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Renal function in the aged

James W. Landers
University of Nebraska Medical Center

RENAL FUNCTION IN THE AGED

James Walter Landers

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TABLE OF CONTENTS

Page

I. Introduction..... 1

II. Review of the Literature..... 3

A. Morphologic Aspects..... 3

1. General Evidence of Renal Senescence..... 3

2. Theories of Genesis of Renal Senescence..... 5

3. Summary of Morphologic Evidence..... 7

B. Functional Changes with Age..... 9

1. Review of Literature..... 9

2. Summary of Present Concepts..... 15

III. An Investigation of Renal Function in Aged Males..... 16

A. Aims and Methods..... 16

B. Results..... 19

C. Discussion..... 23

D. Conclusions..... 24

IV. Summary..... 26

V. Bibliography

I. Introduction.

It is perhaps not surprising that, in a society which places the highest value upon youth, the problems of old age should have for long been almost neglected. However, belated recognition of the fact that the proportion of elderly individuals in our population is steadily increasing, and will continue to do so, has within recent years stimulated a considerable amount of investigation into the biological (as well as social and psychological) implications of ageing.

The problem to be considered here, that of the effect of senescence upon the function of the kidney, has not received the attention which has been accorded other facets of ageing, notably the phenomenon of arteriosclerosis. This is no doubt largely due to the fact that, in non-hypertensive individuals, renal functional impairment due to senile change is clinically unimportant as a primary cause of morbidity and mortality; the kidney, being an organ of large reserve capacity, ordinarily outlasts the heart and the brain. Nevertheless, a significant reduction in this reserve may have important consequences in certain very common situations: e.g., the stress of major

surgery, obstruction of the urinary tract by prostatic enlargement, and congestive heart failure. In the latter instance, a further complicating factor is introduced by the frequent use in therapy of nephrotoxins -- the mercurial diuretics. It seems evident, therefore, that the renal functional alterations which accompany senescence are deserving of study. A good deal has already been accomplished, in the slightly more than a decade since this problem was first attacked, but much more remains to be learned. It is to be hoped that investigation in this field will continue, and that the information obtained will prove of practical clinical value in the steadily enlarging sphere of geriatric medicine.

II. Review of the Literature.

A. Morphologic Aspects.

That atrophic changes do occur in the kidney as a consequence of ageing has been demonstrated in a number of studies carried out on animals. One of the most marked instances of this is the involution which takes place in the kidney (mesonephros) of the daddy sculpin, as described by Grafflin (1). The young fish of this species possesses a glomerular kidney; with ageing, however, marked glomerular degeneration occurs, varying from simple avascular atrophy to cyst formation or actual necrosis. Accompanying the glomerular atrophy, tubular constriction at or near the junction with the glomerulus occurs, and the kidney is thus transformed into the aglomerular structure seen in the adult fish. A similar phenomenon, although less extensive, is seen in the kidneys of other species of fish (2).

MacKay, MacKay and Addis (3) demonstrated that in the rat age has definite influence on the degree of compensatory hypertrophy following unilateral nephrectomy. They found that in rats one month of age the remaining kidney increased in weight by 52.6 per cent (the baseline being one-half the average weight

of both kidneys in a control group); at one year of age, the increase in weight amounted to only 32.3 per cent. Moore and Hellman (4), in a similar experiment, showed that unilateral nephrectomy has no influence on the extent of the senile changes in the rat kidney; they described a decrease in the total number of glomeruli as a consequence of ageing. Arataki (5) also studied the effect of ageing upon the kidney of the rat, and found that the number of glomeruli decreases from an average of 31,000 at maturity to 20,000 in old age (500 days).

General evidence of renal senescence in man has been provided by Roessle and Roulet (6), who showed that the average weight of the human kidney declines from approximately 260 grams at age forty to about 190 grams at age eighty-five; and by Moore (7), who demonstrated a decrease in the number of glomeruli with age in the human kidney. The latter author found that the total number of glomeruli in the human kidney in the seventh decade of life is two-thirds to one-half that during earlier adulthood. Finally, in any discussion of renal ageing it should be remembered that the mammalian urinary system, even at birth, is no stranger to senescence; for the formation and subsequent degeneration, during intrauterine develop-

ment, of the pronephros and mesonephros are necessary antecedents to the development of the definitive excretory organs.

