Renal Function in the Elderly*

MICHAEL M. LUBRAN, M.D., Ph.D.

Harbor-UCLA Medical Center,
Torrance, CA 90502

ABSTRACT

Renal size and volume decrease with age, accompanied by intrarenal vascular changes. The number of glomeruli decreases and the mass of the juxtedudillary nephrons falls. The result is a decrease in the filtration area of the glomerular basement membrane and decreased permeability. The glomerular filtration rate (GFR) is reduced with aging. The GFR is approximated by the endogenous creatinine clearance, which falls in parallel with the inulin clearance (the true measure of GFR) and is always greater because of tubular excretion of creatinine. Analytical methods for serum and urine creatinine overestimate its concentration and suffer, to varying degrees, from interferences, making the normal range method dependent. A further uncertainty arises from the use of a correction to standard surface area. Serum creatinine concentration is an insensitive indicator of renal function in the elderly. Deduction of creatinine clearance from serum creatinine concentration, weight and age using one of many formulae gives only approximate values, usually too high, and is unsuitable for debilitated and seriously ill patients. Tubular function, in general, is decreased in the elderly. The ability of the kidney to concentrate urine maximally after water deprivation decreases with age, as does the ability to excrete a water and salt load, particularly during the night. Nocturnal polyuria is common in the elderly. The aged kidney can maintain acid-base balance under normal conditions, but not when subjected to an acid load.

Introduction

The aging kidney undergoes structural changes which result in quantitative changes in some renal function tests. A major problem in investigating these structural and functional changes is distinguishing between changes caused by disease and those caused by the aging process. Most of the morphological studies have been carried out on autopsy specimens. In these cases, the state of health of the subject has been determined by examination of the clinical records and exclusion from the study of subjects showing features considered by the investigators to indicate disease. However, in these subjects the immediate cause of death might have produced some morphological changes. Further, some diseases in their early stages, for example diabetes mellitus and hyperten-

* Send reprint requests to Michael M. Lubran, M.D., Ph.D., 180 Granville Avenue, Los Angeles, CA 90049.
sion, may not show overt clinical effects, but may nevertheless lead to changes which could be interpreted as caused by aging. Finally, the autopsy subjects in any study are a selected group and not representative of the elderly population in general. It is therefore improper to extrapolate results from a single study to the whole population. However, if a sufficient number of such studies shows similar results, a general conclusion is acceptable with the caveat that some of the changes attributed to the aging process might in reality be due to disease. The anatomical changes briefly described below are believed by most investigators to result from aging.

Anatomy

Kidney size and volume decrease with age after the fourth decade, size by about 20 to 30 percent and volume by about 40 percent by the eighth decade. The loss of renal mass is mainly cortical and is associated with intrarenal vascular changes, described below, which lead to obliteration of the glomerular tuft, creation of a blind arteriole and an increase in the proportion of juxtamedullary glomeruli having continuity of the afferent and efferent arterioles (arteriolae rectae verae). Some sclerotic glomeruli may be resorbed leaving scars and the remaining glomeruli appear crowded. The number of glomeruli decreases from about one million per kidney to about 600,000 or less by the eighth decade, the mesangial cells increase in the glomeruli, but the percentage of cortical interstitial tissue (about 13 percent) remains unchanged. The mass of the juxtamedullary nephrons falls from its adult value of about 15 percent to about 9 percent in the eighth decade. There is some loss of medullary parenchyma and an increase with age of medullary interstitial fibrosis. The length and volume of the tubules decrease with age, but in the same proportion as the decrease in the surface area of the glomeruli, that is, the aging nephron degenerates as a unit and glomerular-tubular balance is maintained. Long-looped juxtamedullary nephrons degenerate earlier than the more peripheral short-looped nephrons. Many distal tubules show diverticula, some of which may harbor bacteria. A marked increase in the size of the malpighian corpuscles, glomerular tufts and the nuclei of the glomerular and tubular cells accompanies the decrease in the number of parenchymal cells in the aged kidney.

