there's another important analogy between the burdens that are being put on nephrologists and other health care providers these days by society. The analogy, is an uncomfortable one from 40 years or more ago and related to the Judenrot. I don't know how many of you remember what the Judenrots were. The Judenrots were the Jewish leaders who the Nazis used to run the ghettos. The Judenrot had the job to make the laws and regulations in the ghettos so that the ghetto society would run well. The SS were very clever. They said to the Judenrot: you have to supply 5,000 Jews per day for relocation to the East, and if you don't do it we're going to come in and do it for you. So the Judenrot went ahead and they made this difficult decision because they wanted to keep the SS out the ghettos and everyday they would supply the required number of Jews. They were honest men, they were leaders of the Jewish communities and they tried their best. You all know what happened to the entire populations of the ghettos and you know what happened to the Judenrots. Those that survived the deportations themselves until the end frequently committed suicide when they realized what they had done; they had become accomplices of basically a criminal society.

I don't want to draw too strong an analogy, but I think Dr. Kjellstrand did not overstress or overstate the case this morning. What our society has done and is doing now raises a number of serious ethical and moral questions. It is up to us to emphasize the consequences of what is happening in society so that we dont become conspiring partners in carrying out what are morally wrong decisions, i.e., reducing necessary medical services in the name of 'cost containment'.

QUESTION FROM THE FLOOR: Please comment on the promotion of basic science research in the developing countries.

DR. FRIEDMAN: That is the rational approach to future planning provided that we must care for those now ill with ESRD.

FROM THE FLOOR: I'm from the Cleveland Clinic. I work directly with dialysis patients everyday. I see an elderly, sick and tragic population. We are in difficult times in dialysis but we need to do our best to give everybody a chance.

Dr. Reiff, I was moved to tears by your presentation, but I also resented your emotional blackmail in the subject matter. As a humanist, as a women, as a Jew, I resent being equated with the mentality of the Third Reich, and yes, I do overthink in an intellectual, 1985 room full of caring people, I will not allow you to put a guilt trip on me.

DR. REIFF: When I have presented this material in other forums, the audience has generally shown one of two reactions. One is a reaction of agreement or support or appreciation for raising some very uncomfortable issues. The other has been an expression of outrage for even making a comparison with the Third Reich. I did preface my remarks with caution about too close an analogy. But I think one of the mistakes we make is sometimes forgetting what Pogo had said: 'We have met the enemy and they is us.'

It is too simplistic to think of the Third Reich and the Nazi era as being all due to evil people and that they were different from us. As we look around our society and at ourselves, more realistically, I think we can see that many of the things that were done -- I'm not talking about the horrendous death camp experiments and the atrocities and the actual gasings on the massive scale -- I'm talking about the acquiscence of the large percentage of the German population with what happened. Most of them were good people. In fact, most of the physicians who took part in the early euthanasia program thought they were doing society a service.

I'm sensitive to your reaction. I appreciated, when you said as a Jew you resented this, and I think an emotional reaction like that is understandable. I think that we have to make ourselves uncomfortable and see that we are not, necessarily, as far away from those who have done some very bad things in the past.

I've come to the conclusion that most of the bad things in the world are done by good people, because 'bad' people rarely get into positions of power to do them. It is the nice people, the good people who, because they bear most of the responsibility are capable of doing the most harm. That includes us, all of us.

DR. KJELLSTRAND: Our job is not to count money. Our job is to take care of patients and to speak up for them.

DR. WILLIAMS: Dr. Oreopoulos, ladies and gentlemen, I have the honor to introduce Dr. Michael Kaye who will provide us with a summary of the symposium. Dr. Kaye who has been a leader in nephrology in Canada for 30 years, is Chaplain at the Montreal General Hospital and also is Director of the Division of Nephrology.

DR. KAYE: Giving a talk is like having a baby: easy to conceive and hard to deliver. Composing a summary of this extraordinary symposium, is like describing a pretty girl: you don't know where to start and once you start, you don't know when to finish.

First I would like to thank Dimitrios Oreopoulos for conceiving and putting together this symposium, which highlights an increasingly critical area of health care as it concerns nephrology.

The symposium looked at a variety of nephrological problems in the older patient. It has become apparent that we face special challenges when we treat the aged. Increased susceptibility to toxic agents, nephrotoxic antibiotics, abnormalities in the cardio-vascular and other systems; impaired immunological responses, and a tendency to malnutrition. These additional risk factors at the extreme of life require special consideration.

However, even with one or several of these abnormalities, most of the elderly can be assured of an acceptable survival. Dr. Lamiere from Gent described comparable recovery rates for young and old with acute renal failure that were most impressive. He has shown what is possible in all nephrology units, including my own.

In end-stage renal disease and chronic renal failure, the experience of Chris Blagg from Seattle and Carl Kjellstrand from Minneapolis, show apparently equal patient satisfaction with life, irrespective of age and type of dialysis. Indeed, these quality-of-life factors were similar to that of the general population. Dr. Kline's data also confirmed this.

Should we put all this technology and effort into the care of the aged with end-stage renal disease, if we are only going to lengthen their lives for a short period. Thus we end up with a moral problem. We can treat, we can dialyze, we can prolong life, but should we? Should we ask those who lived most of their lives, to move over and make room for the young?

I believe the individual has to make the choice; the patient has to decide whether to be treated or not and if life is to be prolonged whether its quality is such as to justify continuation of treatment. I am speaking for individual patient autonomy.

My experience with the aged on dialysis confirms their desire for treatment if there is a reasonable likelihood of success. In this they do not differ from younger patients. If we agree that the patient's wish is decisive, we should initiate treatment irrespective of age. Once we, as a society, or a group of doctors begin to consider criteria of individual worth, which would be applied to treatment options, we are heading for major trouble.

Dr. Isaacs gave us some insight into the social dynamics in the United Kingdom; it suggests that, in this world, the minorities tend to get what the majorities want to give them. We are all adept at rationalizing these decisions and arguments can always be advanced to maintain the *status quoß*.

While the elderly may require more financial expenditure, more nursing care,

more attention from the health care team, I believe we must make that effort. If the chronic care homes in Toronto and Montreal will not accept dialysis patients, they must be made to see the error of their ways, because the signs of inhumanity in our health care world is made visible by how we treat (or don't treat) our minorities, our underprivileged, our poor, our mentally infirm, those who have no voice to speak for themselves and finally, the aged.

Any criteria for choosing treatment should be based on the twin supports of patient desire and acceptance, and medical suitability. We have to rigorously exclude considerations of social worth whether expressed as age or any other basis. This view is the undercurrent of many of statements we have heard during the last two days. All that remains to be done is to make sure that we make clear to our various governments how firm our views are on this matter.

INDEX