THE ASSESSMENT OF RENAL FUNCTION
FOLLOWING AORTIC SURGERY

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ABSTRACT

The Assessment Of Renal Function Following Aortic Surgery

Since the early days of infrarenal aortic reconstruction, renal failure has remained an important cause of post-operative morbidity and mortality. Biochemical testing of renal function following aortic surgery showed evidence of post-operative renal impairment in 47 to 60 per cent of patients. Biochemical testing of renal function is inaccurate.

This study was undertaken to examine the immediate post-operative effects of aortic surgery on renal function and also the long term effects six months after surgery using radionuclide tests; which show minor changes of renal function not detectable biochemically and test the function of individual kidneys.

Glomerular filtration rate (GFR) was measured using $^{51}$Cr labelled EDTA clearance.

Effective renal plasma flow (ERPF) was measured using $^{125}$I labelled Hippuran clearance.

The individual kidney function was assessed using a $^{99m}$Tc labelled DMSA renal scanning and $^{99m}$Tc labelled DTPA renography.

Two age matched groups of patients were used as controls,
1. Patients with arteriopathy who were treated conservatively.
2. Patients undergoing major colonic resection.

The control groups allowed comparison of those patients undergoing aortic surgery with a similar group of patients who suffered from the same disease but were treated without surgery. The second control group of patients undergoing major colonic surgery allowed comparison with those patients having aortic surgery.
The radionuclide tests of renal function were carried out pre-operatively, 10 to 14 days post-operatively and six months later on all aortic patients. The control patients had the tests done twice.

The results indicate that the changes in renal function are specific to aortic surgery. 40 per cent of patients when examined at six months showed a significant deterioration of their renal function. The effects of the operative parameters on the renal function are also discussed.
The work on which this dissertation is based is my own independent work except where acknowledged

Reda W. Awad

Reda Awad

JULY 1987
This thesis is dedicated to my parents Soad and William.
Do not stop to think about the reasons for what you are doing, about why you are questioning. Curiosity has its own reason for existence. One cannot help but be in awe when he contemplates the mysteries of eternity, of life, of the marvellous structure of reality. It is enough if one tries merely to comprehend a little of this mystery each day. Never lose a holy curiosity.

Albert Einstein

1879 – 1955
ACKNOWLEDGEMENTS

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<td>Percentage of function of the left kidney non operative patients</td>
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Aortic Aneurysm Repair Using Dacron Graft
Summary & Objectives Of This Study

"Nothing is so difficult but that it may be found out by seeking."

Terence
185 - 159 B.C.
Summary:

Since the early days of infrarenal aortic reconstruction, renal failure has remained an important cause of post-operative morbidity and mortality. Several mechanisms for this post-operative renal dysfunction have been suggested. Thurlbeck, in 1957, found evidence of embolisation of the renal vascular bed in these patients and suggested that it was the main pathological mechanism of damage. Biochemical studies of renal function have shown evidence of renal impairment post-operatively in 47 per cent to 60 per cent of patients who have undergone aortic surgery (Porter, et al 1968). However, these methods (blood urea estimation, serum creatinine and creatinine clearance) are inaccurate since they show only gross renal changes. Gabriel, in 1966 stated that when the serum creatinine concentration is only just above the normal range then the patient has functionally lost one kidney. Furthermore, tests involving creatinine estimation have poor reproducibility (Garr and Davison, 1975)

This study was undertaken to examine the effects of aortic surgery on renal function using radionuclide tests which are more accurate, reproducible, show minor changes of renal function not detectable biochemically and test the function of each kidney.

The aims of the study were:

1. To investigate the changes in total GFR and ERPF pre-operatively and post-operatively in patients undergoing elective infrarenal aortic surgery.
2. To monitor changes in individual kidney GFR pre-operatively and post-operatively in the same patients as mentioned above.
3. Follow up the changes in total GFR, ERPF, and individual kidney GFR in this group of patients six months after their discharge from the hospital.
4. To compare the changes in renal function in patients undergoing aortic surgery with two control groups:
   A. A group of patients suffering from degenerative arterial disease treated conservatively.
   B. A group of patients undergoing surgery of comparable magnitude.

Methods:
59 patients with infrarenal aortic disease were studied. Radionuclide assessment of renal function was carried out pre-operatively, 10 - 14 days post-operatively and six months later. These radionuclide tests were:
1. Glomerular filtration rate (GFR) measured by $^{51}$Cr labelled ethylenediaminetetraacetic acid (EDTA) clearance. A test of overall renal function.
2. Effective renal plasma flow (ERPF) measured by $^{131}$I-hippuran clearance. This reflects changes in renal blood flow.
3. Differential renal function was studied using $^{99m}$Tc labelled dimercaptoposuccinic acid (DMSA) renal scanning.
4. Clearance and renal perfusion were studied using $^{99m}$Tc labelled diethylenetriaminopentaacetate (DTPA) renography.

By combining the results of test one and test three individual kidney GFR was calculated.

It was important to monitor pre-renal perfusion to ensure that it was not the underlying cause altering the renal function in our patients. Measurement of cardiac output is invasive and may cause morbidity. Therefore radionuclide ventriculography was chosen as an index of pre-renal perfusion, and post-operative cardiac function. This test was performed at the same time as the renal tests. Left ventricular ejection fraction (LVEF) was calculated from the multigated blood pool study.
All operative details were recorded with particular attention to fluid and blood transfusion, blood loss, duration of aortic cross clamping and urine output.

Two age matched groups of patients were used as control:

1. 10 patients with arteriopathy who were treated conservatively.
2. 10 patients undergoing major colonic resection.

These two control groups underwent tests of renal and cardiac functions identical to those patients undergoing aortic surgery. The first control group allowed comparison of those patients undergoing aortic surgery with a similar group of patients who suffered from the same disease but were treated without surgery. The second control group of patients undergoing major colonic surgery allowed comparison with those patients having aortic surgery.

Results:

Patients undergoing elective infrarenal aortic surgery showed no change in their renal function in the immediate post-operative period. Six months later their renal function had deteriorated. Patients in each of the control groups showed no change in renal function. The change in each parameter is discussed separately in the results chapter.
CHAPTER ONE

Introduction & Basic Science
1.1 Introduction & Literature

Solitary, meditative observation is the first step in the poetry of research, in the formation of scientific phantasies, the reality of which we then test with the tools of logic, mathematics, physics and chemistry.