There are two theories extant concerning the genesis of the ageing process in the human kidney. The first of these, and the one favored by the majority of writers, assumes that the atrophic changes which occur in the senile kidney are entirely secondary to the vascular obliteration which results from arteriosclerosis in the renal vessels; the second, that there is a primary parenchymal involution (or at least some component thereof) and that the vascular changes, in part or in toto, are secondary to this phenomenon. The evidence for the latter of these theories will be considered first.

Kaufmann (8) and Furno (9) each described what they believed to be a primary renal parenchymal atrophy, accompanied by no or minimal arteriosclerosis. This Furno considered to be the "typical senile kidney", although, interestingly enough, only ten of the seventy pairs of senile kidneys examined by him showed this change, the remainder manifesting arteriosclerotic alterations of one form or another. Councilman (10), who found sclerosis of the renal arteries of varying degree in three-fourths of the aged kidneys which he

examined, believed that part of the involutional changes seen were due to vascular sclerosis, but not all; no alternative explanation is advanced, however. More recently, Williams and Harrison (11), in discussing the progressive decrease seen with age in the number of glomeruli in the human kidney, propose that the narrowing of the renal arteries and arterioles is one factor, but that there seem to be others, possibly a primary involutionary process. Moritz and Oldt (12) describe a type of renal arteriolar sclerosis (intimal proliferation) which they believe to be common as "adaptive involutional change in vessels whose capillary beds have been reduced by parenchymatous atrophy".

Fahr (13), on the other hand, describes the senile human kidney as a "benign nephrosclerosis" secondary to arteriosclerosis. Loomis (14), working with microdissected material, states that the atrophy of the parenchyma is a result of vascular sclerosis and obliteration, and varies from cloudy swelling and fatty metamorphosis to the final stage of the shrunken arteriosclerotic scar, wherein thirty nephrons in various stages of degeneration have been observed to occupy an area formerly taken up by three normal nephrons. This author also describes compensatory alterations,

consisting of formation of new vascular channels and hypertrophy of tubules of unaffected nephrons. Oliver (15) studied microscopically the kidneys of seventy-five individuals over seventy years of age without primary renal disease, and in each case found vascular changes which he considered sufficient to account for the parenchymal atrophy observed. This writer refers to renal senescence as "a special case of ageing of the vascular system". Similar implications are present in the descriptions of the senile kidney given by Bell (16), Anderson (17), and Fishberg (18), each of whom describes the typical senile kidney as one in which wedge-shaped areas of parenchymal atrophy, due to atherosclerosis in the larger and medium-sized branches of the renal artery, are the prominent feature. Indirect evidence in support of the contention that atrophy is secondary to vascular alteration is found in the work of Gersh (19), who showed that the degeneration of the embryonic mesonephros can be correlated with disappearance or shifting to other organs of the blood supply.

In the opinion of the author, the greatest weight of the available evidence appears to support the contention of Oliver (15) that if a primary parenchymal involution does occur in the human kidney, its effects

are obscured by the manifestations induced by vascular sclerosis and obliteration. Certainly it is difficult to exclude an involutional process; but in the absence of positive evidence thereof, it appears unnecessary and illogical to invoke the concept of primary parenchymal atrophy when, as seems probable, the atrophy observed can be satisfactorily explained on the basis of arteriosclerosis. Whether arteriosclerosis itself is a "normal" part of the ageing process in another problem, far too vast to be considered here; but the extremely common occurence of atherosclerotic manifestations in the aged kidney makes it evident that the concept of renal senescence as consequence of arterial change is the most reasonable working hypothesis.

In brief, then, the typical senile kidney may be described as one in which atherosclerotic involvement of the larger and medium-sized branches of the renal artery, and to a much lesser extent the arterioles, leads to wedge-shaped areas of subcapsular parenchymal atrophy, with loss of a significant number of nephrons, and a moderate reduction in the size and weight of the organ (11, 14, 15, 16, 17, 18). It may be added that, as recently demonstrated by Handler et al. (20), arteriosclerotic changes in the renal

arteries with age are in general more marked in the Negro than in the white race.

B. Functional Changes With Age.

Granted, then, that renal arteriosclerosis, with its resulting atrophic manifestations, is an inevitable corollary of ageing in the great majority of cases, what is the functional significance of this phenomenon?

Agreement is general that "normal" senile changes in the kidney (i.e., uncomplicated by renal disease, including hypertension) rarely give rise to clinically important disturbances of renal function. That some degree of alteration might occur seems plausible, however, when one considers the morphologic changes previously discussed. Nevertheless, until relatively recently little attention has been devoted to this problem.

