decreased considerably because of the research and development achievements of previous years. Training and facility expenditures have remained on the same accelerated level because of the large patient population which is being treated. The major program element is treatment of all suitable patients by transplantation, since this is a one-time treatment. This permanent treatment is, of course, preceded by supportive dialysis and patients in whom the procedure is unsuccessful are also maintained by dialysis pending a second attempt at transplantation. About 12,000 of the remaining patients in renal failure who are not suitable surgery candidates are placed on life-long dialysis.

Under the circumstances of this highly idealized program, about 16,000 lives will be saved annually through transplantation in the vulnerable group. In addition, about 11,400 individuals will be maintained through chronic dialysis; most of these will be carry-over patients from previous years.

This hypothetical program which utilizes $150,000,000 of HEW funds, most of which are devoted to patient treatment, provides treatment for about 55% of the number of patients threatened by death because of end-stage kidney disease during the first year of its operation (1975). It is important to note that advanced age and concurrent disorders prevent the successful application of transplantation and/or chronic dialysis to every one of the approximately 50,000 patients who present themselves each year with end-stage kidney disease.

A comparison summary of the results of the three hypothetical situations with regard to end-stage kidney disease shows that an immediate tenfold increase of HEW expenditures primarily for patient treatment under conditions of the present state of the art would, at best, approach a solution for 15% of the patient population threatened by fatal kidney failure in the first year; thereafter, a progressingly smaller percentage of the vulnerable group could be helped. (This situation is, of course, wholly hypothetical, since there does not exist sufficient medical manpower either qualified or willing to participate in such a program). Advances in the state of the art which can be expected through a judicious doubling of HEW support for research and passage of sufficient time to permit the unfolding of research achievements would make it possible to save the lives of about 55% of the threatened patient population in the first year of such a program with a smaller expenditure of funds for patient care than was postulated for the previously described accelerated level program under the current state of the art, which only starts to take care of 15% of those in need of treatment.

e. Hypothetical Program Attempting Treatment of All Patients with Chronic Kidney Failure

1) Introduction

Whenever consideration is given to the problem of ultimately fatal chronic renal failure, the question is frequently raised of what it would cost to make an attempt at treating all patients threatened by a

uremic death--either with the aid of lifelong chronic dialysis or through attempts at kidney transplantation whenever donor kidneys may be available. This question is usually raised by well-meaning individuals for humanitarian reasons.

Approximately three-fourths of the 50,000 patients who present themselves each year with fatal end-stage kidney disease are known to be above the age of 60. This fact together with the many concurrent other disorders afflicting most of these patients (and the rather stringent requirement for emotional suitability for chronic dialysis) make it extremely unlikely that a large-scale application of either transplantation or chronic dialysis to all or practically all of these 50,000 individuals would be successful. A further discussion of practical restraints in terms of requirements for specialized manpower and facilities is found in Chapter 6 (The Cost of Treating All Patients with Chronic Kidney Failure), Section V. Nevertheless, although the original mission of the Kidney Disease Analysis Group did not include the preparation of an answer to this question concerning the cost of a hypothetical "total push" program, it was felt that an analysis of this cost would be a natural corollary to the preceding analyses of costs and benefits of optimal programs aimed at the major primary kidney diseases and at end-stage kidney disease. In any consideration of

possible programs for the amelioration of the kidney disease problem, an attempt to treat all patients threatened with a uremic death regardless of the possible costs, for humanitarian reasons, represents one extreme in a broad spectrum of possible programs. The committee therefore felt that this hypothetical cost should be ascertained to serve as a maximal bench mark for any intensive attempt at program analysis or planning.

The details of such a hypothetical total push program and the necessary calculations are found in Chapter 6.

2) Calculation of Costs

It was obvious that the mere calculation of the cost of the first year of such a total push program would leave a misleading impression as to the true long-term expense involved if such an approach is chosen. Because of the significant rate of survival from year to year among the patients treated by chronic dialysis, the cost of extending treatment to all those needing it in subsequent years will increase considerably with the passage of time. It was therefore decided to calculate the actual cost of the treatment of all individuals requiring it (the new group of vulnerable uremic patients presenting itself each year, the patients on lifelong dialysis who are survivors from previous years, and the patients in whom transplantation was unsuccessful and who must be maintained with the aid of chronic dialysis) for as many

years as needed after the start of the program until a year was reached which could be considered characteristic of a "steady state." At this particular point in time the number of new patients included each year in this program would equal the number of patients dying in the same year, and in this situation a constant or near-constant yearly cost of the program would be reached.

Calculations showed that under the conditions of this program its yearly cost would increase greatly each year during the first 15 years, that the subsequent yearly increases in cost would be of a somewhat lesser magnitude but still highly significant, and that an asymptotic curve approach would show that the steady state would not yet be reached by the twenty-fifth year. Obviously one can expect research advances to occur well within the first 10 or 15 years which would modify greatly the respective efficacies of transplantation and hemodialysis and their costs. It was therefore decided that it would be unrealistic to report the cost of the hypothetical total push treatment program for end-stage kidney disease in terms of the eventual yearly cost of the steady state after 25 years. Rather, it was felt that it would be sufficiently indicative of the true costs to be expected to report the cost of the first year of such a program (the lowest yearly cost), the cost of

the fifth year (a realistically foreseeable sum which is not likely to be influenced significantly by changes in the state of the art), and the cost of the fifteenth year (which is considerably higher than the cost of the fifth year and begins to approach the markedly higher eventual cost of the steady state year).

To obtain a realistic range of cost, the calculations were done on the basis of two cost assumptions for each treatment modality: A higher "present cost" figure which reflects accurately today's costs of transplantation and chronic dialysis, and a realistically reduced "future cost" figure for these treatment modalities.

3) Results Obtained

First Year

Based on "present cost" figures, the cost of attempting to treat 40,000 patients out of the total vulnerable population of 50,000 during the first year of this hypothetical program, by means of chronic dialysis or kidney transplantation, would be $611,000,000.

(Note: If an attempt is made to treat all 50,000 vulnerable patients, the cost of this program during the first year will be $761,000,000.)

If the calculation for the first year is based on the less likely "future cost" rate, the respective figures

would be $422,000,000 and $522,000,000.

Fifth Year

The cost of this program in the fifth year of its existence will range between $1,043,600,000 (based on the low, "future cost" figure) and $1,543,415,000 (based on the higher, "present cost" figure). In this year, 102,161 patients would be treated under the program by transplantation or chronic dialysis.

Fifteenth Year

The cost of this program in the 15th year of its existence will range between $1,816,000,000 (based on the low "future cost" figure) and $2,702,000,000 (based on the higher "present cost" figure). In this year, 179,401 patients would be treated under this program, by transplantation or chronic dialysis.

In view of the fact that it is anticipated that research advances evolving during and after the first fifteen years of the program would introduce considerable improvements into both treatment modalities and would influence true costs significantly, projected expenses for the twentieth and twenty-fifth year of the program were calculated but not reported. It should be noted, however, that the population which would require treatment during each year of this program would continue to grow and thus the yearly costs would increase, until a point beyond the twenty-fifth year at which a steady state would be reached.

B. A Total Program Aimed at Kidney Disease

1. Introduction

It is evident from the foregoing models that concentration in future programs merely on the treatment of end-stage kidney disease is not likely to solve the problem of annual deaths due to irreversible uremia unless unlimited funds are available for an indefinite continuation of such a program. Thus, steps must be taken to decrease the number of people who enter the irreversible fatal stage each year by a systematic prevention or treatment of the primary kidney diseases which initiate their progressive downhill course. It is obvious from the analyses in the three major kidney disease groups--infectious, hypersensitive and hypertensive--that the otherwise inevitable annual reservoir of patients with irreversible kidney failure can be diminished considerably through vigorous programs activated to deal with each of these groups. The application of relatively minor funds in the group of infectious kidney diseases to stimulate systematic screening of high-risk groups followed by diagnosis and treatment, even within the current state of the art and without awaiting additional advances due to ongoing or future research, can bring about a significant future reduction in the number of end-stage patients. Continued and expanded research activities will be necessary to increase the percentage of patients ultimately benefitted by this approach.

In the area of hypersensitivity diseases involving the kidney there appears to be no promising mode of attack in sight except for the launching of a systematic research effort intended to increase

our knowledge of the disease mechanisms involved. Here, the sooner this effort is started the greater the likelihood of a reduction of the number of end-stage victims in the near future. The promise for benefits to be derived from this type of research effort is such that it should not be postponed--particularly since any new effective treatment or prevention modality would produce major benefits in the entire field of hypersensitivity diseases, such as rheumatic heart disease, rheumatoid arthritis and others.