Theodor Billroth
1829 - 1894
Since DuBost, in 1951 performed the first successful repair of an infrarenal aortic aneurysm, renal failure remains a significant cause of post-operative morbidity and mortality. Cardiovascular surgery is now the most common cause of acute renal failure, (Gornick and Kjellstrand, 1983). Renal failure after vascular surgery has a mortality rate of up to 80 per cent (Gornick and Kjellstrand, 1983). Whether the surgery was emergency or elective had no influence on survival if acute renal failure developed.

The effect of aortic surgery on renal function has been the subject of many investigations. Thorbeck and Castlam, (1957) in a postmortem study demonstrated evidence of atheromatous emboli to the kidneys in 70 per cent of patients; 20 per cent of those patients died because of renal failure. Post-operative impairment of renal function has varied from 1 to 65 per cent in different clinical studies (Tab 1.1). Meekan and Engoll, (1986) showed an increase in the glomerular filtration rate in patients undergoing elective infrarenal aortic reconstruction.

The criteria used to diagnose renal failure vary considerably from one report to another, making interpretation and comparison difficult. For the results of post-operative investigations of renal function to be meaningful, knowledge of the pre-operative status is essential, but this has rarely been investigated. The majority of these reports included both ruptured and intact aneurysms.

Animal experiments have been designed and accurate techniques used to detect the effect of infrarenal aortic cross clamping on renal function and renal circulation. (Abbott, et al 1973). The technique of 'ss-Xenon wash out, and more recently, radionuclide labelled microspheres have been
<table>
<thead>
<tr>
<th>Year</th>
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<th>No. of patients in study</th>
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<th>% of patients with renal failure</th>
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<td>22</td>
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<td>183</td>
<td>47</td>
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<td>434</td>
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<td>May</td>
<td>187</td>
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(Tab. 1.1)
used to study the renal circulation during aortic cross clamping. The results of these animal studies are contradictory (Gagnon, et al 1961).

Powers, et al (1957) concluded from their dog experiments that clamping of the abdominal aorta of the dog for prolonged periods produces the clinical and pathological changes of distal tubular necrosis. The onset of changes in renal haemodynamics appeared after a variable period of aortic cross clamping. The same authors suggested that distal tubular necrosis followed renal ischaemia. In those animals that developed tubular damage, renal blood flow fell to an average of 32 per cent of the control values. Changes in blood flow are difficult to interpret, especially in experimental situations where the mean arterial pressure may vary over a wide range.

Gagnon, et al (1960) showed that cross clamping of the lower aorta immediately distal to the origin of the renal arteries for 1 to 3 hours produced transient changes in renal function in dogs anaesthetised with Pentobarbitone. The filtration rate and plasma flow were reduced by approximately one half upon occlusion of the aorta but these functions returned to control levels before the clamp was removed. All their animals were sacrificed from 2 to 52 days post aortic occlusion with no evidence of renal insufficiency. Histological examination showed no changes related to aortic occlusion.

Howells, et al (1960) found the opposite results to Powers, et al. They concluded that, in dogs, distal aortic occlusion does not contribute to any appreciable renal dysfunction.
Abbott, et al (1973) used the $^{133}$Xenon washout technique in a standard dog model to study renal perfusion. They concluded that deleterious changes in renal blood flow distribution were detected in association with aortic occlusion. The changes in renal blood flow were progressive with time and arrested with termination of the occlusion. These were manifested as renal cortical ischaemia in the presence of only slight variation in total renal blood flow. Although the changes were arrested at the end of the occlusion period, significant cortical ischaemia persisted for at least 60 minutes thereafter. This previously undetected renal cortical ischaemia associated with aortic occlusion may be important in the genesis of clinical renal failure after aortic reconstructive surgery.

Recently Caham, et al (1984) studied the effect of infrarenal cross clamping of the aorta on regional splanchnic and renal circulations in seven dogs. Regional blood flow was determined with differentially labelled microspheres (9 and 15 μm in diameter) injected simultaneously into the left atrium. Their data suggest a shift of blood flow to the juxtamedullary layer of the kidneys during aortic cross clamping.

Although these previous experimental and clinical studies in dogs have been done, the precise effects of elective aortic surgery on renal function in humans are not accurately known. This is because the investigations employed by many researchers do not represent an accurate and reproducible test of renal function. None of the previous studies in humans looked at individual kidney function. Most of the previous clinical research in this field was done using biochemical methods of assessing renal function e.g. blood urea level, serum creatinine level, creatinine clearance test and lysozyme concentration in the urine.
These investigations all measure total bilateral renal function. Normal renal function shows great individual variation, and serial measurements are needed to follow the progress of disease and treatment.

Kerr and Davison, (1975) comprehensively reviewed the subject of assessment of renal function. Glomerular filtration rate (GFR), measurement is seldom performed in clinical practice although precise knowledge of GFR is helpful in detecting early renal disease. It is also useful in following its course and the effects of treatment. Serum urea level is familiar to most clinicians but it is a much poorer guide to GFR than serum creatinine. Serum urea is affected by protein catabolism and urine flow; also its level does not rise unless GFR has been reduced by more than 50 per cent.

Endogenous creatinine clearance is the most popular test of GFR. However, methods of determining creatinine also measure non-creatinine chromogens and thus lead to over-estimation of creatinine particularly in blood (Healy, 1968 Rapoport and Hudson, 1968 Bierans de Haan, 1972). Creatinine clearance has poor reproducibility and high interlaboratory variation in surveys of laboratory accuracy, especially when the result is close to normal (Kerr and Davison, 1975). Conclusions should seldom be based on a single result and large changes in creatinine clearance should always be suspect if the plasma creatinine is not changing in the reverse direction (Kerr and Davison). Effective renal plasma flow (ERPF) can be measured as the clearance rate of para aminohippurate (PAH) on the assumption that PAH is cleared almost completely from the plasma in a single passage through the kidney. Recently I-125-Iodohippurate (I-125-Hippuran) is used instead of PAH, employing the single injection technique and determining the plasma disappearance curve.
Standardisation of GFR and ERPF results:

GFR and ERPF are both related to body size, and surface area and correlates most closely with them in the adult. They are therefore corrected to a standard surface area of 1.73 m² before comparison within the normal range (Holler, et al 1929). This correction is not necessary when the results are used serially to follow the progress of disease.
1.2 Anatomy Of The Kidneys
&
The Ureters

You will have to learn many tedious things,..... which you will forget
the moment you have passed your final examination, but in anatomy it is
better to have learned and lost than never to have learned at all.

