1975

# A study of the clinical and radiological correlations in polycystic disease of the kidneys : the significance of the intravenous urogram

Philip J. Rich
*Yale University*

Follow this and additional works at: http://elischolar.library.yale.edu/ymtdl

A STUDY OF
THE CLINICAL AND RADIOLOGICAL CORRELATIONS
IN POLYCYSTIC DISEASE OF THE KIDNEYS:

THE SIGNIFICANCE OF
THE INTRAVENOUS UROGRAM.

PHILIP J. RICH

1975

A STUDY OF THE CLINICAL AND RADIOLOGICAL CORRELATIONS IN

POLYCYSTIC DISEASE OF THE KIDNEYS:   THE SIGNIFICANCE

OF THE INTRAVENOUS UROGRAM.

PHILIP J. RICH, B.A.

YALE COLLEGE, 1971

PRESENTED TO THE FACULTY OF THE YALE UNIVERSITY SCHOOL OF
MEDICINE, IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR
THE DEGREE OF DOCTOR OF MEDICINE.

DEPARTMENT OF RADIOLOGY

FEBRUARY, 1975

# A STUDY OF THE CLINICAL AND RADIOLOGICAL CORRELATIONS IN POLYCYSTIC DISEASE OF THE KIDNEYS: THE SIGNIFICANCE OF THE INTRAVENOUS UROGRAM.

## TABLE OF CONTENTS

# ACKNOWLEDGMENTS

INTRODUCTION

This thesis explores the pathological and clinical presentation of polycystic disease and their correlation with the findings available during intravenous urography.

Polycystic disease of the kidneys (adult type) is a familiar and congenital pathological disorder transmitted through an autosomal dominant mode of inheritance. It is characterized by variable expressivity of the gene(s) with virtually 100% penetrance, if the patient survives into the ninth decade. Involvment is usually bilateral and pregressive; with the onset of symptons, the patient pursues an inexorable downhill course leading to uremia and death in the absence of operative intervention with renal transplantation.

Polycystic disease is characterized by irregularly shaped cysts of nephronic origin located diffusely throughout the cortical and medullary regions of the renal parenchyma with intervening areas of normal or minimally fibrotic renal tissue. There is a high incidence of associated cystic involvment of other viscera, principally the liver and spleen, cerebral aneurysm and erythrocythemia. (4, 17, 18, 20, 21, 31, 42, 49, 60, 65, 72, 83)

PART ONE:   PATHOLOGY

GROSS PATHOLOGY

On visual inspection, polycystic kidneys are almost always enlarged
and may attain weights of seven or eight kilograms and measure as much as
43 to 48 centimeters.   (31)   The degree of enlargement varies according
to the number of nephrons evidencing cystic involvement and according to
the volume of fluid accumulating within the cysts (29,60); generally,
the degree of cystic change is related to the age of the patient (17, 31).
Enlargement may proceed asynchronously leading to marked asymmetry of
the two involved kidneys.

Although disagreement exists about the existence of unilateral poly-
cystic disease, involvement is usually bilateral.  Bell (4) reported a
unilateral incidence of 8%, by far the highest reported in the pathology
literature; by contrast, Narins and Oppenheimer (50) contend that it is
rare to encounter an adult with unilateral disease.  In those cases of
reported unilateral disease, the contralateral kidney has been described
as either aplastic or hypoplastic.  (4, 17, 29, 50, 59, 70)  Two cases
of polycystic disease in solitary kidneys have been reported and these
underwent compensatory hypertrophy resulting in clinical courses similar
to that of relatives with two kidneys.  (3)

Polycystic kidneys usually present as normally shaped kidneys al-
though increased proportionally in size.  The outer surface of the kidney
is irregular and nodular, studded with translucent vesicles of varying
size bulging from the capsular surface.  The capsule of the kidney usually
is unchanged although it may adhere firmly to the kidney surface and be
difficult to strip.  Examination of the cut surface reveals oval or spher-
ical cysts filled with thin colorless fluid involving both the renal cortex

and medulla. The cysts vary in size from the microscopic up to four to five centimeters. If there has been hemorrhage into a cyst, the fluid may be thickened and may shade in color from bright red to brown. Usually cysts are more numerous and more tightly packed in the cortex, often abutting one another and separated by only a single layer of epithelial cells. A medullary cyst may bulge into the renal pelvis. The normal architecture of the kidney is disturbed; papillae are often absent and the kidney is seldom divided into normal pyramids. (4, 11, 17, 29, 31, 60) The most frequent renal lesions associated with polycystic disease are hydronephrosis and pyonephrosis [usually secondary to compression of the ureter by a lower pole cyst], and pyelonephritis. (34) McNamara (47) in a series of twenty five post-mortem examinations reported a 57% incidence of pyelonephritis in patients with polycystic disease. Tumors and calculosis are less common associations. (31) Generally, the ureters, bladder, and urethra are free of involvment. (29)

HISTOPATHOLOGY

The microscopic appearance of the kidney is generally consonant with the degree of cystic involvment evident on gross inspection of the kidney, the mildest changes being found in those kidneys with a relatively normal gross appearance. (60) Destruction of nephrons may be due to progressive cystic dilatation of a component structure, compression of normal adjacent tissue by enlarging cysts leading to pressure atrophy and fibrosis, hemorrhage, and infection. (47, 60)

In their classic microdissection studies of polycystic kidneys, Osthanondh and Potter (60) discovered that cysts may be found in any portion of the nephron and collecting duct, most commonly at the angle of the

loop of Henle and Bowman's space; however, any individual case may display a preferential involvment for a given structure. As a rule, cysts are multipolar and communicate with the collecting system of the kidney. Glomerular cysts usually arise from a dilatation of Bowman's capsule. Glomerular tufts may be small and incompletely vascularized with capillary loops either separated by large amounts of hyalinized connective tissue or, in occasional specimens, scattered along the inner wall of the cyst. Individual or groups of tubules may dilate forming thin-walled cysts and demonstrate diffuse or saccular enlargment of the proximal tubule, the descending and ascending limbs of the loop of Henle, the distal tubule, or at the junction of the distal tubule and the collecting duct. (41, 60)  Cysts of collecting tubules are generally larger than those of the nephrons and are surrounded by a thick zone of compact connective tissue. (60)  Cyst walls may be lined discontinuously with cuboidal or flattened epithelium; proximal tubular cysts often are lined by characteristic eosinophilic pyramidal cells with a recognizable brush border. (29)

There is a fundamental disorder in the organization of the renal architectureDuring organogenesis, individual tubules of the metanephric blastema may divide asynchronously so that the architecture of minor calyces, papillae and pyramids may be quite different in different parts of the kidney. (60)  Nephrons may attach irregularly to the collecting tubules resulting in a failure to form normal papillae and pyramids. Attachment of several nephrons to the end of a single collecting tubule result in pseudopapilla formation. Arcades may be absent when nephrons attach to collecting tubules proximal to the last generation. (60)  Blood vessels are of irregular size and distribution; interlobular arteries

frequently course beneath cyst walls composed of a single layer of
epithelium leading to considerable hemorrhage with arterial rupture. (31)
Arterioles may be involved by a sclerosing process giving rise to
thickened walls and narrowed lumens. (31, 60)   Nerve trunks often de-
monstrate increased prominence.


ASSOCIATED ABNORMALITIES

The most commonly associated abnormality of polycystic kidney
disease is polycystic liver disease.  The reported association in the
pathology literature varies from 16% (17) to 73% (83); the most com-
monly accepted figure, however, is 33%. (14, 29, 65)   Conversely, the
association of polycystic involvment of the kidneys in patients with a
primary diagnosis of polycystic liver disease is 50%. (14)   Other cystic
disorders associated with polycystic kidney disease are polycystic pan-
creas, approximately 10% (29, 65), spleen, 2% to 5% (29, 65), and rarely,
thyroid, ovary, endometrium, seminal vesicle, epididymus, esophagus, and
cerebellum. (17, 29, 31)

Significant clinically, there is a high association (15%) of
aneurysm of the basal arteries of the brain with polycystic disease;
the anterior half of the circle of Willis is the most frequent location
of these aneurysms. (17, 29)   Conversely, 3.5% of patients with intra-
cranial aneurysm have associated polycystic disease.


ETIOLOGY AND PATHOGENESIS

Numerous theories have been advanced describing the pathogenesis
of polycystic disease; none is adequate to explain fully the disease and

its associations. They may be divided into four general classes: the embryogenic; the metabolic; the neoplastic; and, the inflammatory. The embryogenic theories of Hildebrand (30) and Kampmeier (38, 48) have gained the most wide-spread acceptance. Hildebrand postulates that the condition arises from a derangement in the union of the dual anlagen of the developing kidney; a failure of the union of the ureteric bud with the metanephric blastema deprives the primitive nephrons of an organizing influence giving rise to disturbed renal architecture and cyst formation. Kampmeier proposes that the disease has its origins in a disturbance in the normal processes of division and involution; thus, there is a failure of involution of the first generation of nephrons to differentiate in the metanephrons with eventual cystic degeneration. Potter (60) echoes Hildebrand suggesting that there is a failure of coordination in the patterns of division of the collecting tubules, deriving from the ureteric bud, and the nephrons and connective tissue, deriving from the metanephric blastema. The metabolic theories (18, 61, 72) adduce a toxic metabolite from experimental preparations with cystic disease induced by exogenously administered agents. Additional support for this theory is lacking in that, as yet, there have been no reported cases of polycystic transformation of a kidney transplanted into a patient suffering from polycystic disease of his own kidneys. [There has been a considerable transplant experience in polycystic disease; the last three reports of the Human Transplant Registry (76, 77, 78) indicate that approximately 5% of renal transplants performed annually have been for the treatment of polycystic disease.] The neoplastic theories (17, 33) attribute the disease to hamartomas or cystic adenomas of the renal substance. Finally, the inflammatory hypotheses attribute cyst formation to a variety of insults to

the kidney:  papillitis (31), arterial ruptures into the substance of
the kidney (35), and tubular occlusion resulting in multiple retention
cysts (17).


INCIDENCE

Estimates of the incidence of polycystic disease vary widely be-
tween clinical and autopsy data, but indicate, that there is widespread
failure to recognize the disease ante-mortem.  [Table I]  Men and women
are equally involved, the disease demonstrating no sex predominance.[Table 2]

TABLE 1:   CLINICAL AND AUTOPSY INCIDENCE OF POLYCYSTIC
           DISEASE OF THE KIDNEYS

| SURVEY | DIAGNOSIS ON CLINICAL CRITERIA | DIAGNOSIS BY AUTOPSY |
|---|---|---|
| 1. Mt. Sinai Hospital, New York City | 1:3,666 | 1:  428 |
| 2. Mayo Clinic | 1:3,524 | 1:1,019 |
| 3. Jewish Hospital, Brooklyn, N.Y. | | 1:  158 |
| 4. London Hospital, London, England | 1:4,800 | |
| 5. University of Minnesota | | 1:  509 |
| 6. Nauman | | 1:  650 |
| 7. Cleveland Clinic | 1:4,000 | |
| 8. Dalgaard  Denmark  (17) | | 1:  773 |
| 9. Bell (4) | | 1:  351 |
| 10. Simon and Thompson (22) | 1:2,438 | 1:  323 |

after Higgins (31)

Symptoms of the "adult form" of the disease may appear at any age; how-
ever, it presents most frequently in the fourth or fifth decades of life.
[Table 3]

TABLE 2: CLINICAL INCIDENCE OF POLYCYSTIC DISEASE IN MEN
AND WOMEN

| | NUMBER OF MEN | NUMBER OF WOMEN | TOTAL |
|---|---|---|---|
| Dalgaard (17) | 157 | 193 | 350 |
| Simon and Thompson (72) | 203 | 163 | 366 |
| Rall and Odell (65) | 94 | 113 | 207 |

TABLE 3: AGE OF CLINICAL INCIDENCE OF POLYCYSTIC DISEASE

| AGE (in years) AT DIAGNOSIS | DALGAARD (17) MEN | DALGAARD (17) WOMEN | SIMON AND THOMPSON (72) | RALL AND ODELL (65) |
|---|---|---|---|---|
| 0-9 | | | 2.5% | 3% |
| 10-19 | 0.6% (15-19 years) | 0.5% | 1.1 | 1 |
| 20-29 | 4.4 | 6.8 | 8.7 | 9 |
| 30-39 | 22.9 | 23.0 | 22.4 | 34 |
| 40-49 | 29.9 | 27.9 | 34.2 | 27 |
| 50-59 | 25.4 | 24.8 | 22.4 | 20 |
| 60-69 | 11.5 | 11.4 | 6.8 | 6 [greater |
| 70-79 | 3.8 | 5.2 | 1.9 | than 60 |
| 80-84 | 1.9 | | | yrs. of age] |

PART TWO:   CLINICAL FEATURES

CLINICAL PRESENATION

The diagnosis of polycystic disease is a challenge to the clinician.
The clinical picture is often misleading depending upon the stage at which
the patient presents for diagnosis; none of the signs or symptoms is patho-
gnomonic.