Musser and Phillips (21) found in a series of fifty individuals over seventy years of age that 88 per cent showed indications of renal impairment based upon one or another of the criteria of hypertension, decreased phenolsulfonphthalein excretion, elevation of blood non-protein nitrogen, and albuminuria and

cylindruria. Aside from this observation, the first significant study of age changes in renal function was that of Lewis and Alving (22), on a series of one hundred clinically normal males ranging in age from forty to eighty-nine years. These investigators found a decrease in the urea clearance from 100 per cent at age forty to 55 per cent at age eighty-nine; an increase in the blood urea nitrogen over this age range from 12.03 milligrams per cent to 17.62 milligrams per cent; and a decrease in the concentrating capacity of the kidney from a specific gravity of 1.030 to 1.023. From these data, empirical equations for the decline in urea clearance, the rise in urea nitrogen and the decline in specific gravity were calculated, as follows: for the urea clearance, UC = 136.6 - 0.912 X A, where UC is the urea clearance in per cent of the normal average of 75 cc. per minute (or 54 cc. per minute in those instances in which "standard" clearances were used), and A is the age in years; for the blood urea nitrogen, BN = 7.56 + 0.112 X A milligrams per cent; and for the specific gravity (after the 24-hour fluid restriction regime of Addis and Shevky), SP = 1.036 - 0.00015 X A. The values quoted, from which these conclusions are drawn, are mean values obtained in each decade, and

it has been pointed out by Peters (23) that the individual variations in each decade are considerable; i.e., that the data do not so much indicate a general downward trend in renal function in normal subjects with age as they do an increased frequency of renal functional impairment in later life. While this is to a certain extent a valid criticism, it is likewise evident from analysis of the data (particularly of the urea clearance values) that few if any of the values obtained in the older subjects, especially those over seventy years of age, are comparable to those found in the younger groups; in other words, even the maximum individual urea clearance values among the aged subjects are significantly lower than the mean values for the younger group. Essentially the same remarks apply to the more recent investigations of renal function in age discussed below.

Olbrich et al. (24,25) reported a study of inulin, diodrast and urea clearance tests in fifty subjects over sixty years of age, presumably free of organic disease. These were divided into two groups: those with normal, and those with elevated, diastolic blood pressure; the limit of normal for the diastolic blood pressure was arbitrarily chosen as 100 millimeters of mercury. The following mean values for the various

clearances are given: in the group with normal diastolic pressure, the inulin clearance was found to be decreased 30 per cent (from the normal average for young subjects); the diodrast clearance was decreased 30 per cent; the urea clearance was decreased 25 per cent. In the group with diastolic hypertension, the inulin clearance was decreased 40 per cent; the diodrast clearance was decreased 50 per cent; and the urea clearance was decreased 35 per cent. These investigators attribute the decline in inulin clearance to vascular changes which result in decreased renal plasma flow, rather than to impairment of glomerular filtration; they believe, however, that tubular excretory capacity is impaired, either because of lowered efficiency or because of decreased "tubular mass".

Shock (26,27), in investigating renal function in two small series of Negro males aged sixty to eighty-five, demonstrated that: the mean value for inulin clearance was 60 per cent of the average value for young males; the clearance of diodrast decreased to 45 per cent; the filtration fraction (clearance of inulin/clearance of diodrast) increased by 35 per cent; the tubular maximum excretory capacity for diodrast (diodrast Tm) decreased to 67 per cent;

and the diodrast clearance per unit of diodrast Tm decreased somewhat. Similar results were obtained by Davies and Shock (28) in a larger series of seventy males aged twenty to ninety years, all of whom were free of evidence of renal disease, hypertension, cerebral vascular accident or heart disease. In these subjects the mean values for inulin clearance, diodrast clearance and diodrast Tm were found to decrease linearly beyond the age of thirty years; the magnitude of the decrease between thirty and ninety years was essentially the same as reported in the earlier series by Shock, given above. Miller, McDonald and Shock (29), in a group of 76 males from 24 to 86 years of age, demonstrated a linear decrease in the reabsorptive Tm for glucose which agrees percentagewise almost exactly with the rate of decrease in diodrast Tm with age.