Of Human Bondage

By

U. Somerset Maugham
Anatomy of the kidneys

The kidneys are a pair of bean shaped organs. Each kidney is approximately 11 cm. long, 5 cm. wide and about 3 cm. thick, and it weighs about 130 grams. It possesses upper and lower poles, anterior and posterior surfaces and medial and lateral borders.

Each kidney lies in the upper, deep part of the para-vertebral gutter, lying against the sloping lateral surface of the psoas major, has its long axis parallel to the lateral surface of that muscle, while its medial border faces forwards as well as medially and its anterior surface laterally as well as forward.

The two kidneys are not symmetrical in position; the left is about 1.5 cm. higher than the right and it is slightly more medial. The level of each kidney varies slightly both with the respiratory movements and with posture. During quiet respiration in the recumbent attitude, the transpyloric plane cuts the upper part of the hilum of the right kidney and the lower part of the hilum of the left one.

Each kidney has an intimate relationship to the corresponding suprarenal gland and is enclosed with it in a common investment of weak fascia, known as the renal fascia which is formed by the splitting of the transversalis fascia into anterior and posterior layers. The anterior layer of the renal fascia extends across the aorta and the inferior vena cava as a thin layer which loses its identity superiorly in the connective tissue around the coeliac trunk.

Posterior Relations of the Kidneys

The medial part of the kidney overlaps the lateral side of the psoas
muscle. Lateral to this, and forming the posterior relation of most of the kidney, lies the quadratus lumborum muscle and further laterally the psoas major and quadratus lumborum muscles, so that the superolateral third of the kidney lies in front of the diaphragm. Running downwards and laterally across the front of the quadratus lumborum muscle is the subcostal nerve accompanied by its vessels, and a little lower down the iliohypogastric and below it the ilioinguinal nerve both emerge from the lateral side of the psoas major.

**Anterior Relations of the Kidneys**

The anterior aspect and medial border of the upper extremity of each kidney is covered by the corresponding suprarenal gland. The other anterior relationships of the two kidneys are quite different. All organs in front of the kidney have a less intimate relationship to it, for they all lie anterior to the renal fascia, whereas the suprarenal gland is enclosed with the kidney inside this fascia.

**Right Kidney:** below the area covered by the suprarenal gland about two thirds of the anterior surface of the right kidney is in contact with the posterior surface of the right lobe of the liver. Below the hepatic area the region adjacent to the lower extremity is in contact with the right flexure of the colon, and the region adjoining the hilus is covered by the descending part of the duodenum.

**Left Kidney:** below and lateral to the area covered by the suprarenal gland there is a small triangular region related to the posterior surface of the stomach. Below this gastric area the body of the pancreas lies across the middle of the kidney, and laterally the gastric area is bounded by the line of attachment of the lienorenal ligament. The body of the
pancreas is separated from the kidney by the splenic vein while the splenic artery runs its tortuous course along the upper border of the pancreas. The area lateral to the line of attachment of the lienorenal ligament is related to the spleen. Below the pancreatic area, the lateral part is covered by the left flexure of the colon and the upper part of the descending colon, while the medial part is related to loops of jejunum.

Medial Relations of the Kidneys

Medial to each kidney are the corresponding psoas major muscle, and along the medial margin of the psoas lies the abdominal part of the sympathetic trunk. Anteromedially, each kidney is related to the corresponding suprarenal gland and renal vessels, gonadal vein, and upper end of the ureter. Further medially there is the inferior vena cava on the right side and the abdominal aorta on the left.

Sinus of the Kidney

The sinus is the hollow within the kidney and its long axis corresponds to that of the kidney itself. The floor of the sinus is not flat but presents a series of small cortical elevations called renal papillae, which vary from 6 to 15 in number. On the summit of each renal papilla there are many minute openings, which are the terminal apertures of the tubules of which the kidney is mainly composed, and through which urine escapes into the minor calyces which are cupped over the papillae. The cavity of the sinus is filled with fat, embedded in which lie the major and minor calyces, part of the pelvis of the kidney, branches of the renal artery and tributaries of the renal vein. The artery usually branches and the tributaries of the vein unite a short distance outside the hilus, and, within the sinus, the tributaries of the vein are most anterior, while
Further posteriorly are the calyces of the kidney, with branches of the artery both in front and behind.

The Kidney in Section

The kidney is composed to a large extent of a number of conical masses known as renal pyramids. The pyramids constitute collectively the medulla of the kidney. The pyramids are more numerous than the papillae, two or three usually ending in each papilla in the middle part of the kidney. The bases of the pyramids are separated from the surface by a layer called the cortex of the kidney. The cortex not only covers over the bases of the pyramids, but also sends in prolongations known as renal columns, between the pyramids towards the sinus.

There are five branches of the renal artery within the kidney (segmental arteries) which are visible between the pyramids; these divide into interlobar arteries and some of their main branches can be seen passing across the bases of the pyramids parallel to the surface of the kidney as the arcuate arteries which do not anastomose with one another.

Kidney Tubules

The glandular substance of the kidney is composed of a vast number of minute renal tubules. The wall of each tubule consists throughout of a basement membrane and of an epithelial lining, but the lumen of the tubule and the character of the epithelium vary much in their different parts. Every tubule begins in a thin-walled spherical dilatation known as a glomerular capsule, in which lies a complicated tuft of capillary blood vessels or glomerulus. The capsules with their enclosed capillaries are called renal corpuscles, and they are placed in the convoluted portion of the cortex. The part of the tubule that leads from the capsule to the
proximal convoluted tubule is very tortuous and lies within the convoluted part of the cortex.

The tubule enters the basal portion of the pyramid and diminishing in diameter it pursues a straight course towards the apex of the pyramid, forming the so called descending limb of Henle's loop. Within the apical portion of the pyramid the tubule suddenly bends upon itself, forming the loop of Henle and reversing its direction, passing back again through the base of the pyramid into a medullary ray of the cortex as the ascending limb of Henle's loop. The ascending limb enters the convoluted part of the cortex where it returns to the glomerulus of its own renal tubule and lies in between the afferent and efferent vessels of the glomerulus. The nuclei of the epithelial cells of the tubule are concentrated in one wall of the tubule at this point to form the macula densa. While still within the convoluted part, the tubule again becomes tortuous as the distal convoluted tubule; this tubule finally ends in a short junctioned tubule which passes back into a medullary ray and joins a collecting tubule. Each collecting tubule receives numerous tubules. Finally, several collecting tubules, uniting together, form a papillary duct which opens on the summit of a renal papilla into a minor calyx.