Electron microscopy shows focal thickening and reduplication of the basement membrane of the glomeruli and tubules with age, associated with an accumulation of type IV collagen. The surface area of the glomerular capillary basement membrane is decreased by about 40 percent. The width of the glomerular basement membrane decreases after the fourth decade. There is a progressive reduplication of elastic tissue and thickening of the intima, observed first in vessels larger than arterioles, then extending to arterioles. There is also subendothelial deposition of hyaline and collagen fibers. These changes may result from hypertension, but similar changes have been observed in elderly subjects without a history of hypertension. Further, the size of the lumen of the blood vessels in these subjects is not decreased, in contrast to the decrease found in hypertensive subjects. It is possible that age changes in the blood vessels may be accelerated by hypertension. Xenon washout studies in healthy men and women have shown a progressive decrease in renal blood flow with age, mainly to the cortex, and reduced vasodilation following injection of acetylcholine or a sodium load. However, the response to angiotensin is unaffected by aging. These results are in keeping with the morphological changes described previously.
Renal Function

GLOMERULAR FUNCTION

Kidney function declines progressively with age. Most attention has been paid to glomerular function, because (apart from urinalysis) this was historically the first renal function studied quantitatively in man using readily accessible laboratory procedures. The volume (glomerular filtration rate or GFR) and composition of the glomerular filtrate depend upon the renal plasma flow (RPF), the hydrostatic and oncotic pressure difference across the capillary wall (filtration pressure), the surface area of the glomerular capillaries and their permeability. Renal plasma flow in the adult is about 600 ml/min and GFR about 120 ml/min. Their ratio, the filtration fraction (about 0.2) increases slightly, and RPF progressively decreases with age after the fourth decade, declining about 10 percent per decade. Cortical plasma flow accounts for about 90 to 95 percent of the total flow, but with aging there is some redistribution to the medulla. Autoregulation (i.e., the maintenance of a constant RPF with modest changes in blood pressure) occurs efficiently in the aging kidney in the blood pressure range of 50 to 150 mm Hg. GFR is similarly regulated within the same blood pressure range. The afferent arteriole appears to be the main site of autoregulation, through changes in renal vascular resistance.

The reference method for measuring GFR is inulin clearance. Inulin is completely filtered by the kidney and is neither absorbed nor secreted by the renal tubule in healthy subjects. (Whether or not this is true in patients with renal disease is not clear). However, the technical requirements of measurement of inulin clearance make it essentially a research method. The current clinical method of choice is the endogenous creatinine clearance. This procedure will be discussed in the next section.

Before practical methods for measuring creatinine clearance became available, urea clearance was the accepted measure of glomerular function. In order to establish a normal range, a correction was required for the greatly varying body size of subjects. Originally, it was assumed that clearance varied directly with body weight. Later Addis and co-workers found it varied more closely with surface area in rabbits\textsuperscript{13} and Van Slyke and co-workers\textsuperscript{14} introduced the concept of correcting urea clearance to a standard area of 1.73 square meters. This value was the mean of surface areas of men and women aged 25 years, obtained from actuarial tables. It has since been used as the standard area for all clearance tests. The calculation of surface area is made either from a formula based on height and weight, or more conveniently from tables or a nomogram derived from them.

The most commonly used formula is that of Du Bois and Du Bois,\textsuperscript{15} which is based on the measurement of 9 male subjects aged from 9 months to 40 years. Height was measured in the supine position. The observed and calculated values of the surface areas of these subjects differed by less than 5 percent. The calculated surface area was found by dividing the body into many regular solid figures, the surface area of which could be calculated from well-known geometrical formulae.\textsuperscript{16} Whether or not the Du Bois formula can be applied to all ethnic groups and both sexes has not been determined. In follow-up studies on the same subject, provided height and weight remain essentially constant, surface area is irrelevant, and the uncorrected clearance values can be used. Errors arise when the correction for surface area is applied to grossly obese or wasted subjects, or patients with edema or ascites. Care must be exercised, therefore, in applying this correction in the elderly, especially the sick. Some of the changes
in clearance attributed to the aging process may in fact reflect the error in measuring surface area.