McDonald, Solomon and Shock (30) studied the renal hemodynamic changes produced by the intravenous injection of a pyrogen (killed typhoid bacilli) in a series of fifty-four subjects twenty to eighty-nine years of age. It was found that there was proportionately the same rise in the clearance of para-amino hippurate (which is a measure of effective renal plasma flow) in the aged as in the young subjects during the reac-

tion to the pyrogen, although the baseline values in the aged were lower. This was interpreted to indicate that the arterioles of the aged kidney are capable of dilatation, and that the alterations in renal blood flow with age are not due solely to static structural changes. From these data (and certain theoretical assumptions), Landowne and Shock (31) calculated the alterations with age in renal arteriolar resistance, and concluded that "...(in old age) removable vasoconstriction not only persists but becomes more manifest in the presence of structural changes".

In an effort to determine whether the observed decreases in tubular excretory capacity in the senile kidney are due to a lessened efficiency of tubular mechanisms or to a decrease in renal plasma flow, Miller, McDonald and Shock (32) determined the renal extraction of para-amino hippurate in twenty-seven individuals from twenty-three to seventy-five years of age. In each subject, the right renal vein was catheterized via the antecubital vein, superior and inferior vena cavae, and PAH administered through the femoral artery. It was found that, although the clearance of PAH diminishes with age, the aged kidney retains its ability to extract PAH completely at low plasma levels; in other words, the efficiency of aged

renal tubules is unimpaired, and the observed decreases in tubular excretory capacity are entirely secondary to a reduction of renal plasma flow. These investigators are therefore led to the conclusion that the alterations in renal function with age are secondary to vascular changes, and do not represent a primary cellular involution. This hypothesis is in agreement with the predominant theory of renal senescence arrived at on morphologic grounds, as discussed in the preceding section.

It is evident, therefore, from a consideration of the accumulated data, that a general downward trend in the efficiency of the excretory functions of the kidney occurs with advancing age; furthermore, the evidence is highly suggestive that these alterations may be satisfactorily explained on the basis of reduction in renal blood flow which results from arterial and arteriolar sclerosis. However, to return to the previously cited criticism of Peters, it is also apparent, when the results of any of the above investigations are analyzed individually, that the use of mean values in describing the course of renal functional senescence may be somewhat misleading; for despite the clearly demonstrated general decline, the range of individual variation is great. Thus, for instance, the statement

that there is a linear decrease of a certain magnitude for each succeeding decade of life in a particular renal function, while valid for a group, may be quite inaccurate when applied to the individual. This is perhaps belaboring an obvious consideration, but the author feels that such a qualification is often neglected, and deserves to be made explicit.

II. An Investigation of Renal Function in Aged Males.

A. Aims and Methods.

In order to extend the observations of other investigators to a less highly selected (and therefore, perhaps, somewhat more representative) elderly group, the present investigation of renal function in a small series of aged males was undertaken. No attempt was made to duplicate previous studies employing the more critical and difficult methods of inulin and diodrast clearance, PAH extraction, and the like; instead, relatively simple tests in common clinical usage were performed.

Twenty-one male subjects, nineteen white and two colored, ranging in age from sixty-five to eighty-nine years, were selected from the wards of the Douglas County Hospital and the Clearview (Douglas County)

Home. No particular effort was made to eliminate either patients suffering from chronic diseases, or those with manifestations of arteriosclerosis; the following criteria, however, were used in selecting the subjects: 1) absence of history or clinical findings suggestive of renal disease; 2) absence of hypertension (for the purposes of this study, hypertension was arbitrarily defined as a diastolic blood pressure greater than 90 millimeters of mercury); and 3) absence of congestive heart failure (except in one instance).

The methods of study employed were as follows:

1) Routine urine analysis was performed on voided morning specimens on all subjects, including the Roberts test for albumin, and microscopic examination of the centrifuged urinary sediment. The results are shown in table I.

2) Blood urea nitrogen determinations were done on all of the subjects, by the urease method of Karr (33). These results are shown in table II.

3) Urea clearance determinations were carried out on eighteen of the twenty-one subjects. All tests were performed in the morning. Each subject was given one liter of water to drink between 8:00 A.M. and the beginning of the collection period. The bladder was

then emptied at 9:00 to 9:30 A.M., and again exactly one hour later. 5 cc. of blood was withdrawn by venipuncture shortly after the beginning of the collection period; lithium oxalate was used as an anticoagulant. Urea nitrogen determinations, by the urease method of Karr, were carried out on the urine and on tungstic acid filtrates of the blood. In most instances, urine flow during the collection period was between 1.0 and 2.0 cc. per minute, and calculations of urea clearance were therefore done by the formula for standard clearance, Urea Clearance = $UV^{\frac{1}{2}}/B$, where U = urine urea nitrogen in milligrams per 100 cc., B = blood urea nitrogen in milligrams per 100 cc., and V = volume of urine in cc. per minute. In the two instances in which urine flow was greater than 2.0 cc. per minute, the formula for maximum clearance, UC = UV/B, was employed. The surface area of each subject was estimated from the height and weight, using the formula of DuBois (34), and all values were corrected to 1.73 square meters of body surface. The results are found in table II.