Each medullary ray with its surrounding glomeruli and proximal and distal convoluted tubules which empty into the collecting tubule forming the centre of the ray, constitutes a lobule of kidney tissue. It is demarcated on each side by the interlobular arteries, fine vessels which arise from the arcuate arteries and mostly pass centrifugally, although a few course centripetally to supply the juxtamедullary glomeruli.
Vessels and Nerves of the Kidney

The renal arteries, one on each side, arise directly from the aorta. The left is usually slightly higher than the right. Each artery lies behind the corresponding renal vein, and at or just outside the hilus of the kidney it divides typically into anterior and posterior divisions. The posterior division pass behind the pelvis of the kidney, while the anterior division passes in front of it and divides into two to five branches. Within the sinus each branch divides further. Having entered the substance of the kidney, the larger arteries lie in the intervals between the pyramids and are called interlobar arteries. These vessels divide and form a series of incomplete arterial arches, the arcuate arteries, which pass across the bases of the pyramids. No anastomoses between the branches of the interlobar arteries takes place, each artery which pierces the wall of the kidney sinus being an end artery. The arcuate arteries give off a number of vessels which pass through the convoluted part of the cortex towards the surface of the kidney. They are known as the interlobular arteries and they lie at very regular intervals. From them a number of short branches arise, termed vasa efferentia, each of which proceeds to a renal corpuscle. There the vas efferens breaks up into the capillaries of the glomerulus, which are contained within the invaginated glomerular capsule. Just before breaking up into the glomerular capillaries, the cells of the vas efferens change in character to form the juxtaglomerular cells. The small vessel vas efferens which issues from the glomerulus instead of running directly into a large vein, breaks up, after the manner of an artery, into capillaries which supply the convoluted tubules of the cortex and the longitudinal tubules of the medullary rays. At the bases of the pyramids there are some juxtamedullary glomeruli whose efferent vessels pass fine arterioles into the pyramids where they
break up into a capillary network around the tubules. These clusters of fine arterioles are known as the arterioleae rectae.

The juxta-medullary glomeruli are larger than those in the convoluted part of the cortex and their afferent and efferent vessels are of equal calibre; they are apparently non-functional.

Veins corresponding to the interlobular arteries and arterioleae rectae collect the blood from the capillaries around the tubules and unite to form a series of complete arcuate veins which anastomose freely around the bases of the pyramids.

From the venous arcades, vessels arise which traverse the intervals between the pyramids and reach the sinus of the kidney, where they unite to form the tributaries of the renal vein. Typically three main tributaries issue from the sinus and unite to form the renal vein which runs a direct course to end in the inferior vena cava. The renal veins are anterior to the arteries, and open into the inferior vena cava almost at right angles. The left is thrice the length of the right (7.5 cm. to 2.5 cm.), and crosses the posterior abdominal wall, behind the splenic vein and the body of the pancreas. Near its termination it passes in front of the aorta, just below the origin of the superior mesenteric artery. The left gonadal vein enters it from below, and the left suprarenal vein, enters it above a little nearer the median plane. The left renal vein opens into the inferior vena cava at slightly higher level than the right. Abnormalities of the left renal vein are of surgical importance particularly in aortic reconstruction, occasionally the left renal vein may be double, then one vein passes behind and one in front of the aorta to join the inferior vena cava; or the anterior vessel may be entirely absent. These variations in the left renal vein are due to embryological anomalies of the renal collar.
Variations in the renal vessels are common. Single arteries on right and left sides occur in about 70 per cent of individuals, but they vary somewhat on the two sides and in different individuals, in terms of their level of origin, their calibre, obliquity and precise topographic relationships. *Accessory renal arteries* are common; occurring in up to 30 per cent of individuals. Usually such arteries arise from the aorta, above or below the renal artery; and pursue a course parallel with it to the renal hilum. Higher or lower origins are, however, not uncommon, the accessory renal artery or leash of arteries passing to the superior or inferior pole of the kidney. Very occasionally accessory renal arteries may arise from the coeliac or superior mesenteric arteries, near the bifurcation of the aorta or from the common iliac artery.

The lymph vessels of the kidney end in the aortic lymph nodes. The nerves of the kidney are derived mainly from the coeliac plexus and accompany the branches of the renal artery, forming a renal plexus. The branches of this plexus form bundles of nerve fibres which travel along the branches of the renal artery into the kidney and also run between and supply the tubules.

Variations: A marked difference in the size of the two kidneys is sometimes observed, a small kidney on one side of the body being usually compensated for by a large kidney on the opposite side. Congenital absence of one or other kidney is recorded. A few cases are on record in which an extra kidney was found on one or other side. One or both kidneys may be at much lower level than usual, in the iliac fossa or even in the pelvic cavity.
Anatomy of the ureters

The ureters are the ducts that lead from the kidneys to the urinary bladder. Each ureter begins above in a thin walled funnel shaped expansion, called the pelvis of the kidney which is placed partly inside and partly outside the sinus of the kidney. Towards the lower end of the kidney the part of the pelvis which lies outside the sinus diminishes in calibre, and forms a tube, the ureter, which conveys the urine to the bladder.

The pelvis of the Kidney

Within the sinus of the kidney the pelvis lies among the larger renal vessels. Its volume is about 8ml. It is formed by the junction of three (more rarely two or four) thin walled tubes - the major calyces - each of which has a number of branches called minor calyces. Their wide funnel-like ends enclose the renal papillae and receive the urine. The minor calyces vary in number from five to twenty, but there are usually eight or nine in the adult kidney. The portion of the pelvis that lies outside the kidney has anterior to it in addition to the renal vessels, on the right side, the descending part of the duodenum, and on the left side a part of the body of the pancreas and the peritoneum of the posterior abdominal wall or sometimes the duodenojejunal flexure.

The ureter

The ureter proper is a pale coloured, thick-walled duct with a small lumen. When in situ it has a total length of about 25 cm., and lies throughout its whole course behind and closely adherent to the peritoneum. The upper half of the ureter lies in the abdominal cavity and the lower half in the lesser pelvis.
The abdominal portion of the ureter is directed downwards and slightly medially and lies on the psoas major muscle, crossing it obliquely from the lateral to the medial side. Anteriorly the abdominal portion of both ureters are crossed obliquely by the gonadal vessels while posteriorly, the genitofemoral nerve passes inferolaterally in almost the same line as the vessels. The right ureter has the descending part of the duodenum in front of its upper part and below this is crossed anteriorly by the right colic and ileocolic vessels and by the root of the mesentery shortly before the ureter enters the lesser pelvis. The left ureter is crossed anteriorly by the left colic vessels and by the root of the sigmoid mesocolon.