Glomerular function decreases with age, because of the decrease in the number of glomeruli and the decreased RPF. Creatinine clearance falls slowly with age (about 1 percent per year after the age of 40 years), but there are many exceptions. However, after unilateral nephrectomy, compensatory hypertrophy of the remaining kidney can occur, indicating some functional reserve in the elderly.

Tubular Function

The tubular system converts the glomerular filtrate into urine by a complicated process involving, in addition, aldosterone, renin, angiotensin, antidiuretic hormone, atrial natriuretic factor, among others. Important effects of aging are a decreased ability of the kidney to conserve sodium and a reduced concentrating power. The effects of aging on tubular function are discussed in the section on renal function tests.

Renal Function Tests

Urinalysis

In the absence of renal disease, dipstick urinalysis and microscopy of the urinary deposit are not affected by age. The changes detected by the more sophisticated tests described in the following pages are not revealed by the semiquantitative reactions of the dip-stick or routine microscopy. Specific gravity measured by a urinometer or dip-stick is a less accurate indicator of urine concentration than is osmolality, measured by vapor pressure or freezing-point depression methods.

Proteinuria

In healthy adults, only very small amounts of protein, mainly albumin, appear in the urine. Aging is sometimes accompanied by an increased permeability of the glomerular basement membrane to macromolecules leading to an increase in albumin excretion in apparently healthy subjects. Urinary albumin rises from a mean of 6.7 mg/L in young adults to a mean of 21 mg/L in men and women aged 60 years or more. However, there is considerable overlap of values at the lower end of the range. Mitchell et al found values up to 80 mg/day in subjects over the age of 65 years. The albumin/creatinine ratio is also increased from a mean of 0.57 g/mol in the young adult to a mean of 3 g/mol in healthy subjects over 60 years of age, again with overlap at the lower end of the range. However, the albumin/creatinine ratio provides only a semiquantitative estimate of the amount of protein excreted. Urinary IgG shows a slight increase with age. Although these results were obtained in apparently healthy subjects, the presence of subclinical disease cannot be excluded.

Clearance Methods

Urea Clearance

This procedure is currently seldom used as a test of glomerular function because it is greatly influenced by extrarenal factors such as protein intake and metabolism, by the urine flow rate and by the need for accurate timing of urine collection. Urea is not an ideal substance for clearance measurements because some is reabsorbed by the renal tubules. Blood urea nitrogen (BUN) concentration is still a useful guide to renal disease, but it must be interpreted with caution. Values rise slightly from a mean of 130 mg/L in the young adult to a mean of 150 mg/L in healthy subjects aged 60 years or more and to higher values in the very old. However, BUN increases as the protein content of the diet increases or endogenous protein catabolism increases from
starvation, infection or other causes. Further, BUN does not rise until the GFR has been greatly reduced to perhaps 30 percent of normal. It is also elevated in dehydrated subjects. Dehydration is common in the elderly. Urea clearance and BUN have been replaced by creatinine clearance and serum creatinine measurement.

**Creatinine Clearance and Serum Creatinine**

Endogenous creatinine clearance is used as a measure of glomerular filtration rate. In healthy adults, however, it overestimates GFR by up to 20 percent, when compared with inulin clearance. This overestimation is caused by the secretion of creatinine by the renal tubule. Inaccuracies in the measurement of serum creatinine, however, artifactually decreased the calculated clearance and led to the view that the endogenous creatinine clearance measured the glomerular filtration rate. In some rare instances, creatinine may be absorbed by the renal tubule. For GFR to be equal to clearance of a substance, that substance must not be absorbed, secreted or metabolized in the kidney. Both inulin clearance and creatinine clearance decrease in parallel with age after the age of about 30 years. The decrease in glomerular filtration rate is approximately linear at 8 ml/min/1.73 m². The adult rate is approximately 140 ml/min/1.73 m². The decrease results from decreased perfusion of the renal cortex associated with the decrease in the number of functioning glomeruli and the other anatomical changes described previously.