The onset of the disease is usually insidious; the patient may be
unaware until routine physical examination and laboratory analysis dis-
close renal enlargement, hypertension, proteinuria, microscopic hematuria,
or evidence of asymptomatic urinary tract infection. (17)   Simon and

Thompson (72) report that 133 of 366 patients in their series had no symptons referable to polycystic disease at the time of diagnosis.

The clinical history is invaluable in the diagnosis. Polycystic kidney disease is an autosomal dominant hereditary disease with variable penetrance and expressivity. (17, 18, 20, 62, 83) There is virtually 100% penetrance if the patient survives into the ninth decade of life. [vide supra] Despite this, reports of a positive family history range from 18%, in a series of 366 by Simon and Thompson (72), to 36%, in a series of 94 cases compiled by Higgins (31). The classic presentation is of a middle-aged person with a positive family history and symptons referable to early renal failure. (63) [Table 4] As in the case of most classic presentations, this constellation is encountered infrequently.

TABLE 4: PER CENT INCIDENCE OF CLASSIC FINDINGS IN POLY-
CYSTIC KIDNEY DISEASE

| | Rall and Odell (65) | Simon and Thompson (72) | Daalgard (17) | Higgins (31) | Ward, Draper, and Lavengood (83) |
|---|---|---|---|---|---|
| Cases | 207 | 366 | 350 | 94 | 53 |
| **FINDING** | | | | | |
| Family history (positive) | 34 | 18 | -- | 36 | 32 |
| Gross Hematuria | 48 | 31 | 45 | 41 | 47 |
| Abdominal pain | 28 | 44 | 59 | 64 | 47 |
| Hypertension | 73 | 55 | 46 | 73 | 62 |
| Palpable kidneys (one or both) | 72 | 78 | 61 | 80 | 73 |
| Elevated blood urea nitrogen | 36 | 44 | 44 | 70 | 45 |

Pain is the cardinal presenting symptom for which a patient seeks medical assistance. (17, 31, 65, 72, 83) Most commonly, he complains of a dull nagging ache or pressure in the flank. The pain is usually unilateral, may be intermittent or continuous, and may be so persistent and severe as to be disabling. (17, 31, 65, 72, 83) The pain may result from the excessive weight of the kidney producing tension on the renal pedicle, hemorrhage within a cyst, or the mechanical pressure of expanding cysts on adjacent organs. (72) The reported incidence of flank or abdominal pain ranges from 28% (65) to 64% (31). [Table 4] Acute renal colic is unusual, but may occur with the passage of a clot down the ureter. (72) Loin pain radiating to the back, chest, epigastrium, or groin may also be encountered. Complaints of pain usually occur early in the course of the disease.

Gross hematuria is the second most common complaint. [Table 4] Hematuria is usually self-limited, of short duration, episodic, and seldom heavy enough to cause exsanguination. It is precipitated in most instances by trauma or unusual physical exertion. (17, 31, 72, 83) If persistent, it may be associated with anemia. (83) Bell (4) and Simon Thompson (72) assert that over the course of their disease, between one third and one half of patients will develop hematuria. Appearance of gross bleeding shows no sex predominance and usually appears in the middle of the disease's course. (17)

There is an unusually high incidence of urinary tract infection in polycystic disease suggestive of an increased susceptibility to bacterial invasion. (17) [vide infra] The reported incidence of symptomatic urinary tract infection: frequency, dysuria, fever, chills; ranges from 21% (72) to 69% (31).

In Rall and Odell's series (65), 20% of patients presented to renal clinic following the discovery of renomegaly, either by themselves or the referring physician. On physical examination, renal enlargement was found bilaterally in 51% to 60% of cases and unilaterally in 13% to 25% of cases, with an unexplained predominance of left sided enlargement with unilateral physical findings. (17, 31, 65, 72, 83) Occasionally, enlargement may occur to the point of causing visible distention of the abdominal wall and an increase in the circumference of the abdomen. (17)

Hypertension is a frequent physical finding during the course of polycystic disease and not infrequently is the first sign detected in the disorder. Rall and Odell (65) found that the initial finding of hypertension led to the diagnosis in 16% of their polycystic population; furthermore, they found a 35% incidence of hypertension during the initial visit for the evaluation of the disease. Disparity in the time course at which a patient presents for diagnosis may account for the variations in the incidence of hypertension [35% (65, 72) to 62% (83)] during that initial visit.

CLINICAL COURSE AND LABORATORY DATA

Cysts present at birth (20, 31, 41, 60, 62) remain asymptomatic through the patient's early decades allowing him to pursue a normal life. Symptoms may appear as early as the second decade (17), but these are generally well tolerated until the fourth or fifth decade; as the cysts enlarge and renal function deteriorates the patient seeks medical atten-tion. (17, 31, 65, 72, 83) [Table 3] When the disease first manifests itself in later life, it pursues a more virulent downhill course, with death from hypertension and its sequelae or uremia within a few years.

(17, 31, 83)   Survival following the onset of symptoms is usually less than ten years. (27)   Patients with the disease enjoy a shorter life expectancy than the general population.  Simon and Thompson (72) compared the five and ten year survival of normal and polycystic populations.  They found that the uninvolved group, at age 44 years, had a five year survival rate of 96% and a ten year survival of 90.5%; this compared sharply with a survival rate of 56% and 38%, respectively, in the polycystic group.  Post-diagnosis, eleven of their 366 cases survived more than twenty years, and Dalgaard (17) reported one thirty five year survivor.

Many patients will remain asymptomatic into the seventh and eighth decades, and polycystic disease may be an incidental finding at autopsy. (4, 17, 31)   In their post-mortem series of fifty eight patients with polycystic kidney disease and concomitant polycystic involvement of the liver, Hatfield and Pfister (27) found wide discrepancies between the group of patients who were asymptomatic at the time of death and the symptomatic group and question whether polycystic kidney disease is an unified diagnostic etity.  To summarize their findings:  the average age at the time of death for the asymptomatic group was 73.0 years.  The combined weight of their kidneys was 512 grams [normal:  125 to 170 grams in males; 115 to 155 grams in females].  One fifth of these patients had at least one cyst greater than three centimeters.  The group of patients who were symptomatic ante-mortem averaged 51.8 years at the time of death.  Their kidneys weighed 930 grams, and one half had at least one cyst larger than three centimeters.  Both groups had an equal incidence of asymmetric renal enlargement.  Rather than representing two distinct entities, these findings may also be interpreted as consistent with a hereditary disease of variable expressivity.

Polycystic kidneys may be involved by any of the acquired renal diseases. Inflammatory complications include such entities as pyelitis, pyelonephritis, and paranephritis. (17) The reported incidence of urinary tract infection may approach 65% with problems of recurrence in approximately 11% of cases. (17, 31, 65, 72, 83) [Table 4] The most commonly associated pathogens are E. Coli, P. vulgaris, Staph. albus, and Str. faecalis. (31) Mac Namara (47) examined the kidneys of twenty three patients with polycystic disease who came to necropsy for evidence of pyelonephritis. He found evidence of infection in the kidneys in thirteen patients [57%], eight of whom [35%] had evidence of extensive infection involving more than 50% of the kidney. Of these thirteen patients, only four were expected to have pyelonephritis ante-mortem. Malignancy is rarely associated with polycystic disease; there are fewer than twenty five cases reported including one case each of intracystic papilloma, fibrosarcoma, and angiomyosarcoma. (2, 8, 9, 10, 13, 15, 17, 28, 32, 36, 43, 46, 50, 51, 64, 67, 71, 75, 79, 81) The problems of diagnosis in a kidney with an already deformed gross structure are obvious, and, in most cases, malignancy was not expected prior to surgical exploration or necropsy.

The relentless cystic conversion of the kidneys leads to progressive renal insufficiency in the majority of cases. (17, 31, 72) Dalgaard (17) noted that within a family, the pattern of deterioration had a certain uniformity. Early in the clinical course, urinalysis, renal function tests and serum chemistries are of little value in the assessment of the disease (31); cystic nephrons retain their function and contribute to the functional capacity of the kidney. (11, 17, 41) Normotensive patients with uremia may remain stable for many years, but with the supervention of uncontrolled hypertension, the patient pursues a rapid and inexorable downhill course. (27)

Rall and Odell (65) reported that following the onset of azotemia [BUN·>
40 mg/100ml.] the average life expectancy was 2.2 years.

Serial examination of patients demonstrate that four fifths will
develop hypertension during their clinical course (31, 65, 72); nearly
all will be hypertensive pre-terminally. (83)  Hypertension in combina-
tion with cerebral aneurysm or renal failure augurs an ominous turn in
events; these patients have an average life expectancy fifteen years shorter
than normotensive patients with aneurysm or azotemia. (27)

Despite uremia and recurrent hematuria, polycystic patients are
able to maintain hemoglobin levels in excess of 11 gm/100 ml. (31, 65, 72)
Polycystic patients who come to dialysis tolerate the procedure better
than other uremic patients; they require fewer transfusions to maintain
their hematocrits. (42)  In rare instances, polycystic disease has been
associated with frank polycythemia vera. (12, 24, 25, 37, 73)  The rela-
tive erythrocytosis during dialysis (42) and frank polycythemia (73) are
both corrected by nephrectomy.  No studies, to date, have been published
correlating levels of erythropoietin with erythrocytosis in these patients.
The association suggests that a combination of uremia and high or normal
levels of hemoglobin may lead to an unsuspected diagnosis of polycystic
disease in the patient with renal failure.