Crossing the common iliac or the external iliac artery, the ureter enters the lesser pelvis. Usually the left ureter crosses the common iliac artery and the right ureter the external iliac artery but the arrangement is by no means constant. The pelvic portion of the ureter is 12.5 cm. in length, it passes backwards and downwards on the side wall of the lesser pelvis. In the male at the level of the ischial spine, the ureter is crossed by the ductus deferens; it then bends forwards and medially to reach the lateral angle of the bladder, where it is anterior to the upper extremity of the seminal vesicle. The right and left ureters reach the bladder 5 cm. apart, and piercing the wall of the bladder very obliquely, are embedded within its muscular tissue for nearly 2 cm. Finally they open into the bladder by a pair of minute, slit-like apertures. In the female the ureter descends in a peritoneal fold which forms the posterior boundary of the ovarian fossa. Near its termination it is accompanied by the uterine artery. It passes below the root of the broad ligament of the uterus, where it lies 2 cm. lateral to the cervix uteri, above the lateral fornix of the vagina. Finally it inclines medially to reach the bladder.
Structure of the Ureter

The wall of the ureter, which is thick and of whitish colour, is composed of mucous, muscular and fibrous coats. The mucous coat is lined with a transitional epithelium composed of many layers of cells. When the canal is empty the mucous coat is thrown into numerous longitudinal folds. The muscular coat consists of plain muscle fibres collected into bundles which are separated by a considerable amount of fibrocolar tissue and are arranged some longitudinally, some circularly. The outer adventitial coat of fibrous tissue varies in thickness at different levels. The mucous coat of the calyces and of the pelvis of the kidney has an epithelium like that of the ureter.

Though gravity may play a significant part in the drainage of the upper urinary tract, it is accepted that urine does not simply flow from the kidneys to the bladder but is actively propelled by the muscular components of the pelvi-calyceal systems and ureters. In the renal pelvis and ureter there is no definite arrangement of the musculature into distinct layers of bundles of circular or longitudinal fibres. The bundles are arranged as spirals. The spirals unwind in either direction to form a complex pattern of muscle bundles in ill-defined layers.

Vessels and Nerves of the Ureter

The most constant arteries supplying the ureter are branches from the uterine artery in the floor of the lesser pelvis in the female. In the male, similar branches are derived from the inferior vesical artery. Branches from the renal arteries supply the upper end of the ureters. Usually intermediate arteries are derived either from the aorta, gonadal, common iliac or internal iliac arteries. In the abdomen the arteries
Blood Supply Of The Ureter

Reproduced from Grant's Atlas Of Anatomy
supplying the ureter approach it from the medial side; in the pelvis they approach it from the lateral side. In both abdomen and pelvis the supplying arteries are intimately connected with the peritoneum. The nerves of the ureter are derived from the renal testicular or ovarian and hypogastric plexuses.
CHAPTER ONE

1.3 Anatomy Of The Arterial System
Anatomy of the arterial system

The systemic arteries all stem from the aorta, and by branching and rebranching form what is sometimes spoken of as the arterial tree. The cross sectional area of the arterial tree increases steadily towards the periphery, and the combined sectional area of all of the arterioles greatly exceeds that of the aorta, a fact of profound haemodynamic importance. The manner in which arteries divide varies. The usual arrangement is illustrated by the arteries of the limbs, which give off successive branches yet retain their individuality as main vessels. Some arteries – the aorta is the most notable – end by dividing into two more or less equal branches, in some cases several arteries arise together from a short parent branch, e.g. the coeliac trunk.

Anastomoses

The great majority of arteries communicate with others through branches that unite to form anastomoses. In some regions anastomoses occurs directly between arteries of considerable size, so that there is, potentially, an even distribution of blood to the parts supplied. At the base of the brain the circulus arteriosus is a remarkable example of such an anastomosis. But the most widespread anastomosis takes place between the smaller arteries, and as a rule those between arterioles form extensive networks from which the capillaries arise. Around the limb joints the anastomoses between the medium sized arteries are of clinical importance as the means by which the blood supply is maintained distally by the opening up of a collateral circulation should the main artery be blocked by disease.

End arteries

Small arteries which do not anastomose with others and therefore
(apart from capillary communications) constitute the sole source of blood to these areas they supply are called end arteries; they are of pathological importance since occlusion of such an artery causes death of the tissues it supplies. End arteries are found in the kidney and spleen.

The Aorta

The aorta is the main arterial trunk of the systemic circulation, and for descriptive purposes it is divided into the ascending aorta, the arch of the aorta, and the descending aorta, the last being further divided into thoracic and abdominal parts. Only the abdominal aorta is relevant to this work and will be discussed here.

The Abdominal Aorta

It starts as a continuation of the thoracic aorta at the aortic opening in the diaphragm, opposite the middle of the lower border of the twelfth thoracic vertebra. This vessel extends to the body of the fourth lumbar vertebra where, to the left of the median plane, it bifurcates into the two common iliac arteries.

Relations

Posteriorly it lies on the anterior longitudinal ligament covering the twelfth thoracic to the fourth lumbar vertebrae. Anterior to it lies the aortic plexus of nerves and from above downwards, the coeliac plexus, the omental bursa, the body of the pancreas and the splenic vein, the left renal vein, the horizontal part of the duodenum, the root of the mesentery, the posterior parietal peritoneum and coils of small intestine. It lies at first between the crura of the diaphragm. The thoracic duct and cysterna chyli, and the vena azygos lie between it and the right crus which
Relations Of The Aorta & The Kidneys

Reproduced From Grant's Atlas Of Anatomy
separates it from the inferior vena cava. Below it is in direct contact with the inferior vena cava.

Branches of the Abdominal Aorta
They are classified as follows:

A. Visceral
   1. Paired
      Middle Suprarenal
      Renal
      Testicular or Ovarian
   2. Single
      Coeliac
      Superior Mesenteric
      Inferior Mesenteric

B. Parietal
   1. Paired
      Inferior Phrenic
      Lumbar
      Common Iliac
   2. Single
      Median Sacral

The renal arteries
The renal arteries arise about 1.5 cm. below the origin of the superior mesenteric artery and opposite the first lumbar vertebra. Each artery runs to the hilus of the corresponding kidney, passing anterior to the crus of the diaphragm and the psoas muscle. The left artery lies posterior to the pancreas, the right vessels pass behind the inferior vena


cava, the head of the pancreas, and the descending part of the duodenum. The renal vein lies anterior to the artery.