In the group of hypertensive diseases of the kidney an immediate start, within the current state of the art, of screening, diagnosis and treatment can begin to diminish the number of patients who will eventually require end-stage treatment because of their progressive renal involvement. Simultaneous research efforts are likely to make this particular portion of the overall program more effective as time goes by, in the same fashion in which the new antihypertensive drugs developed during the last ten years have succeeded in decreasing by about 50 percent the mortality due to malignant hypertension.

Thus, a meaningful Federal program to reduce the annual mortality due to kidney disease and aimed at a general reduction of the prevalence of the various kidney diseases must perforce be a multifactorial one which brings into play all of the program components--research, prevention, treatment and education--available in our armamentarium. An optimally proportioned mix of these program components must be present to yield maximum benefits in overall number of lives saved. This last concept includes not only deaths avoided today but deaths to be prevented in the years to come. Needless to say, such a total program, to be meaningful and productive, must be aimed at all three

major primary kidney diseases, as well as at end-stage kidney failure.

2. Structure of Total Program Models

In order to arrive at the overall makeup of such a mixed attack on the problem of kidney disease, Tables I and II were prepared. These Tables outline the composition of four hypothetical overall programs--three at different levels of expenditure and under the conditions of the present state of the art, and the fourth under the conditions of the expected advanced state of the art in 1975. Table III presents the benefits estimated for the four overall programs. Scanning this table horizontally provides an intercomparison of benefits in the four disease categories. A vertical scan of this table provides an indication of the sensitivity of the four kidney disease categories to changes in expenditure levels.

These projected total programs consist of a combination of the individual models of programs aimed at the various major primary kidney diseases and end-stage kidney failure which have been mentioned previously and which are described in detail in Chapter 5. Thus, each hypothetical total program divides a specific level of HEW funding among a rational mix of program components the composition of which, in turn, is based on the conclusions from the previous analyses.

Figures 1 and 2 provide another illustration of the qualitative and quantitative makeup of the first three total programs postulated for the current state of the art in Tables I and II. These pie charts serve to illustrate very graphically the influence of the available level of funding on the relative composition of these hypothetical programs. Thus, under circumstances of small budgets the percentage of treatment funds tends to be small, and that of research tends to

Table I

HEW COST SUMMARY
($1,000)

Program Level	Kidney Disease Categories				Total	
	Infectious	Hypersensitivity	Hypertensive***	End-Stage	Cost	Percent
Current Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	3,803	1,500	4,000	—	9,303	19.92
Diagnosis and Treatment	—	—	—	7,240	7,240	15.50
Sub-Total	3,803	1,500	4,000	7,240	16,543	35.42
Research	4,000	5,250	3,800	12,100	25,150	53.85
Training	400	560	380	1,000	2,340	5.01
Facilities	1,000	170	1,000	500	2,670	5.72
TOTAL	9,203	7,480	9,180	20,840	46,703	100.00
Intermediate Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	5,929	3,000	8,057	—	16,986	14.47
Diagnosis and Treatment	—	—	—	30,000	30,000	25.56
Sub-Total	5,929	3,000	8,057	30,000	46,986	40.03
Research	5,500	8,250	4,650	18,000	36,400	31.01
Training	750	750	500	5,500	7,500	6.39
Facilities	8,000	8,000	8,000	2,500	26,500	22.57
TOTAL	20,179	20,000	21,207	56,000	117,386	100.00
Accelerated Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	9,919	3,000	10,114	—	23,033	7.94
Diagnosis and Treatment	—	—	—	171,000	171,000	58.98
Sub-Total	9,919	3,000	10,114	171,000	194,033	66.92
Research	6,500	10,125	5,500	24,000	46,125	15.91
Training	975	750	1,425	10,000	13,150	4.54
Facilities	10,000	10,000	11,600	5,000	36,600	12.63
TOTAL	27,394	23,875	28,639	210,000	289,908	100.00
Accelerated Expenditure Level--1975**						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	11,308	43,000-Vaccine 13,000	11,732	—	76,040	25.94
Diagnosis and Treatment	—	—	—	132,225	132,225	45.11
Sub-Total	11,308	56,000	11,732	132,225	208,265	71.05
Research	7,410	12,450	9,500	1,500	30,860	10.53
Training	1,110	1,870	3,000	5,000	10,980	3.75
Facilities	11,400	10,000	11,600	10,000	43,000	14.67
TOTAL	31,228	77,320	35,832	148,725	293,105	100.00

* Current State of the Art

** Advanced State of the Art

*** Attributable to renal disease associated with hypertension.

Source: See Chapter 6.

Table II

TOTAL COST SUMMARY
($1,000)

Program Level	Kidney Disease Categories				Total	
	Infectious	Hypersensitivity	Hypertensive***	End-Stage	Cost	Percent
Current Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	11,687	2,000	5,330	—	19,017	7.88
Diagnosis and Treatment	139,388	—	28,032	17,825	185,245	76.73
Sub-Total	151,075	2,000	33,362	17,825	204,262	84.61
Research	5,330	7,000	5,070	12,800	30,200	12.50
Training	530	750	510	1,000	2,790	1.16
Facilities	1,330	225	1,330	1,300	4,185	1.73
TOTAL	158,265	9,975	40,272	32,925	241,437	100.00
Intermediate Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	14,977	4,000	10,954	—	29,931	9.00
Diagnosis and Treatment	140,275	—	32,442	43,200	215,917	64.93
Sub-Total	155,252	4,000	43,396	43,200	245,848	73.93
Research	7,330	11,000	6,200	18,700	43,230	12.99
Training	1,000	1,000	670	5,500	8,170	2.46
Facilities	10,670	10,670	10,670	3,300	35,310	10.62
TOTAL	174,252	26,670	60,936	70,700	332,558	100.00
Accelerated Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	22,097	4,000	13,899	—	39,996	7.60
Diagnosis and Treatment	143,616	—	36,852	189,375	369,843	70.29
Sub-Total	165,713	4,000	50,751	189,375	409,839	77.89
Research	8,670	13,500	7,330	24,700	54,200	10.30
Training	1,300	1,000	1,900	10,000	14,200	2.70
Facilities	13,330	13,330	15,460	5,800	47,920	9.11
TOTAL	189,013	31,830	75,441	229,875	526,159	100.00
Accelerated Expenditure Level-1975**						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	25,190	{200,000-Vaccine 34,000	16,120	—	275,310	33.84
Diagnosis and Treatment	103,721	68,000	53,858	144,875	430,454	52.91
Sub-Total	188,911	302,000	69,978	144,875	705,764	86.75
Research	9,880	16,600	12,000	1,500	39,980	4.91
Training	1,480	2,490	4,000	5,000	12,970	1.60
Facilities	15,200	13,330	15,460	10,800	54,790	6.74
TOTAL	215,471	334,420	101,438	162,175	813,504	100.00

* Current State of the Art

** Advanced State of the Art

*** Attributable to renal disease associated with hypertension.

Source: See Chapter 6.

Table III

PROGRAM BENEFITS

Program Level	Kidney Disease Categories				Total
	Infectious	Hypersensitivity	Hypertensive***	End-Stage	
Current Expenditure Level*					
Short-Term Benefit-Reductions:					
Mortality	70 Deaths	610 Deaths	2,190 Deaths	690 Deaths	3,560 Deaths
Prevalence	3,231,260 Cases	—	27,000 Cases	—	3,258,260 Cases
Morbid Days	15,962,420 Days	—	1,802,000 Days	—	17,764,420 Days
Long-Term Benefit-Reductions:					
Annual	1,750 Deaths	—	4,330 Deaths	—	6,080 Deaths
Cumulative	25,850 Deaths	—	86,560 Deaths	—	112,410 Deaths
Intermediate Expenditure Level*					
Short-Term Benefit-Reductions:					
Mortality	70 Deaths	610 Deaths	2,270 Deaths	1,560 Deaths	4,520 Deaths
Prevalence	3,243,860 Cases	—	34,880 Cases	—	3,278,740 Cases
Morbid Days	16,273,640 Days	—	2,056,820 Days	—	18,330,460 Days
Long-Term Benefit-Reductions:					
Annual	1,770 Deaths	—	4,820 Deaths	—	6,590 Deaths
Cumulative	26,190 Deaths	—	96,300 Deaths	—	122,490 Deaths
Accelerated Expenditure Level*					
Short-Term Benefit-Reductions:					
Mortality	70 Deaths	610 Deaths	2,380 Deaths	7,675 Deaths	10,735 Deaths
Prevalence	3,292,860 Cases	—	42,750 Cases	—	3,335,610 Cases
Morbid Days	17,483,880 Days	—	2,311,340 Days	—	19,795,220 Days
Long-Term Benefit-Reductions:					
Annual	1,870 Deaths	—	4,820 Deaths	—	6,690 Deaths
Cumulative	27,480 Deaths	—	96,300 Deaths	—	123,780 Deaths
Accelerated Expenditure Level-1975**					
Short-Term Benefit-Reductions:					
Mortality	80 Deaths	770 Deaths	9,300 Deaths	27,399 Deaths	37,549 Deaths
Prevalence	5,630,780 Cases	62,250 Cases	289,690 Cases	—	5,991,723 Cases
Morbid Days	26,064,430 Days	2,610,000 Days	5,578,860 Days	—	34,253,290 Days
Long-Term Benefit-Reductions:					
Annual	4,125 Deaths	8,610 Deaths	9,480 Deaths	—	21,090 Deaths
Cumulative	76,500 Deaths	320,000 Deaths	189,660 Deaths	—	586,160 Deaths