Leading causes of death in polycystic disease are uremia, myocar-
dial infarction, cerebro-vascular accident and cardiac decompensation
secondary to hypertensive cardiovascular disease. (72)  [Table 5]

TABLE 5:  LEADING CAUSES OF DEATH IN POLYCYSTIC KIDNEY DISEASE

| Terminal Event | Dalgaard (17) | Rall and Odell (65) | Higgins (31) |
|---|---|---|---|
| Uremia | 59% | 20% | 66% |
| Cardiac disease | 6 | 13 | -- |
| Cerebral hemorrhage | 13 | 9 | -- |

With the advent of hemodialysis, renal transplantation and neph-
rectomy, the natural history of polycystic disease has been altered, im-
proving the long term prognosis. (1, 5, 42, 63, 69)   Lazarus and his
co-workers (42) have reported considerable success in the control of hyper-
tension with dialysis.  All their patients suffered from symptomatic
uremia at the time at which dialysis was instituted; they reported no
unusual complications from the procedure.  Because of the relative ery-
throcytosis of polycystics [vide supra] they discourage routine nephrec-
tomy except in cases with uncontrolled hematuria or life threatening sepsis.
The results of renal transplantation were also encouraging provided that
transplant recipents were first stabilized on hemodialysis and that the
graft survived for at least six months.  Pre-transplant nephrectomy has
been advised to obviate the mechanical problems during surgery from grossly
enlarged kidneys, for control of upper urinary tract infection, hyperten-
sion and vesico-ureteral reflux. (68)

RADIOLOGY

Radiographic diagnosis of polycystic disease becomes feasible with
the progression of the disease to gross involvement.  During the early
course of the disease, radiologic changes are minimal and may pass unde-
tected.  Diagnostic accuracy is increased and earlier detection of changes
made possible through the use of special study techniques such as retro-
grade pyelography (31, 72), infusion pyelography (27, 68, 83), nephro-
tomography (17, 23, 26, 33), and renal angiography (7, 12, 16, 20, 22, 49)

On the plain film of the abdomen, large irregular renal outlines
are suggestive of polycystic involvement.  The kidneys have an embossed

outline and are usually longer than fourteen centimeters. When the kidneys are not visualized on the plain film, displaced loops of bowel are suggestive of enlargement. (7, 17, 21, 22, 40)   With advancing age of the patient, the degree of enlargement increases. Thus, enlargement is found in 11% of patients at age 35 years, 50% at age 50, and 74% at age 75. (17)

Visualization of the renal parenchyma and collecting system with the use of contrast materials allows further delineation of polycystic involvement. [Figure 1]   During the latent phase of the disease small radiolucencies which correspond to areas of cystic involvement produce a non-homogenous nephrogram; in the presence of normal renal function, the nephrogram may be assessed during the first three minutes of urography. (26) During nephrotomography (12, 23, 33) or infusion tomography (27, 83)  [in patients with BUN > 40 mg.%] visualization of cysts as well-demarcated, thin-walled, sharp radiolucencies in the midst of normally functioning areas of parenchyma give rise to a characteristic moth-eaten appearance. The renal calyces appear elongated and crescentic.  Impinged upon by cysts of varying sizes, they are often described as "spidery". (7, 17, 20, 31, 72, 83)   This must be differentiated from the "spider-leg pelvis", a normal variant. (21)  Because of intervening cysts, the renal parenchyma appears thickened (21); measuring greater than three centimeters from the most laterally projecting calyx to the margin of the kidney [normal: 2.7 cm.]. (7, 17)   The longitudinal axis of the kidney shifts from its normal position parallel to the spine. (7, 17)   Multiple cystic impressions impinge upon the renal pelvis which may be shifted laterally due to the enlargement of parenchyma medial to it. (7)   The pelvic ampulla assumes a horn shape; since this is also a normal variant this sign is useful only as

Fig. 1.  Intravenous Pyelographic Findings in Adult Polycystic

Disease of the Kidneys.

A.  Right Kidney:  Urogram demonstrates elongated spidery calyces, sculpted
    by numerous cysts.  Large lower pole cyst extends from L-3 to iliac crest.
    The longitudinal axis of kidney is displaced shifted nearly parallel to
    spine.
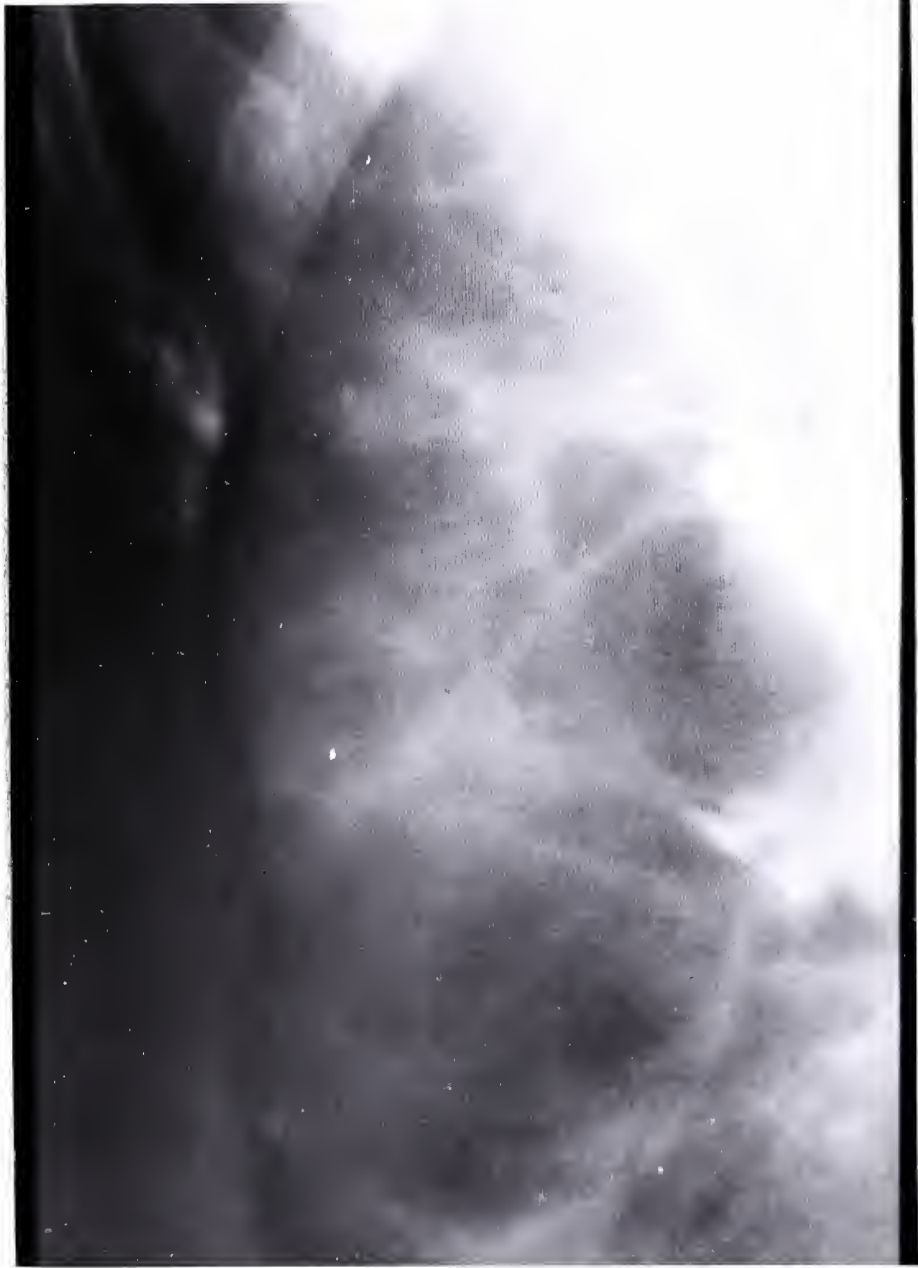
1 B.  Detail of right kidney; Lateral margin and most laterally projecting
      calyx:  Demonstrating attenuation of calyceal system.

1 C.  Left kidney:  Urogram demonstrates knobby, irregular renal outline.
      The calyceal system is sculpted by numerous cysts.  The longitudinal
      axis of the kideny is shifted parallel to spine.

1 D.  Detail of left kidney; lateral margin of kidney and most laterally
projecting calyx:  The calyx is indented by a cystic impression.

further confirmatory evidence in the diagnosis. (7)  Lowman and Haber (44)
recommend simultaneous hepatonephrotomograph in order to detect any co-
existing cystic disorder of the liver.

Because of the risk of ascending infection, instrumentation of
the upper urinary tract must be approached with caution. (17)  Retro-
grade pyelography provides more complete visualization of the collecting
system and may increase the diagnostic accuracy in the case of inadequate
intravenous urography. (72)  The findings on retrograde examination are
similar to those described above. (17, 31, 49, 72)

Angiography is the most discriminating tool in the radiographic
analysis of polycystic kidneys. (7, 16, 22, 49)  During the nephrogenic
phase, the kidneys assume the characteristic moth-eaten appearance. (7, 20,
21, 22, 49)  The arterial phase may reveal deformed, partially atrophic
vessels, with displacement of the interlobular and segmental arteries by
large cystic masses. (88)  The volume of the renal parenchyma may be
estimated from the relative size of the renal outline and its arterial
tree; a small arterial system supplying a large kidney mass indicates a
significant loss of parenchyma. (49)

In a series of twenty three patients reviewed by Hatfield and
Pfister (27), intravenous pyelography proved diagnostic of polycystic
disease in eight patients, suggestive of the disease, but not diagnostic
in another fourteen and interpreted as within the limits of normal in one
case.  Unilateral changes were present in seven patients all of whom
evidenced bilateral disease at autopsy.  In eleven cases where retrograde
pyelography was performed, the examinations were diagnostic in three.  They
were encouraged by the results of infusion tomography, obtaining   the
diagnosis in three cases studied in this way, and recommended it as the
study of choice for evaluation of the suspected case of polycystic disease.

TABLE 6:   RADIOGRAPHIC FINDINGS IN POLYCYSTIC KIDNEY DISEASE

I.   On   Plain Film of the Abdomen
  A.   Large renal outlines:   length greater than 14 cm.;
       with possible displacement of bowel.
  B.   Embossed outline

II.   Intravenous Pyelogram
  A.   Parenchymal thickening:   greater than 3 cm.
  B.   Elongation of the renal pelvis:   greater than 9 cm.
  C.   Elongation of calyces.
  D.   Crescentic, spidery calyces.
  E.   Multiple impressions of cysts in the renal pelvis.
  F.   Lateral displacement of the pelvis.
  G.   Longitudinal axis of the kidney parallel to the spine.

III.   Nephrotomography
  A.   Moth-eaten appearance during nephrogram phase.
  B.   Well circumscribed radiolucencies surrounded by nor-
       mally opacified parenchyma.

IV.   Renal Angiography
  A.   Moth-eaten appearance during nephrogenic phase.
  B.   Well circumscribed radiolucencies surrounded by nor-
       mally opacified parenchyma.
  C.   Deformed, partially atrophic vessels.
  D.   Displacement of interlobular and segmental arteries.

Ultrasound offers the possibility of early diagnosis, before the

characteristic roentogenographic changes appear on intravenous urography.

Lufkin, et. al. (45) studies sixty four patients in a kindred for evidence

of polycystic disease.   Thirty one patients displayed sonographic evidence

of the disease; only fifteen of these evidenced changes on intravenous pye-

lography.