Approaching the hilus of the kidney, each artery divides into three or four branches of which one passes behind the pelvis of the kidney and the rest in front of it. Each renal artery gives off small ureteric branches to the upper part of the ureter, and one or more inferior suprarenal arteries, which pass upwards to the lower part of the suprarenal gland.

Variations

Accessory renal arteries, more common on the left side, may be derived from the aorta, or from the common iliac or internal iliac arteries. They usually enter towards one pole of the kidney, and are end arteries to a portion of the kidney substance.
1.4 Renal Physiology

As every disease we labour under in a disorder of the vital, animal, or natural functions, a thorough acquaintance with these in their sound state is implied before we can pretend to understand their morbid affections, or how to remedy them.

John Morgan
1735 - 1789
The nephron, the functioning unit of a kidney, is a cell lined single tube, the proximal end of which is expanded and inverted to form Bowman's capsule containing a tuft of capillary blood vessels, the whole constituting the glomerulus. The distal end of the tube, together with others, connects to a collecting tube which opens at the apex of a renal pyramid into a minor calyx.

The Glomerulus

This is the site of plasma filtration. Blood from a terminal branch of a renal artery perfuses the glomerular capillary tuft and is filtered out first through the thin wall of the capillary and then through the adjacent Bowman's capsule, so that a cell-free, glomerular, ultra-filtrate passes into the lumen and then to the succeeding first convoluted part of the renal tubule.

The hydrostatic pressure (the blood pressure in the pre-capillary arteriole) provides the filtering force, approximately 75 mm Hg and this is partially opposed by the oncotic pressure (25 mm Hg) produced by the concentration of the plasma proteins in the capillary together with an unknown, but probably low, hydrostatic pressure in the recipient tube.

The Tubule

It is the tubule that modifies the glomerular ultra-filtrate. Driven on by the net filtration pressure, the glomerular filtrate traverses in succession the proximal convoluted part of the tube, the thin descending loop of Henle, the thicker ascending loop of Henle and the distal convoluted part of the tube before reaching the collecting tubule eventually to emerge into a minor calyx as urine.
The Nephron

Reproduced From Jamieson & Kay's Textbook Of Surgical Physiology
Active and passive transfer of many constituents of the glomerular filtrate take place through the cells lining the various parts of the tubule. Some are absorbed partially (water, sodium) or completely (glucose) from the lumen of the tubule into the post-glomerular peritubular capillary venous network which closely surrounds it, while others (potassium, hydrogen ions, ammonia) are excreted from the tubule cells and added to the luminal content.

It has been shown that 80 per cent of the water in the glomerular filtrate is reabsorbed in the proximal part of the tubule, that the main site of sodium and potassium reabsorption is in the proximal tubule, that glucose, phosphate, and amino acids are normally reabsorbed in the proximal tubule and that the synthesis of ammonia, the acidification of the urine, and the secretion of potassium take place in the distal tubule.

Blood Supply

Approximately 25 per cent of the cardiac output perfuses the kidneys; this means that in an adult about 600 ml/min of blood normally flows through a single kidney via the branches of the renal artery. Apart from a small proportion of the volume which supplies the calyces, renal pelvis and the ureter, the major part passes through the glomeruli where it is filtered. The renal blood flow fluctuates widely and decreases follow falls in cardiac output, systemic hypotension, exercise, and even fear. But broadly speaking, the blood flow through the glomerular capillary tuft is not as important as its hydrostatic pressure. Changes in vasomotor tone in the pre and post glomerular arterioles can profoundly affect both the blood flow and the filtering pressure in the glomerular capillaries.
It is difficult nowadays to postulate that changes in vasomotor tone of the renal blood vessels are mediated through the renal nerves because there seems to be little variation from normal in regard to renal blood flow, glomerular filtration and urine production in the transplanted kidney, which is denervated. Myogenic adjustments of arteriolar tone may be initiated by circulating substances and there is evidence to suggest that glomerular filtration is influenced by a feedback mechanism from the convoluted part of the renal tubule.

The interlobular arteries of a kidney are functionally end arteries. There is no collateral circulation and infarction follows arterial occlusion. The return from the peritubular venous plexus to the renal vein or veins, however, is different in as much as a collateral circulation can develop even when a major vein is occluded.

Factors Influencing Renal Function

1. Blood Volume and Atrial Pressure

When a large volume of isotonic saline is rapidly administered intravenously the venous volume expands, the right atrial pressure increases and there is inhibition of the renal reabsorptive mechanisms so that approximately half the infused volume is excreted as urine within a few hours. A comparable diuresis can be induced in laboratory animals by increasing the right auricular pressure with a balloon. This diuresis is not inhibited by ADH.

2. Pituitary, Anti diuretic Hormone (ADH)

Following the ingestion of large volumes of water normal kidneys excrete comparable volumes of low specific gravity, and low osmolality urine. The converse is true when there has been severe water restriction.
These changes are effected virtually entirely by reabsorptive processes in the renal tubules mediated by pituitary activity.

Anti-diuretic hormone (ADH) from the posterior lobe of the pituitary is secreted in response to physical changes in osmo-receptor cells in the supra-optic nuclei which are directly affected by changes in the solute concentration of the extracellular fluid. In this way the kidneys are normally able to maintain the osmotic pressure of the body fluids within a narrow range and this they because ADH increases the water permeability of the cells lining the distal tubules and the collecting ducts. The relative oliguria following major operations is, in part at least, a manifestation of pituitary activity.

3. Adrenals

Sodium excretion by the kidneys is normally determined by the rate of glomerular filtration and the degree of tubular reabsorption. A normal subject with an average sodium intake exerts only 0.5 to 1.0 per cent of the amount of sodium filtered by the glomeruli. If filtration increases, reabsorption is also reduced.

The adreno-cortical steroids profoundly influence renal excretion of sodium and aldosterone is the most important steroid concerned in its reabsorption. Excessive aldosterone secretion giving rise to significantly low urinary sodium outputs, occurs when there has been sodium depletion. It also occurs when the venous return to the heart is reduced. Reduction of the urinary sodium/potassium ratio, occurring within a few hours of accidental or surgical trauma, is an aldosterone induced modification of renal function.
4. Ovaries

It is known that the administration to normal women of small doses of oestradiol causes sodium retention within a few days and that progesterone inhibits the sodium retaining effect of aldosterone.