* Current State of the Art

** Advanced State of the Art

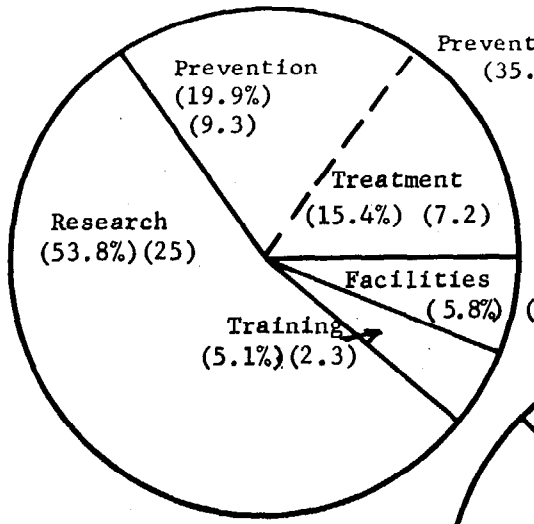
*** Renal disease associated with hypertension.

Source: See Chapter 6.

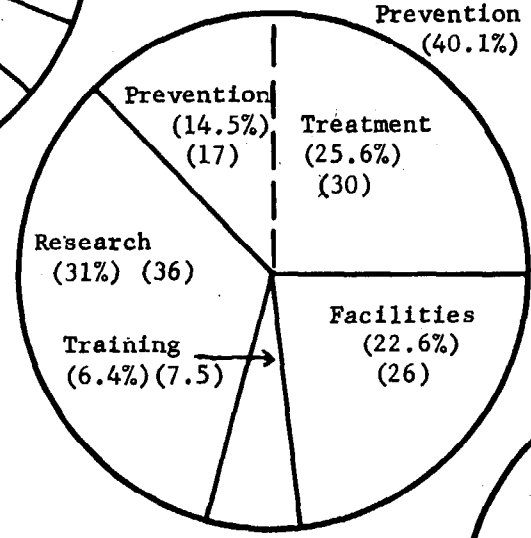
Short-term benefits - reduction in annual mortality, etc., when program is fully operative.

Long-term annual benefits - eventual annual reduction in number of cases reaching end-stage kidney disease.

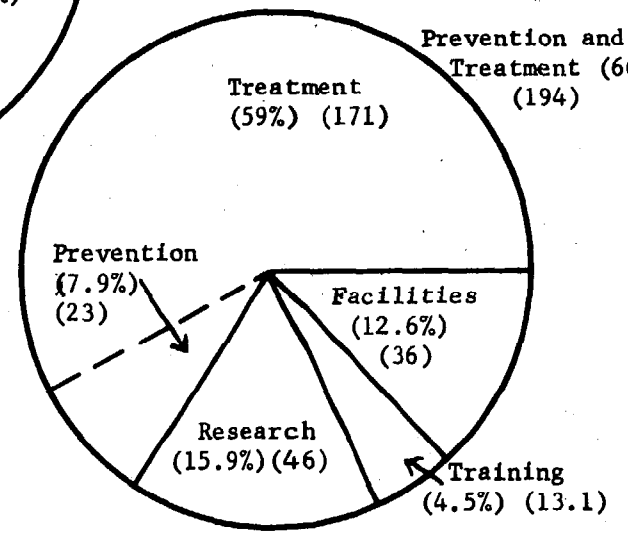
Long-term cumulative benefits - sum total of long-term annual benefits.



Current HEW Expenditure Level
(Current State of the Art)
Total Cost = 46.7*($1,000,000)



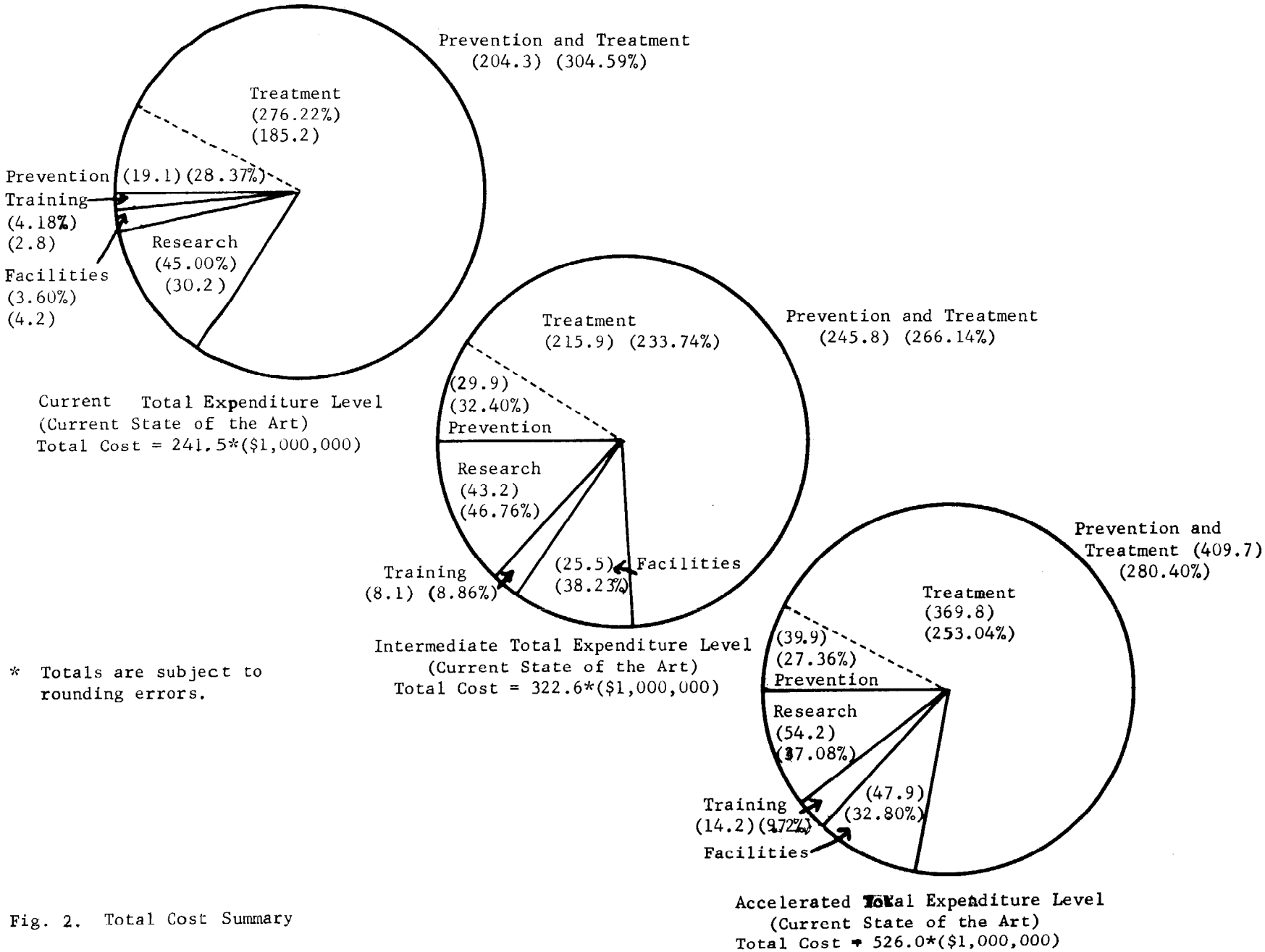
Intermediate HEW Expenditure Level
(Current State of the Art)
Total Cost = 117.4*($1,000,000)



Accelerated HEW Expenditure Level
(Current State of the Art)
Total Cost = 289.9*($1,000,000)

* Totals are subject to rounding errors.

Fig. 1 HEW Cost Summary.



* Totals are subject to rounding errors.

Fig. 2. Total Cost Summary

be large. As the level of expenditure is liberalized this relationship becomes reversed, although in each case the absolute expenditure for each component still grows.