The measurement of creatinine clearance presents many problems, particularly in the elderly, making the assessment of renal function difficult. The problems concern the measurement of creatinine in serum, plasma and urine, the conduct of the clearance test and the establishment of reference ranges for age and sex.

The earliest practical method for measuring creatinine was described by Jaffe using an alkaline picrate reagent. The sensitivity of the method then available was not adequate for measuring endogenous serum or plasma concentrations in normal subjects and creatinine was administered to raise the serum concentration to a measurable level. Endogenous creatinine clearance was first measured by Miller et al in 1952. The original clearance procedure developed by Van Slyke for urea required collection of urine for an accurately timed period of about one hour. In practice, use of such a short collection time was found to lead to considerable error and it has now been replaced by a 24-hour collection period. The use of such a long period is based on the assumptions that endogenous creatinine is excreted at a constant rate (in terms of quantity per minute, not concentration) and that endogenous serum (or plasma) concentration remains constant throughout the day. However, daily urinary creatinine excretion may vary by more than 15 percent.

It is well known that exogenous creatinine, derived from the creatine of meat, is excreted into the urine. Therefore, meat eating should be avoided in the performance of the test.

It is assumed that creatinine is formed at a constant rate from the creatine pool of the body, almost all of which is in the muscle mass. Creatine itself is synthesized by a complex process involving enzymes in the kidney and liver. The conversion of creatine to creatinine is non-enzymatic. Serum creatinine concentration depends on the rates of creatinine formation and excretion; the latter, in health, is almost entirely through the kidney, but in patients with severe renal disease, some creatinine is excreted into the bowel. Tubular secretion may be affected by drugs. In particular, cimetidine completely inhibits tubular secretion of creatinine and serum creatinine
concentration rises. Further, in patients with some liver diseases, synthesis of creatine is impaired and serum creatinine concentrations are low. Prediction formulae for creatinine clearance (described in the following paragraph) are invalid in patients with liver disease.

The interpretation of serum creatinine concentration and the creatinine clearance test in the elderly depends upon establishing a normal range based on sex and age. This is difficult, because of the problem of selecting healthy normal subjects and the great variability of the effects of age on creatine metabolism. The creatine pool, mainly in muscle, diminishes with age to a variable degree in subjects of the same age. It is not certain that the rate of conversion of creatine to creatinine, which is constant in healthy adults, is constant in the elderly, especially if they are debilitated or have some disease. The loss of muscle mass is accelerated by dietary protein deficiency, also common in the elderly, but nevertheless a greatly variable factor. Urinary creatinine excretion may be increased following trauma or fever. Uncertainty also arises from the non-enzymatic conversion of creatine to creatinine which may occur in blood and urine specimens kept at room temperature for 24 hours or more. This occurs when specimens are sent to a commercial laboratory, or are stored (say, over the weekend) at room temperature. Creatinine concentrations may increase by 10 percent or more. Finally, the creatinine values reported by various investigators vary with the method used, its specificity, and precision.

The alkaline picrate method is known to be affected by a large number of substances, collectively known as the non-creatinine chromogens. In healthy adults, the true creatinine concentration is increased by 20 percent or more. Non-creatinine chromogens consist mainly of reducing agents such as glucose, ascorbate and urate, and of substances such as acetoacetate, pyruvate (this is a major source of interference) and other ketoacids, and also protein. The effect of these substances is reduced, but not eliminated, by using a kinetic alkaline picrate method. The results for serum creatinine may still be 5 percent or more too high. Errors are also reduced by continuous flow methods. Urine creatinine concentrations are less affected by non-creatinine chromogens, because of the relatively lower concentration of non-creatinine chromogens. However, in subjects consuming megadoses of vitamins, especially ascorbate, and in subjects excreting considerable amounts of ketoacids, urinary creatinine concentration may be falsely raised. The most effective clinical laboratory methods for measuring true creatinine concentration in both serum and urine are those using enzyme reactions. Enzymatic methods are relatively new. Many are expensive (compared with the picrate methods) and time consuming. Most of them have few interferences. However, while normal ranges for adults have been established using some enzyme reactions, few values have been established for the elderly. The extensive literature on the effect of aging on renal function is based on the alkaline picrate reaction in one of its many forms.