5. Parathyroids

Approximately two-thirds of the phosphate ingested is excreted by the kidneys. A further fraction is excreted from the bowel. The renal excretion is normally determined by the plasma concentration of phosphate and the glomerular blood flow on the one hand, and by phosphate reabsorption on the other. Circulating parathyroid hormone inhibits phosphate reabsorption and thus increases the rate of its excretion in the urine.

6. Blood pH Changes

The kidney is very sensitive to pH changes in the blood and extracellular fluid. One of its most important functions is the elimination of excess hydrogen ions, derived from exogenous and endogenous protein metabolism. The entire nephron, including the collecting tube, is involved in this transfer of hydrogen ions. Ammonia (NH₃) is synthesized by the tubules from amino acids and is converted to ammonium (NH₄⁺) which is excreted in the urine; dibasic phosphate (Na₂HPO₄) is converted to monobasic phosphate (NaH₂PO₄) and when the pH is less than 5 there is also a similar loss of H⁺ ions by conversion of organic acids. In addition, when bicarbonate is reabsorbed, sodium is retained with it and H⁺ ions are, in exchange, secreted by the tubules.

In summary, the kidney rapidly corrects any tendency towards metabolic acidosis or alkalosis by excreting the appropriate anions or
cations. In the absence of urinary infection affecting its acidity, the pH of the urine accurately reflects systemic variation from normal.

7. Obstruction

In unilateral obstruction the healthy contralateral kidney maintains normal body chemistry. On the affected side the obstruction causes increased intratubular pressure but this does not stop glomerular filtration. Renal function continues even when there is complete obstruction although the "urine" that is produced is returned to the circulation.

The relief of partial or total obstruction with a high blood urea, even when of moderately long standing, is followed by a return to normal function if renal parenchyma has not been lost and if the urine is free from infection. When there has been loss of renal parenchyma, renal function is re-established but does not return to normal.

8. Infection

Uncomplicated acute bacterial pyelonephritis seldom gives rise to any significant changes in renal function. Such is not the case when pyelonephritis complicates obstruction for then foci of suppuration develop within and between the tubules, if both kidneys are involved; uraemia rapidly follows. The glomeruli are seldom involved by the suppurative process whereas the renal medulla and the papillae seem to be particularly vulnerable.

9. Glomerular Disease

The designation "glomerular disease" covers a broad spectrum of pathological changes. These may be minimal, perhaps only visible by
electron microscopy, or they may be gross with obliteration of the space between the glomerular tuft and Bowman's capsule; cellular infiltration; oedema and hypertrophy of the glomerular capillary endothelial cells or even hyalinization and sclerosis. A close degree of correlation exists between the severity of the morphological changes and glomerular function. In contrast to glomerular filtration the renal blood flow is often not reduced except in the most severe cases.
1.5 Pathology Of Artarial Disease

Cause of death in the old:

Veins which by thickening of their tunicles in the old restrict the passage of the blood, and by this lack of nourishment destroy their life without any fever, the old coming to fail little by little in a slow death.

Leonardo da Vinci

1452 - 1519
Normal Structure

The innermost layer of the arterial wall adjacent to the flowing blood is the endothelium, composed of a continuous sheath of flattened cells. The integrity of this cell layer is of paramount importance, for damage to it is likely to initiate thrombus formation at the site. The endothelium is separated by a scanty zone of loose mesh connective tissue from the internal elastic lamina. The internal elastic lamina, endothelium, and intervening tissue constitute the intima or internal coat. The media, or middle coat, lies between the internal and external elastic laminae and, in all but the largest vessels, consists mainly of smooth muscle fibres running transversely round the artery. In large arteries, elastic fibres are mingled with the muscle, and in the largest arteries they predominate. The external elastic lamina, on the outside of the media, is less well defined than the internal lamina and is sometimes absent, notably in the cerebral arteries.

The adventitia, or outer coat, consists of loose mesh fibrous tissue and merges with adjacent structures; it is rich in lymphatics and autonomic nerve fibres.

Age changes in arteries

The arterial structure outlined above is that normal in early life; on examining the arteries of middle aged and elderly people certain structural changes are regularly encountered.

Intimal changes

At birth the endothelium lies almost directly upon the internal elastic lamina, but even in childhood these layers come to be separated by
loose mesh connective tissue, which tends to increase in amount and density with the passage of the years (Levene, 1956; Movat, et al 1958). The coronary arteries and the arteries of the lower limbs are the most affected in this way and, in these vessels, the intima, by the age of 60, may equal or even exceed the media in thickness, without any definite pathological state existing.

**Medial changes**

The media of the muscular arteries reach its full development in early adult life. From middle age onward there is a progressive increase in collagen fibres at the expense of muscle cells; there is also a rise in the calcium content accompanying these changes. In medium sized arteries (such as the arteries of the limbs) these changes may lead to dilatation and elongation, so that the artery pursues a tortuous course. In small arteries and arterioles some degree of narrowing may result from this intimal thickening.

**Sclerotic Changes in Arteries**

**Nomenclature**

The nomenclature of this group of diseases is the cause of much confusion, which is heightened by different usages in different countries. The word arteriosclerosis was introduced as long ago as 1833 by Lohstein. He employed it in a generic sense to indicate conditions with thickening and hardening of the vessel walls. It is perhaps, best to use the unqualified word only in a clinical sense for conditions of thickening and hardening of the arteries when the precise pathological state can only be guessed at. Examples from the clinical group may then finally be classified as one of the following:

a. Senile (or presenile) arteriosclerosis.
b. Hypertensive arteriosclerosis.
c. Monckeberg's sclerosis (calcification of the media).
d. Atherosclerosis.

Only atherosclerosis is relevant to this thesis and will be the only one discussed.

Atherosclerosis

Atherosclerosis is at once the most important, the commonest, the most controversial, and the most paradoxical of arterial diseases. It is so universal that a case could be argued for regarding it as a normal concomitant of ageing, and yet it is the main pathogenic factor in two of the commonest fatal diseases of the middle aged and elderly, ischaemic heart disease and cerebro-vascular disease.

So little is known of the true nature of atherosclerosis that, for definition, we are forced back on a brief description. We may then say that atherosclerosis is a disease of the arterial intima, some degree of which is almost universal in the middle aged and elderly; it is characterised by patchy accumulations of lipids, together with irregular fibrous thickening over and around the fatty patches, and by the frequent occurrence of calcification in the affected areas.