DIFFERENTIAL DIAGNOSIS

The major problem in the differential diagnosis of polycystic

disease is the distinction of the condition from renal neoplasm.   Presen-

tation of a patient with non-specific symptoms referable to the kidney,

renal enlargement on plain film of the abdomen or intravenous urography,

and, perhaps, some compromise of renal function immediately raise the

specter of renal neoplasm.  The most useful reontgenographic technique
used to distinguish cystic enlargement from the malignant, is renal angio-
graphy. (7, 12, 49)   During the arterial phase of an angiogram, a neo-
plasm demonstrates a confluence of irregular, small vessels or a puddling
of contrast material in the region of the lesion, the "tumor blush"; dur-
ing the nephrogenic phase, a malignant lesion has a radiographic density
equal to or greater than that of the surrounding renal parenchyma, and
may show areas of necrosis. (12)   A cystic lesion demonstrates an avas-
cular space occupying lesion during the arterial phase, and one or more
round or ovoid lucencies which are well marginated by the surrounding nor-
mal parenchyma during the nephrogenic phase. (12)   Ultrasound has also
been used successfully to differentiate cystic from solid space occupying
lesions within the kidney. (45)

Because of the prognostic implications and the need for accurate
counseling, polycystic disease must be distinguished from other cystic
disorders of the kidney. [Table 7]   Cystosis may cause renal enlargement
detectable on physical examination, and a radiographic picture similar to
polycystic disease. (17)   A diagnosis of retention cysts of the kidney
carries little promise of progressive renal functional impairment.  Simple
cysts may be single, multiple, multilocular or hemorrhagic.  A kidney with
multiple simple cysts may be differentiated from polycystic disease be-
cause it is usually unilateral, causes less destruction of the renal paren-
chyma, and is non-hereditary. (17, 74)   On physical examination, a kidney
with multiple cysts may be palpably enlarged, and, radiologically the in-
volved kidney may resemble the polycystic kidney.  Pyelogenic (peripelvic)
cysts are usually adjacent to the renal pelvis, communicating directly
through a calyx.  A parapelvic cyst is adjacent to the pelvis, but lacks
direct communication.  These two entities may cause lateral deviation of

the renal pelvis, one of the roentgenographic signs of polycystic disease.
Kidney cysts may also arise secondary to the variety of pathologic processes
of the kidney such as calculosis, hypernephroma, tuberculosis, pyelonephri-
tis, hematoma, and echinococcus. (17)    There is some debate in the litera-
ture about medullary sponge kidney as an entity distinct from polycystic
disease. (56)

Other pathologic processes which must be distinguished from polycystic
disease are chronic glomerulonephritis, chronic glomerulonephritis with
associated hypertension, pyonephrosis, bilateral hydronephrosis, nephropto-
sis, and tumors and cysts in adjacent organs. (17)    Radiographically en-
larged, poorly functioning kidneys must also be distinguished from renal
amyloidosis, leukemic infiltration of the kidney, multiple myeloma, and
the collagen vasculidides.

---

TABLE 7:   DIFFERENTIAL DIAGNOSIS OF CYSTIC LESIONS OF THE
           KIDNEYS


1.   Retention or inflammatory cysts
2.   Simple cyst
       a.   Single cyst
       b.   Multiple cyst
       c.   Multilocular cyst
       d.   Hemorrhagic cyst
3.   Peripelvic cyst
4.   Parapelvic cyst
5.   Pathologic cyst
       a.   Calculosis
       b.   Hypernephroma
       c.   Echinococcus
       d.   Other

after Dalgaard (17)

TABLE 8:  DIFFERENTIAL DIAGNOSIS OF BILATERAL RENAL ENLARGEMENT

1.  Polycystic disease
2.  Renal neoplasm
3.  Chronic glomerulonephritis
4.  Bilateral hydronephrosis, pyonephrosis
5.  Cystosis
6.  Renal amyloidosis
7.  Leukemic infiltration
8.  Multiple myeloma
9.  Collagen vascular disease

PART THREE:  CLINICAL AND RADIOLOGICAL CORRELATIONS AND THE SIGNIFICANCE
OF THE INTRAVENOUS UROGRAM

MATERIALS AND METHODS

Recently, Lalli and Poirier (40) contended that serial intravenous pyelography constituted a useful tool in the evaluation of the progression of polycystic disease and the prognostication of its clinical course.  They based their conclusions on a sample of twenty patients drawn from the Cleveland Clinic's pool of 509 cases.  [Table 9]  From this data, they concluded

TABLE 9:  RESULTS OF SERIAL PYELOGRAPHY IN TWENTY PATIENTS WITH POLYCYSTIC DISEASE OF THE KIDNEYS

| | No. of Patients | Family History | Uremia | Hypertension | Death | Hematuria | Observation Period (yr.) Aver. | Range |
|---|---|---|---|---|---|---|---|---|
| Enlarged | 9 | 4 | 6 | 8 | 2 | 4 | 11 | 2-21 |
| Minimal Enlargement | 8 | 4 | 3 | 5 | 0 | 5 | 5.1 | 2-11 |
| Not Enlarged | 3 | 2 | 2 | 2 | 0 | 1 | 13 | 8-18 |
| Total | 20 | 10 | 11 | 15 | 2 | 10 | 9.7 | 2-21 |

after Lalli and Poirier (40)

that correlations were made between advancing renal size and the presence of clinical complications, and that an observed increase in renal size was in fact correlated with the severity of the disease and could be used as an indicator of probable shortened life expectancy.

Chi square analysis of the data, however, leaves a less definitive impression than this conclusion would imply. Because of the sample size, the data from the minimally enlarged and unenlarged groups were pooled for interpretation. Lalli's data are not statistically significant. In terms of the sequelae of polycystic disease, uremia [$p < 0.50$] and hypertension [$p < 0.20$], the data do not present a valid statement of prognosis. The increase of mortality, although not significant [$p < 0.10$] is suggestive and merits further investigation of the experimental hypothesis.

Intravenous pyelography is a relatively non-invasive, benign procedure. Accurate prognosis on the basis of IVP would permit a more thorough orchestration of the patient's clinical management, allowing the selection of a compatible kidney donor while the patient is yet able to maintain himself on his own diminishing renal function and before multiple transfusions during dialysis have sensitized him to possible donor antigens. Timely use of transplant and nephrectomy [vide supra] would have a salutory effect on the natural history of the disease process. (5, 42, 68, 69, 77, 78)

The experimental population was derived from a review of the records of ninety six cases of polycystic disease at the Yale-New Haven Hospital, the West Haven Veteran's Administration Hospital, the Hospital of St. Raphael, New Haven, Connecticut, and the Waterbury Hospital, Waterbury, Connecticut. Intravenous pyelograms were available on thirty patients, eleven of whom had undergone serial examinations which were still on file. The eleven patients had a total of thirty urograms which were examined independently by the author and six staff radiologists at the Yale-New Haven Hospital. The radiologists were asked to evaluate the parameters of renal length and width, calyceal length and the thickness of the renal parenchyma from the most lateral projecting calyx to the lateral margin

of the kidney. [Figure 2]   Names of the patients were masked, and the examinations randomized in order to prevent comparison with a patient's previous pyelogram.  Films for a given examination were reviewed independently by the six radiologists and a statistical mean drawn.  These results were used as a standard of accuracy to gauge the reliability of the author's assessment of the material reviewed independently.  Normal values were taken from literature controls. (54, 55, 80)  [See Appendix A]   No controls for the length of the calyceal system were available.  A control group was drawn from seventy five consecutive cases performed at the Yale-New Haven Hospital from February 1 to April 23, 1974, and interpreted to be within the range of normal by the attending staff radiologist.  [See Appendix B]

DISCUSSION

In the evaluation of clinical history, the cohort of thirty patients was divided into groups according to the presence or absence of urinary tract infection, uremia, and hypertension.  The mean lengths of the kidneys in these groups on intravenous urography were compaired using a one tailed "t" test; a correlation was considered statistically significant if $p < 0.05$. Analysis of data indicated a statistically significant correlation between an increased kidney length and an increased incidence of infection documented by culture of the urine.  The longer kidney was measured and the mean length of the kidneys in patients with infection was $18.6 \pm 2.2$ cm. and without infection, $16.3 \pm 2.8$ cm.  [$p < 0.025$]   Thus, not only is there an increased incidence of infection among patients with polycystic disease (79), but that incidence increases as the kidneys enlarge.  Similar data in patients with uremia, while not statistically significant were suggestive of a pos-

Fig. 2: Polycystic Kidney Disease -- Adult Type; Assessment of Renal Parameters. (See text) L= Length, W = Width, C = length of calyceal system, P = width of renal parenchyma measured from the lateral margin of the kidney to the most laterally projecting calyx.

sible correlation between kidney length and uremia; the mean length of kidneys in uremic patients was $19.5 \pm 3.0$ cm. and in non-uremic patients $17.2 \pm 2.9$ cm. [p < 0.10] There was no significant difference demonstrated with hypertension; the mean length of the kidneys in hypertensive patients was $17.9 \pm 3.1$ cm. and in normotensive patients $17.2 \pm 2.6$ cm. [p < 0.30] The data for infection may be viewed from another perspective. [Table 10]

TABLE 10: CORRELATION OF KIDNEY LENGTH AND URINARY TRACT INFECTION

| Kidney length (cm.) | No. of patients with infection | No. of patients without infection | Total |
|---|---|---|---|
| <15 | 2 | 6 | 8 |
| 15 to 18 | 5 | 4 | 9 |
| >18 | 8 | 5 | 13 |
| Total | 15 | 15 | 30 |

The group of eleven patients for whom serial examinations were available was broken down into groups according to the interval development of urinary tract infection and uremia, and the eventual development of renal failure [the institution of hemodialysis]. Thus, a patient manifesting hypertension at the time of initial urography was eliminated from consideration in the cohort that developed elevated blood pressures. A one-tailed "t" test with a value $p \leq 0.05$ was considered significant. The size on the population developing interval infection and uremia [one case each] precluded meaningful analysis. The analysis of increasing kidney size and hypertension was not statistically significant, a finding consistent with Lalli's data (40); the interval change in patients developing hypertension was $1.0 \pm 2.3$ cm. and in those remaining normotensive $3.0 \pm 2.8$ cm. [p $\leq$ 0.30] During the period of follow-up, two patients developed renal failure and began chronic hemodialysis. The interval change in patients going on to dialysis was $3.0 \pm 1.1$ cm., and for the group not requiring dial-

ysis $1.8\overset{+}{-}2.5$ cm. [p < 0.025]. Because of the small population involved, this finding is not definitive, but merits further investigation.

This study provides statistical confirmation of the clinical impression expressed in the literature that the collecting system of the kidneys is elongated in polycystic disease. (7, 17) The mean length of the calyceal system of the right kidney was $7.1\overset{+}{-}0.9$ cm. for the series of seventy five uninvolved patients and $10.2\overset{+}{-}2.2$ cm. for the series of thirty polycystic patients [p < 0.01] similarly, the calyces of the left side measured $7.2\overset{+}{-}0.9$ cm. and $10.4\overset{+}{-}2.8$ cm., respectively. [p < 0.01] [Appendices A, B]

The measurements by the six staff radiologists were compared using a "t" test to analyze the data [Appendix A]. The precision of varian ce obtained was 1.1 cm. for the length of the kidney, 0.7 cm. for the width, 0.7 cm. for parenchymal width, and 1.0 cm. for the length of the calyceal system. These measurements may be applied clinically as general statements on the precision of measurement of any one event. In this study, they provide a guide to the precision of the author's.

A retrospective study of hospital records is fraught with imponderable variables. Of 96 cases on record at the four institutions involved in this study, urographic examinations were available on only 30. Due to problems of storage, X-rays are sent for reprocessing of silver salts after seven years at the Yale-New Haven Hospital and after only four years at the Waterbury Hospital, if, during that period, the patient has not had further radiologic evaluation. Patients with polycystic disease may run a clinical course as long as thirty six years (17) during which time they may remain largely asymptomatic, not requiring medical assistance with consequent removal of early examinations from their records. Simple loss of films is a frustrating experience with which all clinicians are

familiar and which further compounds the problems of assembling a series such as this. Higgins (31) noted that during exacerbation of the disease patients develop hematuria pain and nitrogen retention which subside during periods of remission. It is during these periods of active disease, that the patient is most likely to present to the hospital or the hospital clinic for evaluation; thus, in many cases, the data available from hospital records may not be representative of the patients prevailing clinical status for much of his course. Assessment of the polycystic patient's data has been on the basis of "clinical gestalt," a combination of history, physical findings, and a laboratory evaluation which varies from physician to physician. A prospective evaluation is needed comparing the efficacy of serial serum chemistry (BUN, creatinine), glomerular function (24-hour creatinine clearance), tubular function (PSP), urologic, and sonographic evaluations as a means of following a patient and determining the prognosis. A prospective study is now in progress at the Yale-New Haven Hospital in which polycystic patients and their families are being evaluated sonographically.