C. Future Shifting Proportions of Program Components

Figures 1 and 2 have illustrated the influence of the amount of available funds on the relative proportions of the various program components in such total efforts. Another factor which will influence these proportions very significantly is the prevailing state of the art with respect to the various primary kidney diseases and end-stage kidney failure. This was evident in the program analyses involving the individual groups of kidney diseases; the same principle holds in relation to overall programs as illustrated on Tables I and II. Here too, the total program mixes illustrated do not and should not represent static proportions to be followed in future years. Depending on advances in knowledge and methodology which will be derived from ongoing research efforts, these proportions will have to be changed each year to obtain maximal benefits in terms of lives saved both in the long run and in terms of the immediate future. Thus, as survival figures for transplantation improve, more patients who would otherwise be maintained permanently with the aid of dialysis will be treated by kidney transplant, and proportionately more funds should be channeled in this direction. As improved methods of primary prevention are developed (such as an anti-streptococcal vaccine) more funds will have to be allocated for the applications of the new techniques since their successful use will reduce the long-term mortality at a relatively small per capita expense.

D. Outlook

With an advancing state of knowledge and with the passage of time, the proportions of the optimal mix for a total program for the solution or

amelioration of the kidney problem will follow the general outlines of the diagram presented in Figure 3. It illustrates a gradually increasing emphasis on successful prevention and effective treatment of the various primary kidney diseases with progressively lesser needs for the saving of lives due to end-stage kidney disease. Given such a set of circumstances there will be a continued need for a repeated searching re-evaluation of the entire kidney disease problem, so that program decisions will continue to bring maximum benefits to patients afflicted with kidney disease.

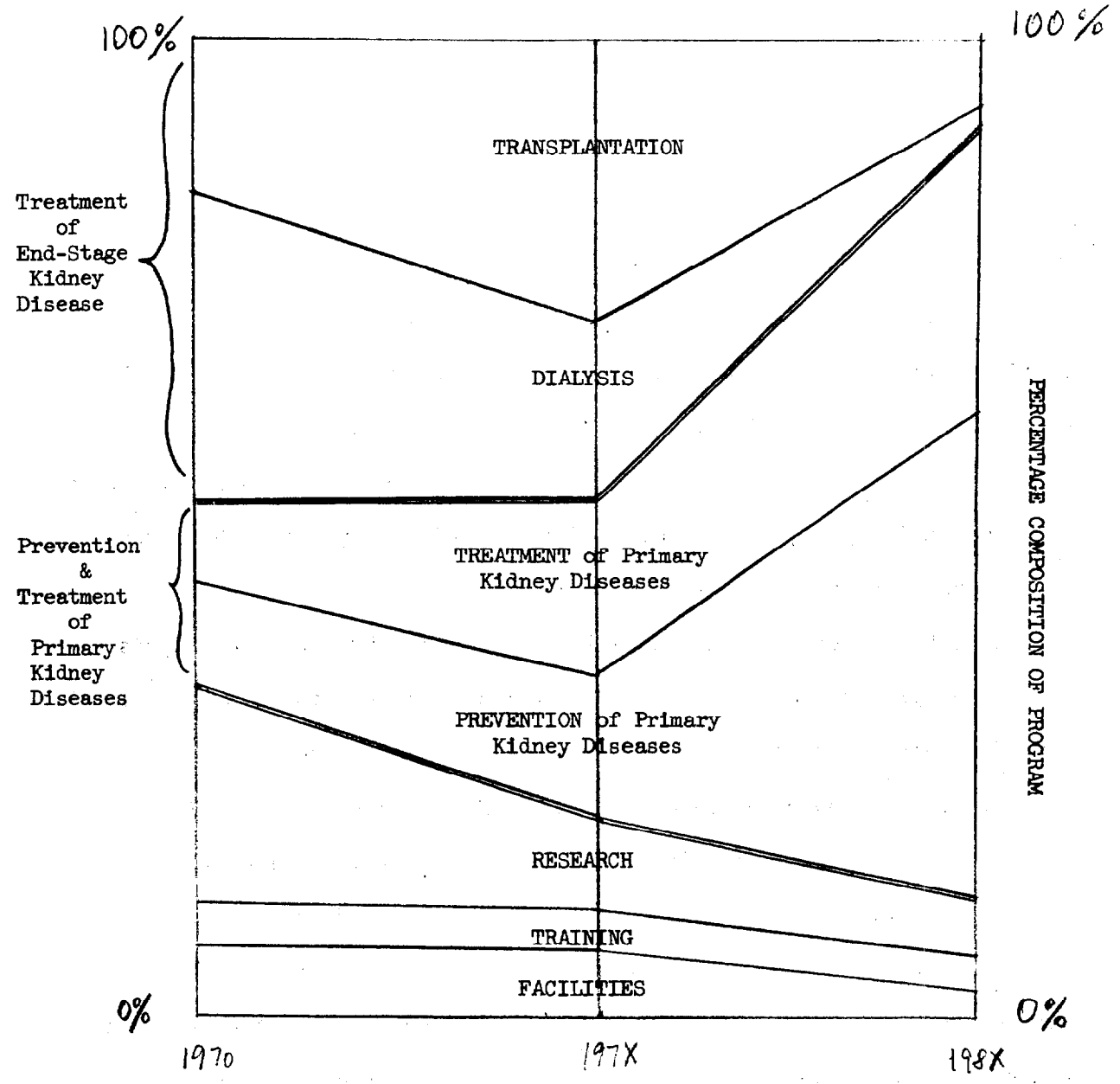


Figure 3. EFFECT OF ADVANCING STATE OF THE ART ON FUTURE PROGRAM COMPOSITION
(Percentages are wholly arbitrary and merely serve to illustrate shifting trends.)

Chapter 2

Kidney Disease--Current Status

I. INTRODUCTION

Dramatic advances in the treatment of end-stage renal failure have sparked new hope for people suffering from this hitherto fatal condition. Today hundreds are living useful and productive lives while undergoing chronic hemodialysis. Hundreds more have received successfully transplanted human kidneys and carry on life with minimal interruption in their daily activities. Current programs to increase research and development in transplantation and chronic hemodialysis, and training of personnel to supervise these complex procedures promise a wider application.

Yet, though dramatic and usually successful, chronic hemodialysis and renal transplantation are difficult procedures associated with considerable morbidity and mortality. At best these procedures are now applicable to a relative few patients who reach the terminal stages of renal failure.

A rational program in kidney disease, therefore, requires that opportunities to interrupt all processes leading to renal disease be sought and pursued vigorously. We must fill the gaps in our understanding of the pathogenesis of renal disease; we must define and isolate the etiologic factors, and careful and detailed study must settle the areas of controversy.

II. THE DISEASE PROBLEM

As indicated in Chapter 1, diseases of the kidney have steadily gained in significance as an area of social importance for both federal and nonfederal research and service efforts during the last five years--primarily because of the development of hemodialysis and kidney transplantation. In general,

however, mortality from kidney disease and other urinary system diseases has steadily declined since 1900 from about 100 deaths per 100,000 population in 1900 to 17.2 in 1964. Total mortality for all age groups among the four disease groups mentioned in Chapter 1 for 1964 was 58,788. The distribution of mortality among these disease groups is depicted in Figure 1. As can be seen, hypertensive renal cardiovascular diseases accounted for the greatest percentage (36%) of deaths among the kidney disease groups considered in the analysis.

Figures 2-5 graphically present the importance of morbidity associated with kidney diseases in terms of prevalence, days of restricted activity, days of bed disability and total work loss days. In general, there is little morbidity associated with hypersensitivity diseases of the kidney. Total morbid time of all types is generally evenly distributed among the remaining disease groups. During the period of July 1964 - June 1965, kidney diseases accounted for about 140,000,000 total days of restricted activity, 63,500,000 days of bed disability, 17,000,000 work loss days, with a prevalence of about 7,800,000 cases.