Because of the difficulty and errors associated with collecting a 24-hour urine specimen in elderly subjects, some of whom may be bedridden, mentally confused, or otherwise incapacitated, attempts have been made over the years to deduce creatinine clearance from serum creatinine concentrations, taking into account sex, weight and age. Many formulae have been suggested, derived by statistical treatment of creatinine clearance measurements of groups of subjects of different ages. Clearance is defined as $U \times V/P$, where $U$ and $P$ are respectively the creatinine concentration
of urine and plasma (or serum: serum and plasma concentrations are equal) measured in the same units (mg/L or \(\mu\)mol/L) and \(V\) is the urine volume per minute in ml, obtained by dividing the 24-hour output by 1440. It is usual to use fasting blood; sometimes the mean of the fasting blood concentrations at the beginning and end of the collection period is used.

A widely used formula is that of Cockcroft and Gault\(^\text{34}\), who measured serum and urine creatinine by a continuous flow method. The steps in deriving their formula were: measurement of \(U \times V \times 1440\), (the excretion of creatinine in the 24-hour period); calculating the creatinine excretion per kg body weight; calculating the mean value of this for each decade; plotting this mean against the mean age for each decade; calculating the regression line for creatinine/kg against age; rounding off the constants in the regression equation; creating the clearance formula. They found the regression equation to be \(UV \times 1440/kg\) body weight = 28 - \((0.2 \times \text{age in years})\).

From this they derived the formula: 24-hour creatinine clearance = \((140 - \text{age}) \times \text{(weight in kg)}/(72 \times \text{serum creatinine in mg/dl})\). The study group comprised 249 males, apparently healthy, aged between 18 and 92 years, of whom 112 were 60 years or older. No females were studied, but Cockcroft and Gault\(^\text{34}\) suggested that the calculated clearance should be multiplied by 0.85 to give values for females. The simplicity of the formula has made it popular, despite its limitations. The formula assumes that creatinine excretion depends only on weight and age, \(i.e.,\) it is constant from day to day so long as the weight remains constant. It is well known that daily creatinine excretion may vary by 15 percent or more, even on a constant diet. Body weight is ambiguous — it may or may not include clothing.

Several other formulae have been proposed and their effectiveness determined against measured creatinine clearances.\(^\text{35,36,37,38}\) The results correlate fairly well in the case of healthy subjects but the values obtained are, on the whole, overestimates of the measured clearances. The values given by the formulae are misleading in the case of debilitated patients. At the very best, the formulae can give only a semi-quantitative evaluation of the true clearance.

Accurate reference methods for serum creatinine have been described.\(^\text{39,40}\) These methods employ isotope dilution mass spectrometry and are available only in specialized laboratories. Recently, an enzymatic reference method has been described which appears to be suitable for routine use in the clinical laboratory.\(^\text{41}\) Many automated chemistry analyzers use enzymatic methods, and other techniques have been used, for example, capillary zone electrophoresis.\(^\text{42}\)

Serum creatinine concentration in the elderly is about the same as in the adult, but with a wider range. The decrease in creatinine excretion occasioned by the loss of muscle mass with aging is compensated by a parallel decrease in glomerular filtration rate. However, a small change in either can upset the balance and alter the serum creatinine concentration. A normal serum creatinine concentration does not necessarily imply normal renal function, nor does a raised value always mean impaired renal function. The balance can be disturbed as a result of illness not related to the kidney, by changes in protein consumption, malnutrition and other factors. Interpretation of serum creatinine concentration as a guide to renal function must be made with care; only small increases in concentration may occur in severe renal disease if creatinine production is well below normal. A long-term study of creatinine clearance has shown that the decline of renal function with age does not occur in an appreciable number of elderly subjects.\(^\text{43,44,45}\)
Disorders of water and electrolyte homeostasis are common in the elderly. Hyponatremia and hyperosmolar states often occur in elderly institutionalized patients. Postural hypotension, a major sign of sodium depletion, is common in the elderly irrespective of the presence or absence of hyponatremia. Other tests are therefore required. The ability to concentrate urine maximally after water deprivation decreases with age. Simple tests are available to test the kidney’s ability to handle water and sodium.