SUMMARY

Thirty patients with polycystic disease of the kidney were studied. A radiologic sign of increased length of the calyceal system in the kidneys of patients with the disease over normal was described. Correlations of the clinical course of the disease and increased kidney length were made. There is a statistically significant correlation between the incidence of urinary tract infection and the increased length of the kidney. No such correlations were found for hypertension or uremia. Analysis of interval changes in kidney length in eleven patients with serial examinations, revealed a significant correlation between an interval change of

3.0 cm. on diagnostic urograms and the development of renal failure. The data did not support an association of the development of hypertension with increasing kidney length.

Twenty nine intravenous pyelograms were examined by six staff radiologists of the Yale-New Haven Hospital. They were asked to measure the length of the calyceal system on each kidney on each examination. The precisions of variance obtained when this was analyzed were: length = 1.1 cm.; width = 0.7 cm.; parenchymal thickness = 0.7 cm.; and, calyceal length = 1.0 cm. These values may be used by the clinician as a guide to the precision of measurement of a urogram by a radiologist on any one occasion.

This study constitutes a necessary preamble to a study, now in progress, comparing the efficacy of intravenous pyelography and ultrasound in the investigation of polycystic disease. In order to evaluate the contributions available from ultrasonic investigation, it was necessary to define the limits of the currently accepted evaluative tool, intravenous urography.

APPENDIX A

| | Moell 1956 (55) | Moell 1961 (54) | Vourinen (80) |
|---|---|---|---|
| **RADIOGRAPHIC MEASUREMENTS* OF NORMAL KIDNEYS** | | | |
| **MEN** | | | |
| Right Kidney | | | |
| Length | 12.7 ± 0.78 | 12.9 ± 0.80 | 12.4 ± 1.02 |
| Width | 6.3 ± 0.49 | 6.2 ± 0.45 | 6.2 ± 0.72 |
| Left Kidney | | | |
| Length | 13.2 ± 0.82 | 13.2 ± 0.79 | 12.7 ± 1.12 |
| Width | 6.4 ± 0.55 | 6.3 ± 0.49 | 6.2 ± 0.45 |
| **WOMEN** | | | |
| Right Kidney | | | |
| Length | 12.4 ± 0.66 | 12.3 ± 0.79 | 12.0 ± 1.08 |
| Width | 5.9 ± 0.37 | 5.7 ± 0.46 | 5.7 ± 0.56 |
| Left Kidney | | | |
| Length | 12.8 ± 0.77 | 12.6 ± 0.77 | 12.5 ± 1.29 |
| Width | 6.1 ± 0.38 | 5.9 ± 0.42 | 6.2 ± 0.61 |

* all measurements in cm. ± 1 S. D.

RESULTS OF SERIAL PYELOGRAPHY IN ELEVEN PATIENTS AS READ BY SIX STAFF
RADIOLOGISTS AT THE YALE–NEW HAVEN HOSPITAL

LEFT KIDNEY*

| Patient | Length | Interval Change in Length | Width | Calyceal Length | Parenchymal Width |
|---|---|---|---|---|---|
| M.B. | 15.2 $\pm$ 0.2 | | 6.4 $\pm$ 1.0 | 9.7 $\pm$ 1.2 | 2.5 $\pm$ 0.6 |
| | 14.7 $\pm$ 0.3 | -0.5/ $2^{2}$/12 yr. | 7.4 $\pm$ 0.4 | 9.6 $\pm$ 0.6 | 2.7 $\pm$ 0.7 |
| S.C. | 18.6 $\pm$ 0.4 | | 9.4 $\pm$ 0.4 | 12.3 $\pm$ 0.5 | 3.0 $\pm$ 0.2 |
| | 18.4 $\pm$ 0.2 | -0.2/ $3^{4}$/12 yr. | 9.8 $\pm$ 0.9 | 11.6 $\pm$ 0.9 | 2.8 $\pm$ 0.2 |
| C.D. | 15.9 $\pm$ 0.5+ | | 6.6 $\pm$ 0.4 | 9.5 $\pm$ 1.7 | 2.6 $\pm$ 1.8 |
| | 16.8 $\pm$ 0.5+ | | 6.0 $\pm$ 0.3 | 10.6 $\pm$ 0.4 | 3.1 $\pm$ 0.4 |
| | 16.6 $\pm$ 0.4 | +0.7/ 3 yr. | 6.8 $\pm$ 1.0 | 9.4 $\pm$ 1.0 | 3.3 $\pm$ 0.8 |
| | 18.1 $\pm$ 1.1 | +1.5/ $4^{10}$/12 yr. | 7.0 $\pm$ 0.4 | 9.9 $\pm$ 0.5 | 2.7 $\pm$ 1.1 |
| | | +2.2/ $7^{10}$/12 yr. | | | |
| F.D. | 16.7 $\pm$ 0.5 | | 9.4 $\pm$ 0.6 | 9.0 $\pm$ 1.2 | 3.2 $\pm$ 0.2 |
| | 16.5 $\pm$ 1.9 | -0.2/ $3^{6}$/12 yr. | 8.6 $\pm$ 0.6 | 10.3 $\pm$ 0.9 | 3.0 $\pm$ 0.0 |
| G.G. | 14.1** | | 8.0** | 7.5** | 2.5** |
| | 15.1** | +1.0/ $3^{1}$/12 yr. | 7.3** | 7.0** | 3.5** |
| | 14.8 $\pm$ 0.4 | -0.3/$10^{1}_{2}$/12 yr. | 8.0 $\pm$ 0.4 | 8.7 $\pm$ 0.7 | 3.0 $\pm$ 0.7 |
| | | +0.7/$13^{2}$/12 yr. | | | |
| G.J. | 16.3 $\pm$ 0.7 | | 9.5 $\pm$ 0.9 | 12.8 $\pm$ 0.3 | 3.7 $\pm$ 0.9 |
| | 17.8 $\pm$ 0.3 | +1.9/ $1^{3}_{10}$/12 yr. | 9.6 $\pm$ 0.6 | 13.1 $\pm$ 0.5 | 2.3 $\pm$ 0.6 |
| | 17.1 $\pm$ 1.2 | -1.1/ $3^{10}$/12 yr. | 9.6 $\pm$ 0.5 | 12.6 $\pm$ 1.2 | 2.7 $\pm$ 0.5 |
| | | +0.8/ $5^{1}$/12 yr. | | | |
| | 21.0 $\pm$ 1.0 | +3.9 $1^{1}$/12 yr. | 10.6 $\pm$ 0.9 | 12.4 $\pm$ 1.4 | 2.9 $\pm$ 0.6 |
| | | +4.7/ $6^{2}$/12 yr. | | | |
| C.L. | 18.1 $\pm$ 2.3 | | 8.4 $\pm$ 1.0 | 12.0 $\pm$ 0.8 | 3.0 $\pm$ 0.6 |
| | 20.9 $\pm$ 1.3 | +2.8/ $7$/12 yr. | 8.5 $\pm$ 0.6 | 11.8 $\pm$ 0.3 | 2.5 $\pm$ 0.5 |
| J.M. | 20.5 $\pm$ 0.5 | | 9.0** | 16.0 $\pm$ 0.6 | 4.4 $\pm$ 0.2 |
| | 20.4 $\pm$ 2.0 | -0.1/ $3^{7}$/12 yr. | 8.4 $\pm$ 0.7 | 11.7 $\pm$ 3.9 | 2.6 $\pm$ 1.4 |
| A.M. | 18.7 $\pm$ 1.0 | | 9.2 $\pm$ 0.5 | 12.7 $\pm$ 0.5 | 2.8 $\pm$ 0.7 |
| | 18.1 $\pm$ 0.1 | -0.6/ $4$/12 yr. | 9.0 $\pm$ 0.1 | 13.3 $\pm$ 0.6 | 4.5** |
| G.S. | 14.9 $\pm$ 0.3 | | 8.0 $\pm$ 0.6 | 8.2 $\pm$ 0.6 | 2.3 $\pm$ 0.5 |
| | 15.8 $\pm$ 0.3 | +0.9/ $4$/12 yr. | 8.1 $\pm$ 0.2 | ----- | ----- |
| M.T. | 17.5 $\pm$ 1.4 | | 8.5 $\pm$ 0.6 | 8.9 $\pm$ 1.1 | 2.8 $\pm$ 0.4 |
| | 19.1 $\pm$ 2.1 | +1.6/ $7$/12 yr. | 7.8 $\pm$ 0.3 | 11.9 $\pm$ 0.2 | 2.8 $\pm$ 0.2 |
| | 16.1** | -3.0/ $1^{1}_{8}$/12 yr. | 7.5** | 11.7** | ----- |
| | | -1.4/ $1^{8}_{2}$/12 yr. | | | |
| | 16. 7** | +0.6/ $1^{2}_{10}$/12 yr. | 7.9** | 11.0** | 2.7** |
| | | -0.8/ $2^{10}$/12 yr. | | | |

\* all measurements in centimeters $\pm$ 1 S.D.

\** read by only radiologist

+ performed during same hospital admission; the first examination is
an intravenous pyelogram, the second a tomogram