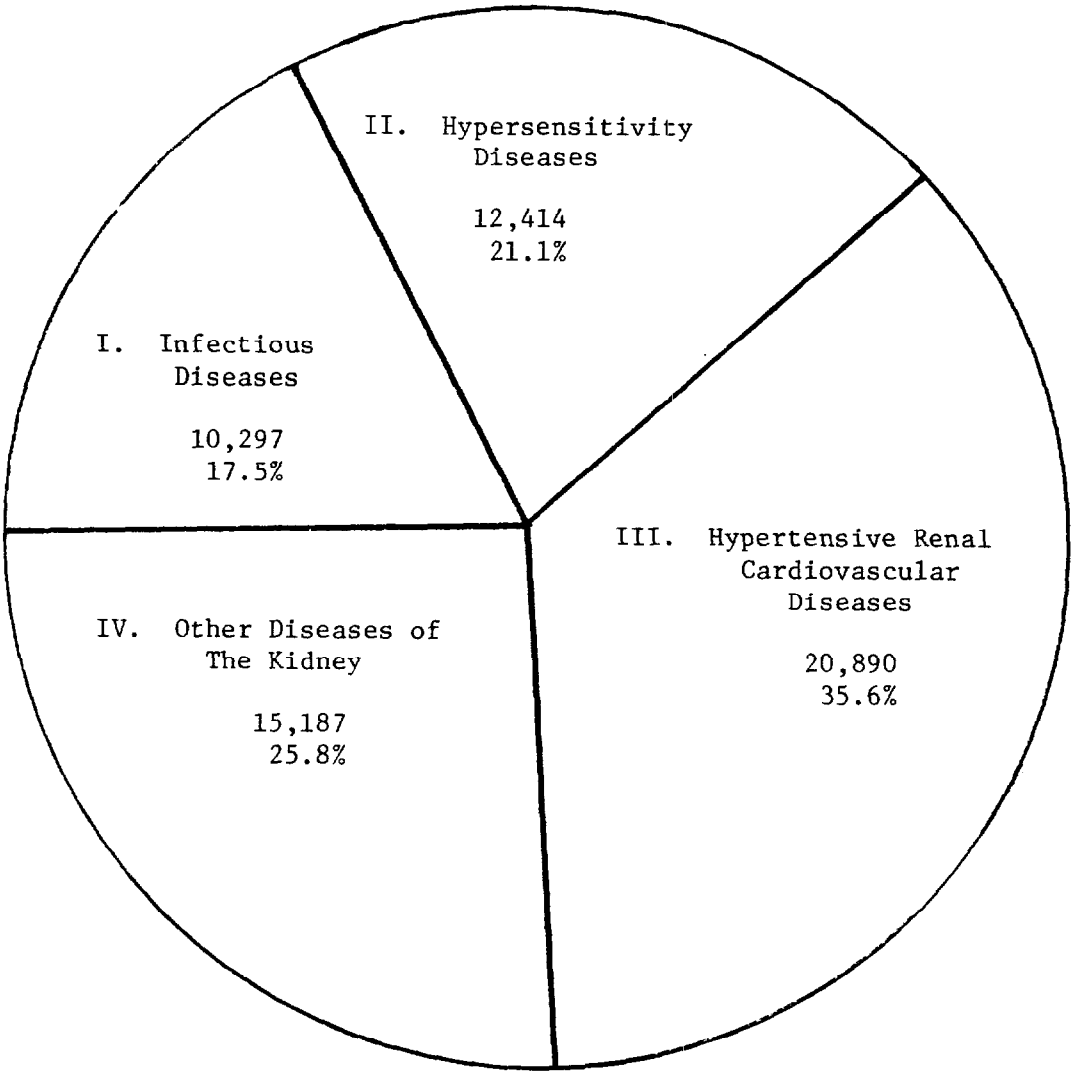
III. DISEASES OF INTEREST

A. Hypertension

1. Introduction

Arterial blood pressure is maintained by a variety of mechanisms and is subject to a number of influences such as posture, emotional state and exercise. When measured correctly in the steady resting state a diastolic blood pressure in excess of 90mm. of mercury is considered abnormal.

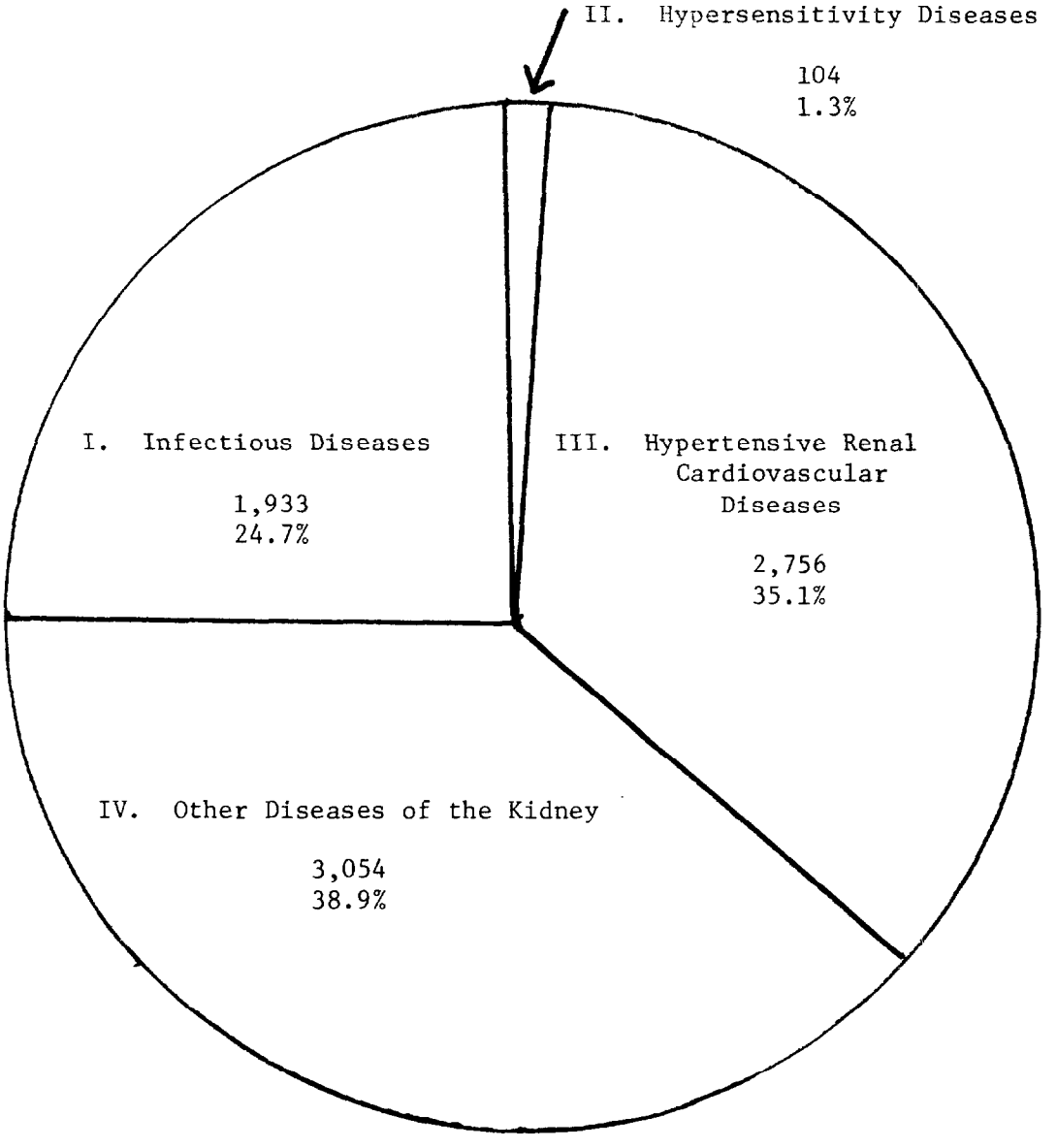
The conditions characterized by established diastolic hypertension



Total Mortality--58,788

Fig. 1. Mortality from Kidney Disease in 1964 by Disease Group.