### Water Load

The ability to excrete a water load (20 ml/kg body weight) after 9 hours of fluid deprivation is impaired in the elderly compared with young adults. In a water load test reported by Faull et al., plasma osmality was essentially unchanged, but urine osmolality and the plasma concentration of arginine vasopressin (AVP) immediately after water deprivation in the elderly were markedly decreased. Four hours after the water load, both young adults and the elderly excreted about 90 percent of the ingested load, but most of the water was excreted by the young in the first hour. The free water clearance was 1.6 ml/min in the young and 0.04 ml/min in the elderly 60 minutes after the load. The osmolality of the pooled 4 hour collection was 392 mOsmol/l in the young and 225 mOsmol/l in the elderly. Thus, the elderly excrete a water load more slowly than the young, and the urine is more dilute. Free water clearance is defined as volume of urine excreted per minute times the ratio of urine to plasma osmolality. It is the volume of urine required to excrete all urinary solutes in an isoosmotic solution. The free water clearance is positive when the urine is hypertonic compared with the plasma and negative when it is hypotonic.

Nocturnal polyuria is common in the elderly of either sex (therefore prostate problems can only be a factor in males). Decreased urinary concentrating power and possibly a deficiency of AVP may be factors (see also the following). The effect of aging on plasma AVP concentration is uncertain. Arginine vasopressin is important in water homeostasis. Extracellular osmotic pressure controls, by a neurohypophysial mechanism, the release of vasopressin from the hypothalamus. Arginine vasopressin acts on receptors in the basolateral membrane of the renal collecting tubule, resulting in increased permeability of the cell wall to water and the transfer of water into the renal medulla.

Plasma AVP concentration (supine position) averages 1.8 pmol/L in the young adult and 1.7 pmol/L in subjects over 61 years of age. After water deprivation, plasma AVP falls more in the elderly than in the young. Plasma osmolality, sodium concentration and potassium concentration are not affected by age. Age does not influence plasma osmolality or AVP concentration after an overnight fast.

Thirst is an important factor in water homeostasis. Thirst is regulated by the hypothalamus-neurohypophysial system in response to plasma osmolality changes. When measured in terms of water drunk after prolonged dehydration, thirst declines with age. The mechanism is not well understood. The extracellular hypovolemia caused by water deprivation stimulates the production of renin. The renin-angiotensin-aldosterone system preserves sodium balance and influences thirst. The effect of age on this system shows wide variations. In general, basal plasma renin activity decreases with age after the fourth decade, reaching about half the adult value by age 80 years, but plasma renin substrate and inactive renin do not
change with age. Angiotensin II does not decrease with age but plasma and urinary aldosterone concentrations fall progressively. The renin-angiotensin-aldosterone system responds normally to the appropriate stimuli (posture, sodium-volume depletion), but the responses are more marked in the presence of sodium depletion. It is possible that the morphological changes associated with aging result in decreased secretion of renin by the kidney, or decreased activation.

**Tests of Sodium Excretion**

The generation of a positive free water clearance during a sustained maximal water diuresis after a water load test is an index of the reabsorption of sodium chloride in the diluting segment of the nephron and the maximal volume of urine excreted per minute an index of sodium chloride delivery to this segment. The diluting segment includes the ascending limb of the loop of Henle, the distal convoluted tubule, the cortical collecting duct and possibly the medullary collecting duct. The aging kidney has a decreased ability to conserve sodium (tested by measuring urinary sodium excretion in subjects on a prolonged low sodium diet) and older subjects excrete sodium more slowly than do young subjects. Compared with the young, older subjects excrete sodium, potassium and total solutes at a higher rate at night, which may also be a cause of the nocturnal polyuria of the elderly. An extrarenal factor influencing the diluting segment in relation to sodium is antinatriuretic peptide (hANP). The mean basal concentration of hANP is markedly increased in men older than 64 years (120 pg/ml) compared with young men (25 pg/ml). The action of hANP on the kidney is to increase GFR and to induce natriuresis, by activating guanylate cyclase in the renal vasculature; cGMP rises in urine and plasma. Following infusion of an isotonic sodium chloride load, hANP rises to a greater degree in elderly men than in young men, but cGMP rises to the same degree. These findings suggest that there is reduced activity of the hANP receptors in the elderly.