RIGHT KIDNEY*

| Patient | Length | Interval Change in Length | Width | Calyceal Length | Parenchymal Width |
|---|---|---|---|---|---|
| M.B. | 15.5 ± 0.8 | | 6.9 ± 0.3 | 8.7 ± 1.0 | 2.2 ± 0.4 |
| | 14.0 ± 0.5 | -1.5 $2^2$/12 yr. | 7.2 ± 0.2 | 8.2 ± 0.2 | 2.2 ± 0.4 |
| S.C. | 19.4 ± 0.7 | | 8.7 ± 0.3 | 13.5 ± 0.7 | 3.1 ± 0.6 |
| | 21.6 ± 0.5 | +2.2/ $3^4$/12 yr. | 8.4 ± 0.7 | 13.0 ± 1.6 | 3.9 ± 0.7 |
| C.D. | 12.0+** | | ------ | ------ | 3.6** |
| | 12.4+** | | 7.5** | ------ | 2.7 ± 0.3 |
| | 10.7 ± 0.4 | -1.3/ 3 yr. | 8.0 ± 1.3 | 6.0** | 2.5 ± 0.0 |
| | 13.0 ± 0.9 | +2.3/ $4^{10}$/12 yr. | 7.7 ± 0.2 | 6.7 ± 0.7 | 2.9 ± 0.3 |
| | | +0.6/ $7^{10}$/12 yr. | | | |
| F.D. | 13.8 ± 0.5 | | 8.5 ± 0.3 | 7.9 ± 0.7 | 2.8 ± 0.3 |
| | 15.8 ± 1.3 | +2.0/ $3^6$/12 yr. | 8.3 ± 0.9 | 8.4 ± 0.5 | 2.8 ± 0.5 |
| G.G. | 13.6** | | 6/7** | 7.5** | 3.0** |
| | 14.5** | +0.9/ $3^1$/12 yr. | 6.2** | 7.5** | 2.5** |
| | 15.4 ± 0.5 | +0.9/$10^1$/12 yr. | 6.7 ± 0.2 | 8.7 ± 0.2 | 2.4 ± 0.4 |
| | | +1.8/$13^2$/12 yr. | | | |
| G.J. | 16.5 ± 1.8 | | 9.7 ± 0.5 | 9.5** | 3.0 ± 0.1 |
| | 18.2 ± 0.7 | +1.7/ $1^3$/12 yr. | 9.3 ± 1.1 | 11.3 ± 0.4 | 2.9 ± 0.6 |
| | 19.0 ± 3.2 | +0.8/ $3^{10}$/12 yr. | 9.1 ± 0.7 | 13.4 ± 1.0 | 3.2 ± 0.7 |
| | | +2.5/ $5^1$/12 yr. | | | |
| | 19.4 ± 0.2 | +0.4/ $1^2$/12 yr. | 10.3 ± 1.2 | 13.4 ± 0.2 | 2.6 ± 0.3 |
| | | +2.9/ $6^2$/12 yr. | | | |
| C.L. | 17.8 ± 1.0 | | 7.8 ± 0.3 | 10.1 ± 0.7 | 3.0 ± 0.4 |
| | 24.9 ± 0.9 | +7.1/ $7$/12 yr. | 9.1 ± 0.8 | 10.3 ± 2.1 | 3.2 ± 0.6 |
| A.M. | 20.3 ± 3.2 | | 8.9 ± 0.5 | 11.2 ± 0.4 | 2.8 ± 1.5 |
| | 17.6 ± 0.6 | -2.7/ $4$/12 yr. | 9.1 ± 0.3 | 11.2 ± 1.5 | 3.8 ± 1.2 |
| J.M. | 20.6 ± 0.8 | | 9.5 ± 0.0 | 13.3 ± 1.0 | 4.0 ± 1.3 |
| | 20.2 ± 2.0 | -0.4/ $3^7$/12 yr. | 8.5 ± 0.6 | 13.7 ± 1.2 | 3.4 ± 0.9 |
| G.S. | 14.3 ± 0.4 | | 7.0 ± 0.0 | 8.7 ± 0.3 | 2.2 ± 0.4 |
| | 15.2 ± 0.6 | +0.9/ $4$/12 yr. | 7.4 ± 0.9 | ------ | 4.5** |
| M.T. | 14.0 ± 0.0 | | 7.9 ± 0.5 | 8.2 ± 0.4 | 3.0 ± 0.3 |
| | 14.2 ± 0.6 | +0.2/ $7$/12 yr. | 8.0 ± 0.3 | 7.5 ± 0.5 | 2.7 ± 0.3 |
| | 14.0** | -0.2/ $1^1$/12 yr. | 8.3** | 8.3** | ------ |
| | | 0.0/ $1^8$/12 yr. | | | |
| | 14.3** | +0.3/ $1^2$/12 yr. | 8.0** | 8.3** | 2.5** |
| | | +0.1/ $2^{10}$/12 yr. | | | |

* all measurements in centimeters ± 1 S.D.
+ performed during same hospital admission; the first examination is an intravenous pyelogram, the second a tomogram
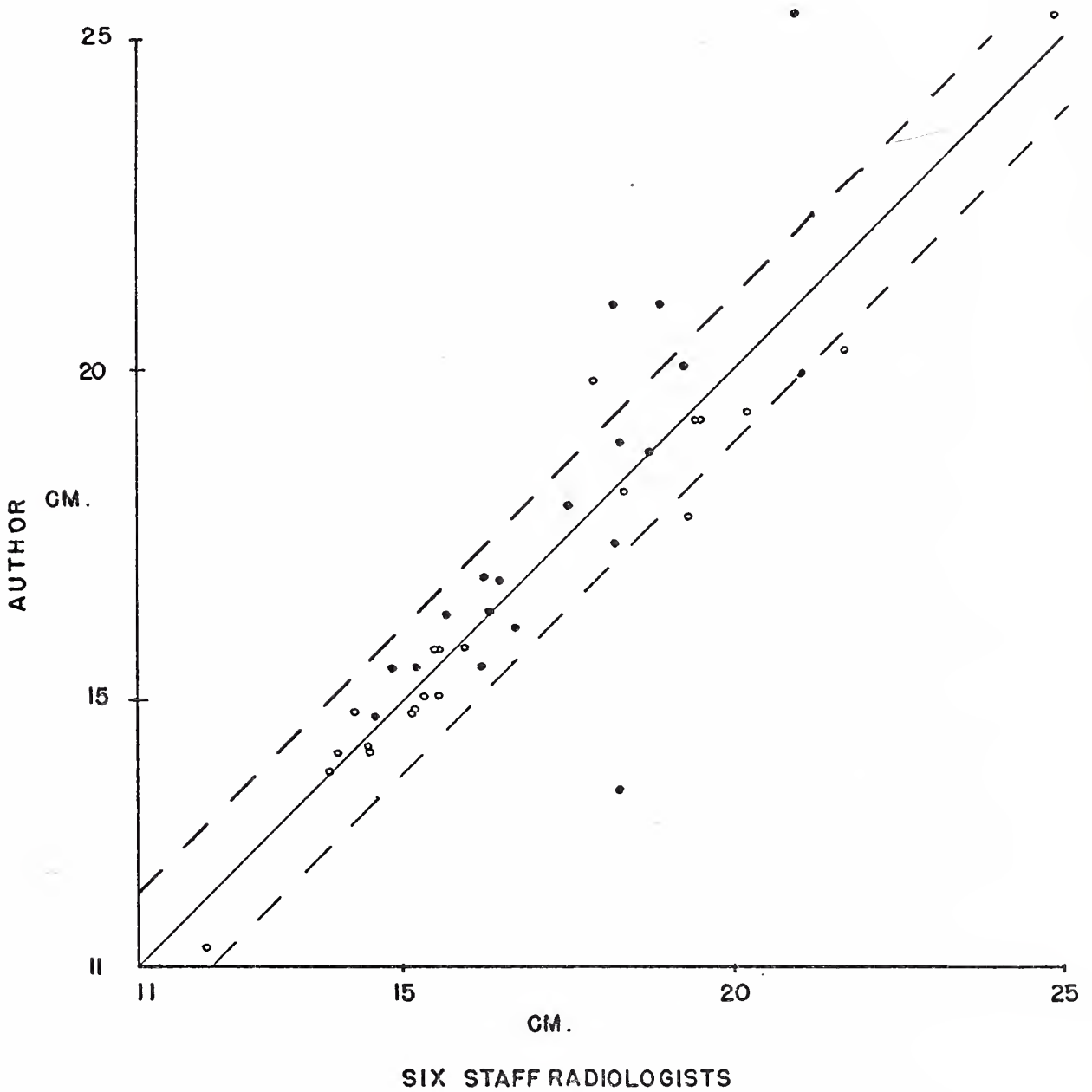** read by only one radiologist

RESULTS OF SERIAL PYELOGRAPHY IN ELEVEN PATIENTS AS READ BY SIX
STAFF RADIOLOGISTS AT THE YALE-NEW HAVEN HOSPITAL:

PRECISION OF VARIABILITY***

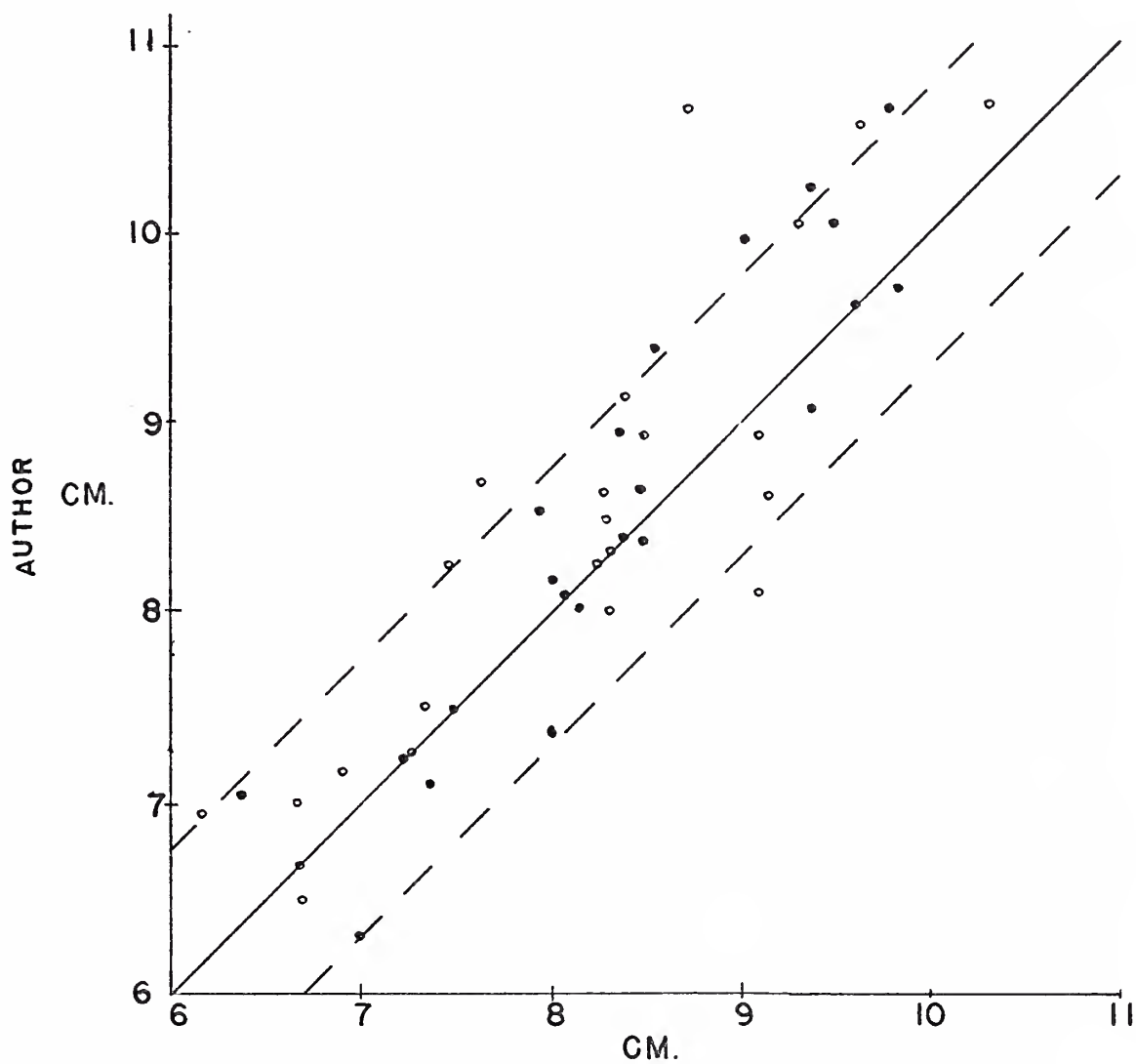|  | Length | Width | Calyceal Length | Parenchymal Width |
|---|---|---|---|---|
| Right kidney | ± 1.1 | ± 0.7 | ± 0.9 | ± 0.7 |
| Left kidney | ± 1.1 | ± 0.7 | ± 1.1 | ± 0.7 |