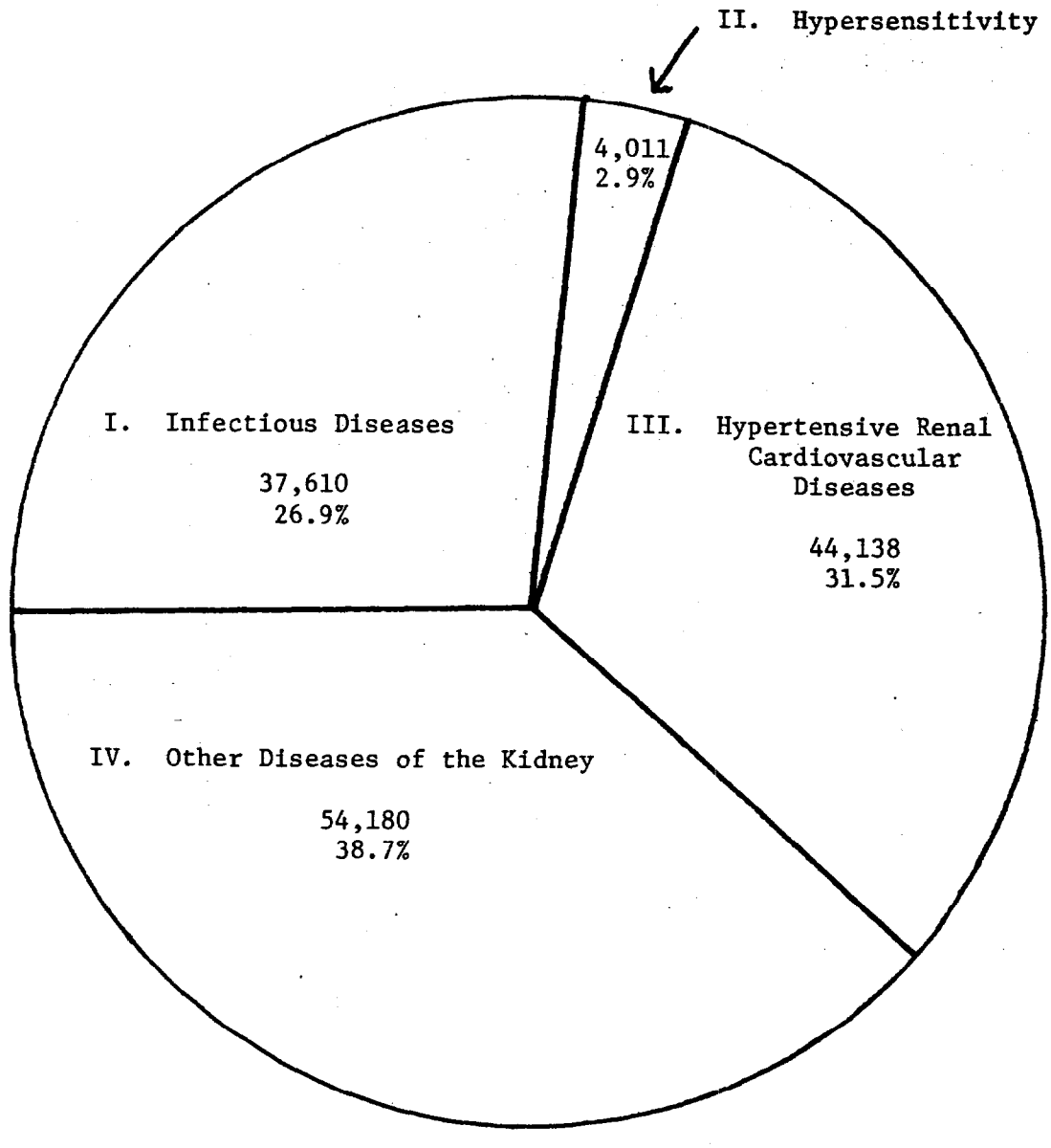
Source: Unpublished data from the U.S. Department of Health, Education, and Welfare, Public Health Service, National Center for Health Statistics, Washington, D.C.



Total Prevalence - 7,847

Fig. 2. Selected Chronic Conditions, Prevalence (1000's), United States, July 1964 - June 1965.

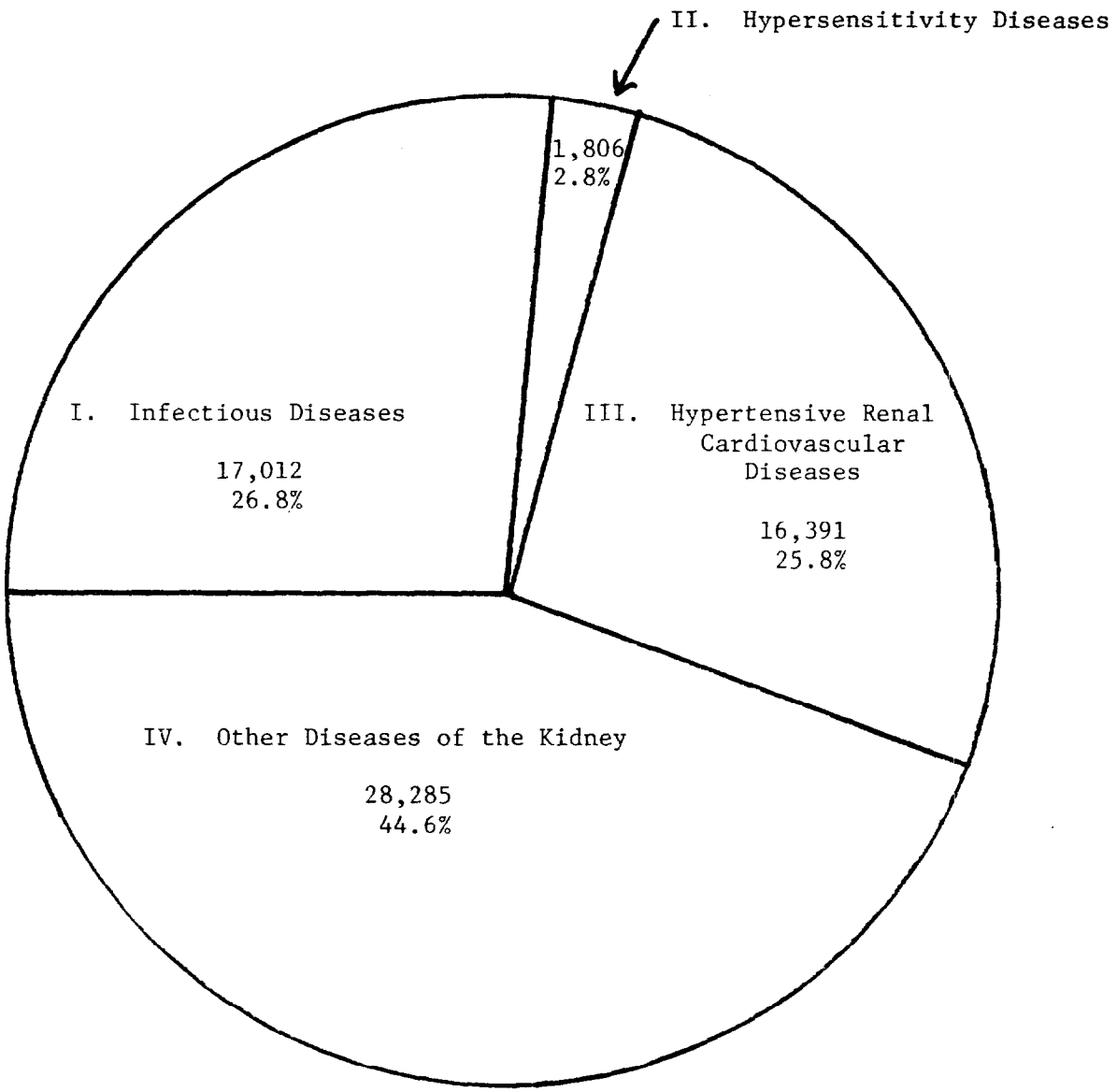
Source: For civilian non-institutional population from unpublished data from the U.S. Department of Health, Education, and Welfare, Public Health Service, National Center for Health Statistics, Washington, D.C.



Total Days of Restricted Activity - 139,939

Fig. 3. Selected Chronic Conditions, Days of Restricted Activity (1000's), United States, July 1964 - June 1965.

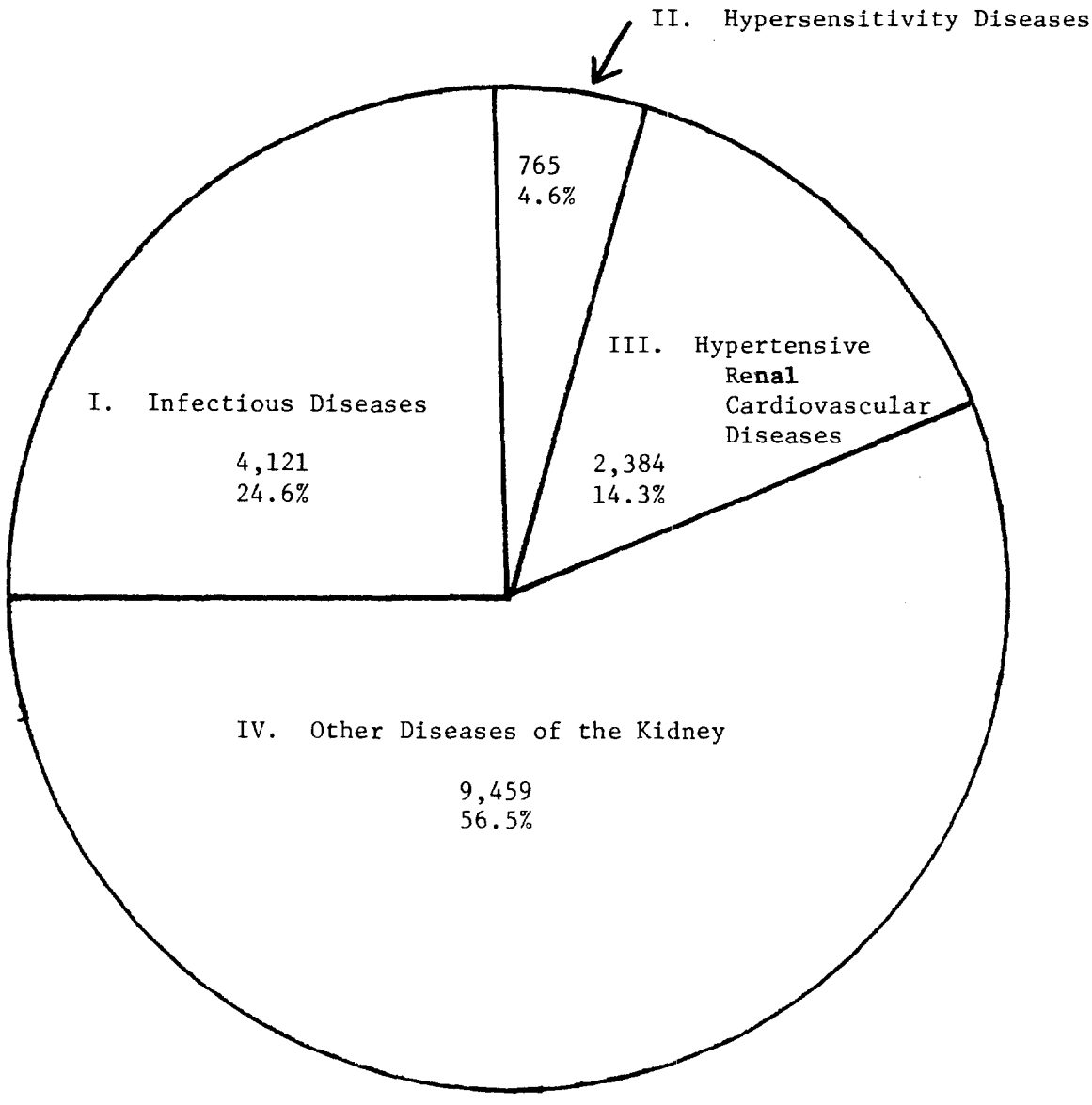
Source: For Civilian non-institutional population from unpublished data from the U.S. Department of Health, Education, and Welfare, Public Health Service National Center for Health Statistics, Washington, D.C.