4) Phenolsulfonphthalein excretion, by the fifteen-minute intravenous method, was determined in fifteen of the twenty-one subjects, in the following manner: each subject was given approximately 500 cc.

of water to drink. Fifteen minutes later 1 cc. (6 milligrams) of sterile phenolsulfonphthalein was injected intravenously. Exactly fifteen minutes following injection of the dye, the bladder was emptied. The percentage of dye excretion was determined by means of the Leitz photoelectric colorimeter. The results are given in table III.

B. Results.

Table I

Subject	Age	Blood Pressure	Urinalysis*	Remarks
F.K.	65	128/80	A tr. C /	
F.J.	65	146/72	A tr. C /	
H.H.	66	180/90	NA	
P.H.	66	112/70	NA	Bronchiectasis
E.P.	67	116/88	A tr. C ///	
G.B.	68	120/70	C ±	Arteriosclerosis obliterans of legs
A.E.	70	116/90	A /	
S.G.	70	132/82	NA	Rheumatoid arthritis

Table I (Continued)

Subject	Age	Blood Pressure	Urinalysis*	Remarks
J.U.	70	128/68	A ∕ C ∕∕	
C.J.	72	118/60	A ∕∕ C ∕∕∕	Pulmonary tuberculosis
G.C.	72	108/74	A ∕	Arteriosclerosis obliterans of legs
T.A.	73	142/82	C ∕	
H.S.	73	108/66	A tr. C ∕	
E.N.	73	118/76	NA	
E.G.	77	144/80	NA	
C.S.	78	140/70	A ∕∕ C ∕∕∕	
B.H.	78	110/68	NA	
A.A.	79	98/62	C ∕∕∕	
F.B.	79	130/60	A ∕ C ∕	Arteriosclerotic heart disease
J.W.	80	130/62	NA	
F.K.	89	116/76	A tr.	Arteriosclerotic heart disease, early decompensation

* A: Albumin in urine: graded from trace (tr.) to ∕∕∕∕ in the usual manner.
C: Cellular elements in urinary sediment: ∕ = rare; ∕ = few; ∕∕ = moderate number; ∕∕∕ = many.
NA: No abnormalities.

Table II

Subject	BUN in mg. per 100 cc.	Urea Clearance cc./1.73 sq. m./min.	Urea Clearance per cent of normal*
F.K.	14.9	68.0(max.)	90.7
F.J.	21.9	--	--
H.H.	12.6	41.0	75.9
P.H.	16.1	40.2	74.4
E.P.	20.6	29.9	55.4
G.B.	14.0	21.0	39.0
A.E.	15.8	48.4	89.6
S.G.	13.6	27.2	50.4
J.U.	19.4	38.6	71.4
C.J.	14.7	69.2(max.)	92.0
G.C.	15.8	37.7	69.8
T.A.	18.8	57.6	107.0
H.S.	12.6	30.5	56.5
E.N.	11.6	39.0	72.2
E.G.	13.6	17.0	31.5
C.S.	15.8	34.1	63.1
B.H.	21.9	21.2	39.3
A.A.	15.3	--	--
F.B.	14.8	22.9	42.4
J.W.	20.3	28.3	52.4
F.K.	24.4	--	--

Table II (Continued)

	BUN in mg. per 100 cc.	Urea Clearance cc./1.73 sq. m./min.	per cent of normal*
Mean	16.6	35.2	65.2

* Average normal for standard clearance is 54 cc. per minute; for maximal clearance, 75 cc. per minute.