*** measurements in centimeters

FIGURE I: COMPARATIVE MEASUREMENTS OF KIDNEY LENGTH

LEGEND
— — RANGE OF VARIABILITY
• LEFT KIDNEY
∘ RIGHT KIDNEY

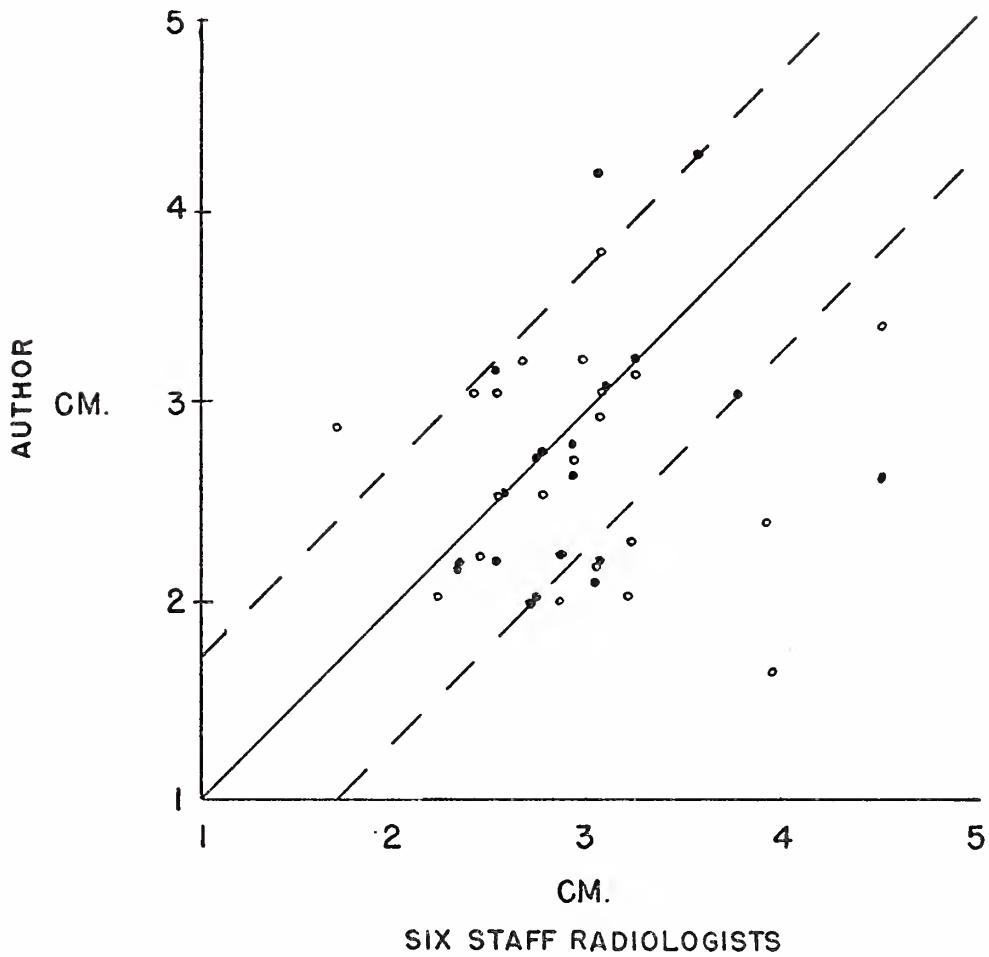FIGURE 2: COMPARATIVE MEASUREMENTS OF KIDNEY WIDTH

SIX STAFF RADIOLOGISTS

LEGEND

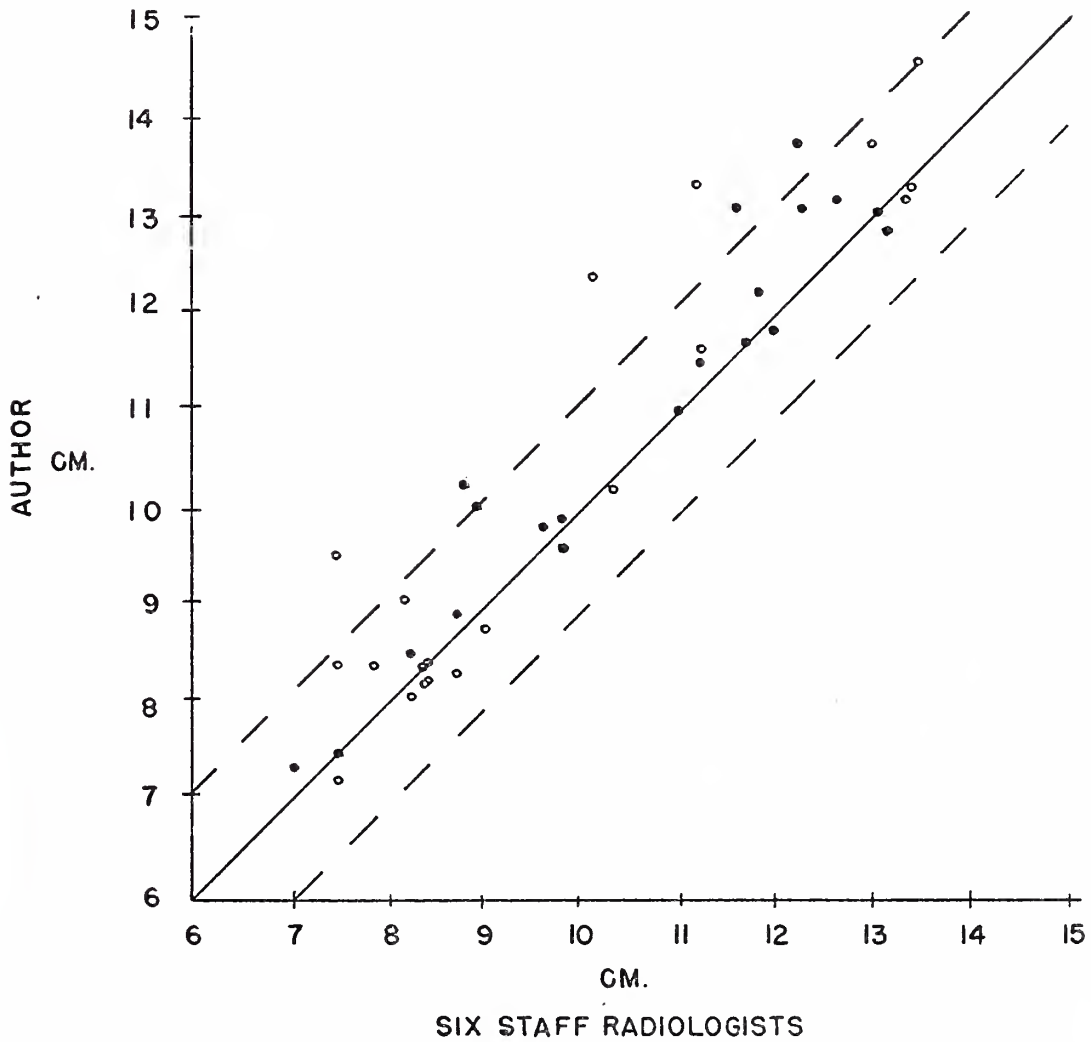— — RANGE OF VARIABILITY
- • LEFT KIDNEY
- ∘ RIGHT KIDNEY

FIGURE 3: COMPARATIVE MEASURENTS OF RENAL
PARENCHYMAL WIDTH

LEGEND

—— RANGE OF VARIABILITY
•   LEFT KIDNEY
∘   RIGHT KIDNEY

FIGURE 4: COMPARATIVE MEASUREMENT OF RENAL
CALYCEAL LENGTH

SIX STAFF RADIOLOGISTS

LEGEND

— — RANGE OF VARIABILITY
•  LEFT KIDNEY
◦  RIGHT KIDNEY

APPENDIX B

INDICATIONS FOR INVESTIGATION IN SEVENTY FIVE PATIENTS WITH NORMAL
INTRAVENOUS PYELOGRAMS

| Indication on Radiology Requisition | Number of Cases |
|---|---|
| Hypertension | 17 |
| Recurrent urinary tract infection | 13 |
| Hematuria | 8 |
| Flank or back pain | 7 |
| Benign hypertrophy of the prostata | 5 |
| Ureteral colic | 4 |
| Fever of unknown origin | 4 |
| Diabetes Mellitus | 4 |
| Carcinoma of the cervix | 3 |
| Diverticulosis | 2 |
| Pancreatitis | 2 |
| Crohn's disease | 1 |
| Tuberculosis | 1 |
| Carcinoma of the breast | 1 |
| Mycosis fungoides | 1 |
| Kidney donor | 1 |
| Testicular pain | 1 |

CALYCEAL LENGTH IN NORMAL KIDNEYS *

|  | Men | Women | Total |
|---|---|---|---|
| Right kidney | $7.3 \pm 0.80$ | $6.8 \pm 0.84$ | $7.1 \pm 0.87$ |
| Left kidney | $7.4 \pm 0.86$ | $7.0 \pm 0.84$ | $7.2 \pm 0.87$ |

* all measurements in cm. $\pm$ 1 S. D.

REFERENCES

1.  Amamoo, D.G., Woods, F.E., and Anderson, C.F.:  Renal Transplant
    in End Stage Polycystic Renal Disease,  J. Urol. 112: 443-4, 1974.

2.  Baurys, W. and Morton, W.:  Papillary Carcinoma in a Polycystic
    Kidney,  Urol. and Cutan. Rev. 54: 662, 1950.

3.  Bear, R.A.:  Solitary Kidney Affected with Polycystic Disease:
    A Report of Two Cases,  Urol. 3: 566-567, 1974.

4.  Bell, E.T.:  Renal Diseases,  Philadelphia, pp. 85-109, 1946.

5.  Bennett, A.H., Stewart, W., and Lazarns, J.M.:  Bilateral Neph-
    rectomy in Patients with Polycystic Renal Disease,  Surgery,
    Gynecol. Obstet. 137: 819-820, 1973.

6.  Bernstein, J.:  Heritable Cystic Disorders of the Kidney:  The
    Mythology of Polycystic Disease,  Pediatr. Clin. North Am.
    18: 435-446, 1971.

7.  Billing, L.:  The Roentgen Diagnosis of Polycystic Kidneys,  Acta
    Radiol. 41: 305-315, 1954.

8.  Bobbitt, R.M.:  Secondary Pathologic Changes in Polycystic Kidney
    Disease,  J. Urol. 50: 131, 1943.

9.  Borski, A.A. and Kimbrough, J.C.:  Bilateral Carcinoma in Polycystic
    Renal Disease--An Unique Case,  J. Urol. 71: 677, 1954.

10. Brannan, W., Miller, W., and Crisler, M.:  Co-existance of Renal
    Neoplasms and Renal Cysts,  So. Med. J. 55: 749, 1962.

11. Bricker, N.D. and Patton, J.F.:  Cystic Disease of the Kidneys:
    A Study of Dynamics and Chemical Compostion of Cyst Fluid,  Am.
    J. Med. 18: 207-219, 1955.

12. Chynn, K.Y. and Evans, J.A.:  Nephrotomography in the Differentia-
    tion of Renal Cyst from Neoplasm: A Review of 500 Cases,  J. Urol.
    83: 21-24, 1960.

13. Clemmesen, J.:  Familiaent Malignt Hypernephrom i en Slaegt Med
    Hereditaer Cystenyre,  Nord. Med. 14: 1472, 1942, cited in
    McFarland, et.al., J. Urol. 107: 530, 1972.

14. Cloete, G.N.P. and Van Rooyen, R.J.:  A Case of Polycystic Disease
    of the Liver and Kidneys,  S. Afr. Med. J. 48: 185-186, 1974.

15. Cole, A.T. and Gill, W.B.:  Dual Renal Cell Carcinomas in a Uni-
    lateral Polycystic Kidney,  J. Urol. 109(2): 182-185, 1973.

16. Cornell, H.S.:  Angiography in Polycystic Disease of the Kidney,
    J. Urol. 103: 24-27, 1970.

17. Dalgaard, O.Z.:  Bilateral Polycystic Disease of the Kidneys:  A
    Follow-Up of 284 Patients and Their Families,  Acta Med. Suppl.
    328: 1-255, 1957.

**REFERENCES**

18. Darmady, E.M., Offer, J., and Woodhouse, M.A.:   Toxic Defects in Polycystic Disease of the Kidney:  Evidence for Microscopic Studies. Lancet, I: 547-550, 1957.