Total Days of Bed Disability - 63,494

Fig. 4. Selected Chronic Conditions, Days of Bed Disability (1000's), United States, July 1964 - June 1965.

Source: For civilian non-institutional population from unpublished data from the U.S. Department of Health, Education, and Welfare, Public Health Service, National Center for Health Statistics, Washington, D.C.



Total Work Loss Days - 16,729

Fig. 5. Selected Chronic Conditions, Work Loss Days (1000's), United States, July 1964 - June 1965.

Source: For civilian non-institutional population from unpublished data from the U.S. Department of Health, Education, and Welfare, Public Health Service, National Center for Health Statistics, Washington, D.C.

include primary (essential) hypertension, of unknown cause, comprising 80-90% of the total, and secondary hypertension accounting for 10-20% of the hypertensive population. In the secondary group, the hypertension can be traced to some underlying process. This group is especially important because often the hypertension can be cured. Processes leading to secondary hypertension include: adrenal tumors, renal artery stenosis, pyelonephritis, acute and chronic glomerulonephritis, pheochromocytoma, coarctation of the aorta, and certain disorders of the central nervous system.

2. Primary (Essential) Hypertension

a. Incidence

Primary hypertension occurs in 5-10% of the adult population of the United States. In 1965 it was estimated that 9,200,000 individuals had hypertension. It is twice as common in women as in men and there is a strong familial tendency. The average age of detection is about 32 and onset after 50 years of age is most unusual. When followed from the onset of hypertension, the average patient lives for a period of 20 years. (The average life expectancy at 32 is 41.5 years.) The course of the individual patient varies. Some patients may enter an accelerated phase in a few months; others may survive with few complications for 40 or more years.

Of those with essential hypertension 5-10% develop an accelerated or malignant form which is fatal if untreated.

b. Clinical Course--Benign Hypertension

Initially there may be no symptoms and the patient is often unaware of the illness until informed by his physician. The clinical course roughly divided into an uncomplicated phase lasting an average of 15 years and a complicated phase with progressive damage to the heart, kidneys, brain, eyes, and other systems.

During the uncomplicated phase about 2/3 of the patients have a variety of usually minor symptoms including fatigue, nervousness and headaches. After an indefinite period, complications appear. Atherosclerosis is common. Hypertension accelerates arterial damage and predisposes to the deposition of lipid materials. In most there is gradual enlargement of the heart. Congestive heart failure is eventually responsible for about 25% of the deaths and is a contributing factor in another 25%. About 10% of hypertensives die of a myocardial infarction while another 10% die following cerebral thrombosis or hemorrhage. Thus, some 70% die from major vascular problems.

In the kidneys, damage to the small arteries is found in a high percentage of patients. Approximately one-half eventually develop some evidence of renal damage (manifested by polyuria, diminished concentrating power, or proteinuria), but uremia is only rarely the cause of death unless there is an accelerated or malignant phase of disease.

c. Accelerated or Malignant Form

Some 5-10% of patients with essential hypertension develop an accelerated phase with progressive renal damage and higher fixed diastolic blood pressure. The onset is usually abrupt and is characterized by headaches, failing vision, nausea, and weight loss. Unless the course is interrupted by treatment, complications develop rapidly and death from brain, heart or kidney damage usually occurs within two years. About one-third of these patients die with severe renal complications. Early treatment of this group is important since progressive changes in the small arteries of the kidney develop rapidly. After these changes have developed to an advanced state,

lowering blood pressure may precipitate renal failure. Therapy started early significantly prolongs life in this group. The impact of successful drug therapy for malignant hypertension can be inferred from an almost 50% decline in the death rate from hypertensive heart disease since the introduction of antihypertensive agents in 1952.

3. Secondary Hypertension

In every patient with established diastolic hypertension, the possibility of secondary hypertension should be considered. Known causes must be systematically excluded by history, physical examination, appropriate laboratory tests and X-rays. The incidence of secondary hypertensions is estimated at from 10 to 20% of the total hypertensive population. Of these 5-15% are caused by renovascular (renal arterial) lesions. Another group of potentially curable hypertensives are those having hypertension secondary to aldosterone-producing adrenal tumors. Presently experts differ on the incidence of aldosterone-producing tumors in the hypertensive population. It is variously estimated that these tumors account for from 1 to 20% of the hypertensive population. Most investigators are now finding that 1% of their hypertensive patients have this condition. Other causes of secondary hypertension such as coarctation of the aorta, various renal diseases, Cushing's disease, pheochromocytoma and central nervous system disorders can be excluded only by careful and often extensive examination.

4. Etiology of Primary Hypertension

The cause or causes of hypertension have been and are the subject of intensive study by many distinguished investigators. There are three major theories relating to the development of hypertension. Some have stressed the importance of neurogenic factors and psychologic stress,

others have emphasized excessive sodium intake and abnormal endocrine control, while still others have concluded that renal circulation and renin are of primary importance in the development of hypertension. There is much evidence supporting each theory. Possibly one or all of these factors operates in a given individual who may be genetically predisposed to the development of hypertension. In this brief review emphasis will be placed on the renal relationships with hypertension without intending to imply that renal factors are the underlying cause of all primary hypertension.

The association between pyelonephritis and hypertension exists but the exact nature of the relationship has not been clarified. Patients with hypertension have a reported incidence of pyelonephritis varying from 14% to 51%. Conversely, from 12% to 85% of patients with histologic evidence of pyelonephritis are reported as having hypertension. The high incidence of pyelonephritic kidneys in hypertensives suggests that hypertension either predisposes to renal infection or is the direct cause of pathologic changes which are indistinguishable from those usually caused by infection. It has also been postulated that chronic renal infection is a major cause of hypertension. Current evidence is substantial regarding these views, but is not yet conclusive.

The relationship between hypertension and arteriolar nephrosclerosis (damage to the small arteries of the kidney), of the kidneys is also a subj of continuing controversy. Clearly, most hypertensives have nephrosclerosi to a greater or lesser extent. Now most investigators think that the nephrosclerosis is secondary to the hypertension. Some, however, maintain that the renal arteriolar lesions may be the precipitating cause of the hypertension. Whatever the underlying cause, it seems clear that once

established, hypertension accelerates the development of renal arteriolar stenosis and conversely that the arteriolar lesions may sustain and aggravate the increase in blood pressure. In malignant hypertension, renal ischemia leads to increased renin output with secondary hyperaldosteronism and an accelerated rate of hypertension which in turn leads to further renal arteriolar damage.

Further clarification of these important areas will have far-reaching therapeutic implications.

5. Management of Hypertension

With proper screening of the hypertensive population it is probable that 10-20% will be found to have underlying causes amenable to permanent cure. In malignant hypertension and in advanced diastolic hypertension (blood pressures in excess of 110mm. in men and 120mm. in women) early drug therapy and dietary management have been demonstrated sharply to reduce morbidity and mortality. In patients with lesser elevations of blood pressure the evidence favoring treatment is less substantial. Treatment must be individualized balancing the risks inherent in any chronic treatment against the potential benefits. Current long-term studies will help clarify this area.