**Other Tests of Tubular Function**

The Tm for glucose decreases linearly with age, but because the GFR is decreased, glucosuria does not occur at normal serum glucose concentrations.

The tubular phosphorus threshold (TmP/GFR) is a good index of tubular reabsorption of P. In males, it falls progressively with age, but in females the threshold rises.

**Acid-base Metabolism**

The renal tubule plays an important role in maintaining the constancy of the plasma pH, through its ability to control bicarbonate and hydrogen ion excretion, and to generate bicarbonate. Hydrogen ion excretion depends on excretion of both hydrogen ions and ammonium ions into the tubular fluid. In the urine, the hydrogen ions are associated with the phosphate buffer system. Titratable acidity is measured by the amount of alkali required to restore the pH of a standard volume of urine to the plasma pH value; the hydrogen ions required to form the ammonium ion from ammonia can also be measured in terms of alkali. The sum of the two measurements (total acidity) is a measure of the total hydrogen excretion of the kidney and is the basis of tests for acid-base balance.

Measurement of abnormal handling of bicarbonate by the kidneys is demanding, both technically and on the patient and is essentially a research procedure. It involves measuring the Tm for bicarbonate. Acid-base balance testing is straightforward and technically simple. The subject is given an oral dose of ammonium chloride (0.1 g/kg body weight) and the
urine passed between 5 and 7 hours after the dose is collected (the maximal effect occurs in this interval).

Blood specimens are drawn before and 2 hours after the dose to determine the pH and electrolyte concentrations. The pH of the urine is measured and also the titratable acidity and ammonium ion concentration. In healthy young adults urine pH should be less than 5.3, total acidity should exceed 60 μmol/min, titratable acidity should exceed 25 μmol/min and ammonium excretion should exceed 35 μmol/min. Basal values of plasma pH and bicarbonate do not change with age, but acute acid load results in a decrease in ammonium excretion; titratable acid is unchanged. These results suggest that the elderly can maintain urinary acidification under normal conditions, but not under conditions of acid load.

The effect of aging on other functions of the renal tubule has been investigated for some other metabolites. In the case of calcium and phosphate, the efficiency of the homeostatic mechanisms which maintain calcium and phosphate is impaired (as well as the mechanisms for maintaining the balance of other electrolytes). As a result, hypocalciuria and hyperphosphaturia may be found. Elderly patients immobilized by paralysis or fracture rapidly excrete calcium in excess of 500 mg/24 hours (the upper limit of normal in healthy adults). The effect of aging on the Tm for phosphate has been discussed above. Parathyroid hormone concentrations increase with age, but calcitonin decreases, more in women than in men. The renal tubule is involved in vitamin D metabolism through the hydroxylation of 25-OH-D to 1,25(OH)₂-D by a 1-hydroxylase enzyme. The activity of this enzyme decreases with age. The resulting diminished production of the dihydroxy-compound may be responsible for the increased production of parathyroid hormone in the elderly. Extrarenal factors complicate the interpretation of the role of the kidney in diseases of calcium and phosphorus metabolism.

Diet may influence renal function tests, particularly dietary protein, and may be important in the elderly because so many are malnourished or eat low protein diets. In addition, the effects of aging on renal function tests has been investigated for the most part by comparing values in healthy young adults, predominantly male, and presumably healthy elderly. The effect of non-renal illness on these tests is not clear. Most studies have not commented on the ethnic composition of the test subjects. Normal values may well be different in different ethnic groups. Few data have been published.

In general terms, renal function tests supply only supporting evidence of renal function. The clinician must take all factors into consideration when evaluating a particular test.

References