Table III

Subject	Per cent excretion of PSP
F.K.	29.0
H.H.	21.5
P.H.	22.5
E.P.	21.4
A.E.	29.0
S.G.	23.3
J.U.	17.2
G.C.	20.0
T.A.	23.5
H.S.	31.5
E.N.	25.5
E.G.	15.5
C.S.	20.6

Subject	Per cent excretion of PSP
B.H.	22.0
F.B.	33.5
Mean	23.7

C. Discussion.

1. Blood urea nitrogen: as shown in table II, the mean value for the blood urea nitrogen in the twenty-one subjects was 16.6 milligrams per cent. The normal range for this substance in the blood is usually given as 9 to 17 milligrams per cent, so the mean value for this group falls near the upper limit of normal. It is evident, however, from simple inspection, that there is a wide individual variation in these values; the lowest found was 11.6 milligrams per cent, and the highest 24.4 milligrams per cent. The average deviation from the mean (MD) is 2.9; the standard deviation (SD) is 4.63. The standard error of the mean (SDm) is 1.01, and the probable error of the mean (PEm) is 0.15.

Inspection of the data reveals no particular correlation, within the group, between age and blood urea nitrogen values. This is borne out by analysis of the data, which shows a coefficient of correlation (r) of only 0.32, which is not significant. (Since the group was made up entirely of elderly men whose ages fell within a fairly narrow range, and there is no control group of younger subjects, a lack of cor-

relation with age is not surprising).

2. Urea clearance: the mean urea clearance value for the eighteen subjects tested is, as shown in table II, 65.2 per cent of the average normal value for standard urea clearance of 54 cc. per 1.73 square meters of body surface per minute. For this group of values, MD equals 16.9; SD equals 27.3; SDm equals 6.4; and PEm equals 4.3. In other words, the range of individual variation is great, as is true of the blood urea nitrogen values. Again, as for the latter, there is no significant correlation within the group between age and urea clearance values.

3. Phenolsulfonphthalein excretion: the mean value for P.S.P. excretion by the fifteen-minute intravenous method is 23.7 per cent. This is only slightly below the normal minimum for this test of 25.0 per cent. Again the rather marked spread of the individual results should be noted. For these data, MD equals 3.4; SD equals 4.84; SDm equals 1.25; and PEm equals 0.84. There is no significant correlation between age and P.S.P. excretion in this group.

D. Conclusions.

Although the series presented here is too small

to have a great deal of statistical significance, the results are in general confirmatory of the findings of other investigators in indicating a moderate impairment, on the average, in renal function with age.

One point which is well demonstrated by these data, and which has been repeatedly emphasized, is the wide range of individual deviation from the mean in renal functional efficiency among the aged subjects tested. This is a phenomenon which has not been stressed by other writers; however, critical scrutiny of their data reveals its presence. This fact is of obvious clinical importance, since it implies that in dealing with an individual aged patient, any assumptions regarding the renal functional capacity which are based upon the mean are likely to be misleading. In other words, kidney function may be essentially normal, or it may be significantly reduced, in an aged person in whom there is no suspicion of renal disease; and in situations where this is of some importance (the example of administration of mercurial diuretics has been mentioned), special attention to the elderly patient's excretory capacity would seem appropriate.

III. Summary.

The general subject of renal senescence in man, with particular attention to the functional aspects, has been reviewed.

Various authors have shown that with ageing there is a gradual decrease in the number of nephron units in the human kidney, and the typical senile kidney has been described as one which shows sclerosis of the larger vessels with coarse scarring and moderate reduction in the amount of parenchyma. The question of whether the parenchymal atrophy is primary, or secondary to renal atherosclerosis, has been discussed, and it is concluded that the bulk of the evidence favors the interpretation that the vascular alterations are primary.

The results of a number of investigations of changes in renal function with age have been reviewed. It has been demonstrated that with senescence the blood urea nitrogen tends gradually to rise, and that glomerular filtration, effective renal blood flow, and tubular excretory capacity undergo a significant reduction. It has also been demonstrated, however, that at least part of the reduction in renal blood flow is due to functional renal arteriolar constric-

tion; and that the efficiency of the individual renal tubules remains umimpaired. It is suggested that the concept of the primacy of vascular change in the genesis of renal involution appears most probable from functional, as well as morphologic, evidence.

The results of kidney function studies in twenty-one males aged sixty-five to eighty-nine years are reported. The mean value for blood urea nitrogen was found to be 16.6 milligrams per cent; for urea clearance, 65.2 per cent of the average normal clearance; and for phenolsulfonphthalein excretion, a mean value for the fifteen-minute intravenous test of 23.7 per cent. It is pointed out that the data, both in this series and in those of other investigators, show a wide range of individual variation, and that clinical appraisal of renal functional status in aged patients must therefore be an individual matter.

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