B. Pyelonephritis and Infections of the Kidney

During the past 30 years since the reports of Longcope and Winkenwerder, and Weiss and Parker, the term pyelonephritis has been widely used to imply a pathologic process resulting from the immediate or late effects of bacterial infection of the kidneys. Unfortunately, the criteria used to diagnose pyelonephritis are not uniform.

1. Incidence

The incidence of chronic pyelonephritis varies widely among various

autopsy series from as low as 2% to as high as 35%. Reasons for these differences are the varying criteria used by pathologists to diagnose pyelonephritis and the differing populations studied. Kidney infections are more common in older populations, are more frequent in Negroes, and occur in higher incidence among lower socio-economic groups. In one careful study, pyelonephritis was found in 3.3% of 4,596 autopsies. Only 10% of these cases of pyelonephritis had demonstrable bacteriuria at death although previous treatment may have resulted in eradication of bacteria in some cases. In this same series 1.6% of 4,596 deaths were attributed to uremia. In another study acute and chronic pyelonephritis was found in 10% to 20% of the autopsies at two hospitals but was judged to be a major factor causing death in only one-third of these cases.

On a national basis in 1964, about 10,000 of the 1,800,000 deaths or 0.5% were attributed to infections of the kidney. This figure must be analyzed. It represents data from a wide variety of sources where there are considerable differences in the diagnostic criteria of pyelonephritis. It does not include cases of obstructive uropathy due to prostatic hypertrophy and prostatic cancer when these were ruled the underlying cause of death though renal infection may have precipitated death. On the other hand, this figure includes cases of renal disease in which there was no documentation of infection by bacteriologic or pathologic means. In other cases renal infection may have been recognized, but the underlying urologic or metabolic defect may not have been apparent.

Such incidence data of kidney infection and pyelonephritis must, therefore, be approached with caution in program planning. The final diagnosis of the cause of death is at best a good interpretation of events in the current state of the art. Many cases of infection are certainly

missed and others are classified erroneously as infection. The margin of error is unknown, but could be large. A rational approach to the control of pyelonephritis must include further research into all causes of chronic interstitial nephritis as well as the search for methods to control kidney infection.

2. Acute Pyelonephritis

Acute pyelonephritis is a common problem usually caused by gram negative bacterial invasion of the kidney. The onset is usually abrupt with characteristic symptoms although at times clinical symptoms may be subtle or absent. The acute symptoms generally subside rapidly although bacteriuria may persist without adequate treatment. Recurrences are common, particularly during and following pregnancy. In recurrent cases, a careful search for underlying predisposing factors such as prostatic hypertrophy, stones, diabetes mellitus and congenital malformations should be made. Remedial procedures are indicated where feasible.

3. Chronic Pyelonephritis

Symptoms of infection are frequently absent in patients with chronic pyelonephritis although there may be a history of previous urinary tract infection. The onset is usually insidious with gradual development of the manifestations of chronic renal failure. This period of relative renal insufficiency may be long. During this period many patients live in comfort for years despite azotemia. Bacteriuria may be absent or present only intermittently making accurate diagnosis difficult during life. In such cases, other causes of nephritis must be considered. Eventually, end-stage renal failure is reached unless intervention is undertaken.

4. Bacteriuria and Urinary Tract Infection

Bacteriuria may be defined as the presence of over 100,000 organisms per cc. of urine on a culture of clean fresh urine. Defined in this manner persistent bacteriuria indicates infection of the urinary tract. There has been much debate about the role of bacterial infection in the pathogenesis of chronic pyelonephritis. Repeated bouts of kidney infection whether manifest or silent lead to renal scarring and eventual renal failure. But in many cases bacteria cannot be isolated from kidneys in which the pathologic diagnosis is pyelonephritis. One current and controversial theory to explain this discrepancy is that bacteria may initiate a self-sustaining destructive process which persists after bacteria have been eradicated. Another possibility is that some cases classified as pyelonephritis are due to non-bacterial causes. It is not known how often bacteriuria per se is the forerunner of chronic pyelonephritis. Since bacteriuria is present in patients who do not subsequently develop pyelonephritis and since the source of bacteria may be the urethra, bladder or other lower urinary tract sites, there must be many cases in which ascending infection does not develop. On the other hand, bacteria in the lower urinary tract may lead to kidney infection, particularly in the presence of predisposing factors such as obstruction, stones, diabetes and gout. Furthermore, such bacterial infection can act as a source of virulent organisms in the development of septicemia. Thus, while bacteriuria may not always lead to the development of chronic pyelonephritis, its presence should be taken seriously, and careful consideration given to management.

In young patients persistence of bacteriuria should be confirmed by a minimum of two cultures of clean voided specimens. If bacteriuria persists in an asymptomatic patient, a short course of antibiotic treatment should be followed with repeat culture at intervals. If bacteriuria still persists, investigation to detect underlying correctable lesions is indicated.

In later stages of pregnancy about 6% have asymptomatic bacteriuria. Of these, at least 40% will develop pyelonephritis. It seems reasonable to treat bacteriuric pregnant women for the duration of the pregnancy. In older patients in whom the incidence of bacteriuria may be 10 to 20%, treatment must be undertaken with some caution. The eradication of bacteriuria in the elderly is difficult and the risk of complications from over-zealous treatment seems great.

Carefully controlled long-term studies are necessary to determine in which cases vigorous treatment of bacteriuria will prevent the development of chronic pyelonephritis. Judicious application of current techniques to control infection may result in eventual reduction in the number reaching the end-stages of pyelonephritis.

Hypersensitivity Diseases

1. Acute Glomerulonephritis

Acute glomerulonephritis is a common disease affecting all age groups, but it occurs predominantly in children. Almost all cases follow by one to four weeks infection with hemolytic streptococci. These bacteria initiate an immune process which is almost certainly responsible for the subsequent renal damage. Only certain nephritogenic types of streptococci are responsible for acute glomerulonephritis. Thus, in some epidemics of hemolytic streptococcal infections, glomerulonephritis is not seen,

while in others the attack rate is high, the disease often striking several members of the same family.

Most cases are mild and some may go unnoticed. In mild symptomatic cases, renal damage is manifested by blood in the urine and puffiness due to salt and water retention. In more severe cases hypertension, anemia, and even acute renal failure may develop. As a rule most patients recover completely, but currently, about 2% of hospitalized patients die of acute renal failure. In 1964, 585 deaths were attributed to acute nephritis. An additional 2,900 died of nephritis not specified as acute or chronic. A few patients with the acute form enter a protracted subacute course with gradual deterioration of renal function over a 6 to 12 month period. Nephrosis seldom occurs in the acute phase.

In another group, comprising probably not much more than 1% of the total with acute post streptococcal glomerulonephritis, healing is incomplete. These patients show continuing proteinuria and eventually develop one type of chronic glomerulonephritis. Failure to heal is more common in adult cases of acute glomerulonephritis and seems to be associated with non-epidemic streptococcal infections. Estimates vary, but about one-tenth to one-third of all cases of chronic glomerulonephritis are post streptococcal in nature.

2. Chronic Glomerulonephritis

Chronic nephritis and nephrosis accounted for 8,800 deaths in 1964. Chronic glomerulonephritis cannot be defined as a single disease entity and probably has multiple causes. In most cases the etiology is obscure. In various autopsy series its frequency has been reported from 0.5% to 1.5% and is about one-third as frequent a cause of death as pyelonephritis. The onset occurs in all age groups. If those presenting with the nephrotic

syndrome are excluded, the greatest number are first noted between age 10 and 40.

Chronic glomerulonephritis usually begins quietly and progresses slowly. The first manifestation is frequently persistent protein in the urine. In other instances onset is abrupt with rapid development of nephrotic syndrome characterized by edema and massive proteinuria. Hypertension rarely appears until renal damage is severe. The course is variable lasting from one to about forty years. In one series the average duration was seven and one-half years in those who have died, however, many in this series are still living. The course may be punctuated by episodes of nephrosis and may terminate abruptly. Signs of renal failure appear gradually, but once azotemia appears, progress to end-stage renal failure is usually a matter of only a few years.

3. Nephrotic Syndrome

Massive loss of protein in the urine may be caused by a variety of renal diseases and leads to the development of the nephrotic syndrome. Clinically this syndrome is characterized by massive swelling of the body and face known as generalized edema. Underlying renal diseases such as lupus erythematosus, diabetic nephropathy and post streptococcal glomerulonephritis are occassionally recognized, but more often no underlying cause can be detected.

4. Idiopathic Nephrotic Syndrome

Nephrotic syndrome due to unknown causes is a major cause of morbidity and mortality, most often in children between the ages of one and six. The annual occurrence in this age group is estimated at 2 per 100,000.

Patients with the nephrotic syndrome present a variety of clinical pictures. In the idiopathic form glomerular lesions lead to urinary