19. Edsman, G.:  Angionephrography in Polycystic Kidneys,  Acta Radiol. [Suppl.] 155: 98-104, 1957.

20. Elkin, M. and Bernstein, J.:   Cystic Diseases of the Kidney: Radiological and Pathological Considerations,   Clin. Radiol. 20: 65-82, 1969.

21. Emmet, J.L. and Witten, D.M.:  Clinical Urography,  Philadelphia, 1971, pp. 981-1006.

22. Ettinger, A., Kahn, P.C., and Wise, H.M., Jr.:  The Importance of Selective Renal Angiography in the Diagnosis of Polycystic Disease, J. Urol. 102: 156-161, 1969.

23. Evans, A., Monteith, J.C., and Dubilier, W., Jr.:  Nephrotomography, Radiology 64: 655-663, 1955.

24. Forsell, J.:  Nephrogenous Polycythemia,  Acta Med. Scand. 161: 169-179, 1958.

25. Friend, D.G., Hoskins, R.G., and Kirkin, M.W.:  Relative Erythro-cytemia and Polycystic Kidney Disease with Uremia:  Report of a Case with Comments on the Frequency of Occurrence,   N. Eng. J. Med. 264: 17-19, 1961.

26. Halpern, M., Dalrymple, B., and Young, J.:   The Nephrogram in Polycystic Disease:  An Important Radiographic Sign,   J. Urol. 103: 21-23, 1970.

27. Hatfield, P.M. and Pfister, R.C.:  Adult Polycystic Disease of the Kidneys (Potter type 3),  J.A.M.A. 222: 1527-31, 1972.

28. Hayward, W.G.:  Hypernephroma in a Polycystic Kidney,  J. Uro. 56: 190, 1946.

29. Heptinstall, R.H., ed.:  Pathology of the Kidney,  Boston, 1974, pp. 89-93.

30. Hildebrand, O.:  Weiterer Beitrag zur Pathologischen Anatomie der Nierengesstwultie III Congenitale Cystenniere mit Sarkombildung, Arch. Klin. Chir. 48: 348, 894, cited in Heptinstall, Pathology of the Kidney, Boston, 1974.

31. Higgins, C.C.:  Bilateral Polycystic Kidney Disease:  Review of 94 Cases,  A.M.A. Arch. Surg. 65: 318-328, 1952.

32. Howard, R.M. and Young, J.D., Jr.:  Two Malignant Tumors in a Polycystic Kidney,  J. Urol. 102: 162, 1969.

33. Hurwitz, R.A. and Weigel, J.:  Polycystic Kidneys:  A Diagnostic Study with Continuous Drip Infusion Pyelograpy, Nephrotomography and Renal Scans,  J. Urol. 94: 639-646, 1965.

34. Ivemark, B.I., Lagergren, C., and Lindvall, N.:   Roentgenologic
    Diagnosis of Polycystic Kidney and Medullary Sponge Kidney,
    Acta Radiol. [Diag.] 10: 225-235, 1970.

35. Ivemark, B.I. and Lindblom, K.:   Arterial Ruptures in the Adult
    Polycystic Kidney,   Acta Chir. Scand. 115: 100-110, 1958.

36. Johnson, W.F.:   Carcinoma in a Polycystic Kidney,   J. Urol. 69:
    10, 1953.

37. Kurlle, G.R.:   A Case of Gaisbock's Disease,   Med. J. Aust. I:
    777-780, 1954.

38. Kampmeier, O.F.:   Hitherto Unrecognized Mode of Origin of Congenital
    Renal Cysts,   Surg. Gynecol. Obstet. 36: 2081, 1923.

39. Lalli, A.F.:   Renal Enlargement,   Radiology 84: 688-691, 1966.

40. Lalli, A.F. and Poirier, V.C.:   Urographic Analysis of the Develop-
    ment of Polycystic Kidney Disease,   Am. J. Roentgenol. Radium Ther.
    Nucl. Med. 119: 705-709, 1973.

41. Lambert, P.P.:   Polycystic Kidney Disease:  A Review,   Arch. Pathol.
    44: 34-58, 1947.

42. Lazarus, J.M., et.al.:   Hemodialysis and Transplantation in Adults
    with Polycystic Disease,   J.A.M.A. 217: 1821-4, 1971.

43. Lewis, E.L. and Kimbrough, J.C.:   Bilateral Hypernephroma Associated
    with Polycystic Disease,   Urol. and Cutan. Rev. 56: 79, 1952.

44. Lowman, R.M. and Haber, S.:   Hepatonephrotomography,   Angiology 12:
    583-8, 1961.

45. Lufkin, E.G., et.al.:   Polycystic Kidney Disease:   Earlier Diagnosis
    Using Ultrasound,   Urol. 4: 5-12, 1974.

46. McFarland, W.L., Wallace, S., and Johnson, D.E.:   Renal Carcinoma
    and P lycystic Disease,   J. Urol. 107: 530-532, 1972.

47. McNamara, J.J.:   Pyelonephritis in Polycystic Disease of the
    Kidney,   Am. J. Surg. 109: 178-81, 1967.

48. McKenna, C.M. and Kampmeier, O.F.:   Consideration of Development of
    Polycystic Kidney,   J. Urol. 32: 37, 1934.

49: Meaney, T.F. and Corvalan, J.G.:   Angiographic Diagnosis of
    Polycystic Renal Disease,   Cleve. Clin. Q. 35: 79-84, 1968.

50, Medart, W.S., Fr.:   Case Report:  Congenital Heart Disease, Uni-
    lateral Polycystic Kidney and Neuroblastoma,   So. Med. J. 67:
    516, 1974.

51. Melicow, M.M. and Gile, H.H.:   An Hypernephroma in a Polycystic
    Kidney:  Reviw of Literature and Report of Case,   J. Urol. 43:
    190, 1946.

52. Melnick, P.J.: Polycystic Liver, Arch. Path. 59: 162-172, 1955.

53. Mitchell, T.S., Halasz, N.A. and Gittes, R.F.: Renal Transplanta-
    tion: Selective Preliminary Bilateral Nephrectomy, J. Urol.
    109: 796-801, 1973.

54. Moell, H.: Kidney Size and Its Deviation From Normal in Acute
    Renal Failure, Acta Radiol. [Supple.] 206: 5-74, 1961.

55. Moell, H.: Size of Normal Kidneys, Acta Radiol. 41: 305-15, 1954.

56. Nemoy, N.J. and Forsberg, L.: Polycystic Renal Disease Presenting
    as Medullary Sponge Kidney, J. Urol. 100: 407-411, 1968.

57. Newcombe, D.S.: Gouty Arthritis and Polycystic Kidney Disease,
    Ann. Intern. Med. 79: 605, 1973.

58. Nixon, R.K., et.al.: Nephrogenic Polycythemia, Arch. Inter.
    Med. 106: 797-802, 1960.

59. Oppenheimer, G.D. and Narins, L.: Unilateral Polycystic Kidney
    Disease, J. Urol. 61: 866-869, 1949.

60. Osthanondh, V. and Potter, E.L.: Pathogenesis of Polycystic
    Kidneys, A.M.A. Arch. Pathol. 77: 459-512, 1964.

61. Perey, D.Y.E., Herdman, R.C., and Good, R.A.: Polycystic Renal Dis-
    eases: A New Experimental Model, Science 158: 494-496, 1967.

62. Perkoff, G.T.: The Hereditary Renal Disorders, N. Eng. J. Med.
    277: 79-85, 1967.

63. Pickens, R.L.: The Early Diagnosis of Polycystic Kidney Disease,
    Urol. 2: 188-190, 1973.

64. Puigvert, A.: Polykystose Renal et Cancer Bilateral, J. Urol. Med.
    Chir. 64: 30, 1958, cited in McFarland, et. al., J. Urol. 107:
    530, 1972.

65. Rall, J.E. and Odel, H.M.: Congenital Polycystic Disease of Kidneys:
    Review of Literature and Data on 207 Cases, Am. J. Med. Sci.
    218: 399-407, 1949.

66. Rivera, J.V.: Gout and Polycystic Disease of the Kidney, Ann.
    Intern. Med. 80: 427, 1974.

67. Roberts, P.F.: Bilateral Renal Carcinoma Associated with Polycystic
    Kidneys, Br. Med. J. 3(874): 273-4, 1973.

68. Rosenberg, J.C., et.al.: Indications for Pretransplant Nephrectomy,
    Arch. Surg. 107(2): 233-41, 1973.

69. Salvatierra, O., Jr., Kountz, S.L., and Belzer, F.O.: Polycystic
    Renal Disease: Treatment by Renal Transplantation, Surg., Gynecol.
    Obstet. 137: 431-434, 1973.

70. Sellers, A.L., Winfield , A., and Rosen, V.:  Unilateral Poly-
    cystic Kidney Disease,   J. Urol. 107: 527-529, 1972.

71. Siegelman, S.S., Zovod, R., and Hecht, H.:  Neurofibromatosis,
    Polycystic Kidneys and Hypernephroma,  N.Y. State J. Med. 71(20):
    2431-3, 1971.

72. Simon, H.B. and Thompson, G.J.:  Congenital Renal Polycystic
    Disease:  Clinical and Therapeutic Study of 366 Cases,   J.A.M.A.
    159: 657-662, 1955.

73. Singh, A., Singh, S., and Singth, N.:  Association of Polycythemia,
    Polycystic Kidneys, Diabetes Mellitus, and Portal Hypertension,
    J. Indian Med. Assoc. 27: 25-26, 1974.

74. Spence, H.M.:   Congenital Unilateral Multicystic Kidney:  An
    Entity to be Distinguished from Polycystic Kidney Disease and
    Other Cystic Disorders,   J. Urol. 74: 693-706, 1955.

75. Tallarigo, A.:  Su un rar caso di associazione tra rene poloicistico
    e tumor ipernefroide,  Riv. Anat. Pat. E. Onc. 3: 510, 1950, cited
    in McFarland, et.al., J. Urol. 107: 530, 1972.

76. The Eleventh Report of the Human Renal Transplant Registry,  J.A.M.A.
    226: 1197-204, 1973.

77. The Ninth Report of the Human Transplant Registry,  J.A.M.A. 220:
    253-260, 1972.

78. The Tenth Report of the Human Renal Transplant Registry,  J.A.M.A.
    221: 1495-1501, 1972,

79. Tomoff, W.:  Hypernephroma dex. mit policystischer Degeneration,
    Ztschr. f. Urol. 31: 67, 1937, cited in McFarland, et.al. J. Urol.
    107: 530, 1972.

80. Vuorinen, P., et.al.:   Renal Cortical Index and Other Roentgenographic
    Measurements,   Acta Radiol. [Suppl] 211: 5-54, 1962.

81. Vander Vuurst de Vries, J.H.J.:  Un cas de tumeur dans un gros rein poly-
    kystique, J. d'urol. 46: 130, 1938, cited in McFarland J. Urol. 107:530, 1972.

82. Wahlqvist, L.:   Cystic Disorders of the Kidney:  A Review of Patho-
    genesis and Classification,   J. Urol. 97: 1-7, 1967,

83. Ward, J.N., Draper, J.W., and Lavengood, K.W., Jr.:   A Clinical
    Review of Polycystic Kidney Disease in 53 Patients,   J. Urol.
    98: 48-53, 1967.

d
he

t

YALE MEDICAL LIBRARY

Manuscript Theses

Unpublished theses submitted for the Master's and Doctor's degrees and
deposited in the Yale Medical Library are to be used only with due regard to the
rights of the authors. Bibliographical references may be noted, but passages
must not be copied without permission of the authors, and without proper credit
being given in subsequent written or published work.

This thesis by                                                        has been
used by the following persons, whose signatures attest their acceptance of the
above restrictions.

_____ Bonita Stanton _____

_____ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ ‎ _____

NAME AND ADDRESS                                          DATE