Adams, (1964) has pointed out the fact that the process appears to be at one and the same time both proliferative and degenerative in nature, the key events in genesis of the plaque being:

- Accumulation of intra and extracellular lipids, most of which seem to be derived from the plasma.
- Proliferation of smooth muscle cells within the arterial intima.
The disease affects in a totally irregular manner, large and medium sized arteries, and it falls away in the small arteries to disappear well above the pre-arteriolar segments.

For convenience of description, three stages in the development of the lesions can be considered — fatty streaking, atheroma formation, and fully developed atherosclerosis — but it is important to realise that these stages regularly coexist in the same individual and indeed in adjacent segments of the same artery.

Fatty streaking of the intima

The earliest stage in this sequence of events may be seen even in young children and infants. The lesions are best seen in the aorta, but may also appear in the carotid arteries and other branches of the aorta, including the coronaries. They appear as faintly yellow streaks, about a millimetre wide, running along the lining for some distance. In the aorta they often extend from the region of the arch down to the bifurcation, favouring the posterior wall and tending to divide and surround the orifices of branches. Microscopical examination shows the streak to be composed of a collection of large mononuclear cells stuffed with fat and lying immediately beneath the endothelium.

The possible influence of haemodynamic factors on the topography of these lesions is suggested by the fact that fatty streaks in the ascending aorta, just above the aortic valve ring tend to lie at right angles to the direction of the blood flow rather than along its axis as is seen more distally.
However, differences of opinion exist as to whether or not the fatty streaks progress to more advanced lesions. These lesions are not amenable to observation during life and views on their natural history, regression or development must be of a speculative nature.

The Atheromatous Plaque

Seen in the postmortem room the uncomplicated plaque appears as a smooth, yellow or white button-like lesion, circular in outline, 3 to 15 mm in diameter and slightly raised above the surrounding surface. Microscopical examination of atheroma shows a sizable collection of fat lying in and thickening the intima. The fat is partly intracellular, but in the central parts of the collection the cells have often disintegrated to liberate a structureless fatty mass. It is the material which may accumulate in quite large amounts in large aortic plaques that gives the condition its old name of atheroma, derived from the Greek word for a porridge substance.

How and why this sterol accumulates in the arterial intima is clearly a matter of first importance. Turnover studies of labelled cholesterol suggest that the bulk of cholesterol in the human aorta is derived from plasma (Field, et al 1960).

The association between atherosclerotic lesions and the presence in those lesions of relatively large amounts of plasma derived lipids and other plasma constituents suggests that the process must be accompanied either by a focal increase in the permeability of the endothelial barrier or a decline in the efficiency of the mechanisms which clear the plasma derived molecules from the arterial wall.
The Fully Developed Lesion

The condition may never advance beyond the stages mentioned above but all too often the development of fatty accumulations in the intima is accompanied by widespread proliferation of fibrous tissue around and in between the plaques. In this way the entire intima becomes grossly but irregularly thickened, along large stretches of the vessel. It is no longer possible for this thick layer to be nourished throughout by diffusion from the lumen, and blood vessels extend into it through the media from the vasa vasorum. The intima, normally avascular, may thus become a highly vascular structure (Winteritz, et al 1938). The progressive thickening of the intima is likely, especially in smaller arteries.

Certain further developments are liable to ensue in severely affected vessels, namely calcification, ulceration, mural thrombosis and occlusive thrombosis. Calcification as a generalisation can be said to occur mainly in older people and in the most advanced lesions. The distal part of the aorta is especially prone to calcification and may come to be lined by a rigid intima which fractures like an egg shell when the vessel is incised. Microscopical examination shows the calcification to be sited mainly in the deepest part of the intima and at the sides of the fat collections. Ulceration of the plaques is also best observed in the distal part of the aorta though it may occur in smaller vessels too. It appears to result from softening in the hyaline fibrous tissue that separates the fatty debris from the lumen. When this layer gives way, the porridgy material may escape into the blood. The atheromatous ulcer is quite shallow, with ragged edges and recognizable lipid debris in its base. It usually absorbs pigments from the blood and becomes much darker than the surrounding intima. Not unexpectedly mural thrombosis over the ulcerated area is of common occurrence.
Postmortem Specimen Of The Infrarenal Aorta Showing

The Pathology Of Atherosclerosis
Mural thrombus consists mainly of fibrin, with a varying admixture of blood cells; it soon becomes covered with endothelium and a slow process of organisation converts it into a dense layer of hyaline fibrous tissue, thus leading to further thickening of the intima. The formation of small fibrin thrombi over and round atheromatous plaques, and their subsequent incorporation into the intima, are common occurrences, not limited to grossly ulcerated areas. The mechanism of their formation is not fully understood.

**Effect on Arterial Calibre**

The effect of atherosclerosis on the calibre of the affected artery is extraordinarily variable and unpredictable, and we are faced with a paradox that this single disease process may leave the affected vessel occluded, stenosed, unchanged or dilated, even to the extent of aneurysm formation. The explanation seems to lie in the varying severity of the secondary degenerative changes that affect the media. Blood pressure too must play its part, dilatation being more liable to occur in the largest vessels and in hypertensive subjects. The main site at which dilatation is encountered is the aorta. A severely atherosclerotic aorta may be dilated throughout its length, but the most characteristic lesion is a fusiform aneurysm of its distal part.

**Special Features in Particular Sites**

In the aorta the lesions have a characteristic distribution. There may be a few plaques in the arch, but the lesions always increase in concentration and severity along the course of the aorta from the arch to the bifurcation. In severe examples they are commonly confluent below the level of the renal arteries and it is in this region that complications such as calcification, ulceration, mural thrombosis and aneurysm formation...
are likeliest to ensue. There is a strong tendency for plaques to form round or adjacent to the orifices of branches. On occasion the plaques may impair the entry of blood into the branches and lead to ischaemic changes in the areas supplied.

Mural thrombosis in the aorta is occasionally sufficient to impede significantly the flow of the blood, and sometimes complete occlusion occurs near the bifurcation. The femoral, popliteal, and tibial arteries are also commonly affected by severe atherosclerosis with thrombosis.

**Aetiology and Pathogenesis**

Discussion of these important aspects is hindered by confusion between atherosclerosis itself and the main clinical syndromes associated with it, notably myocardial ischaemia. Nearly all the statistical studies contributed to the subject are based on myocardial ischaemia as the criterion of atherosclerosis, but the assumption that that syndrome is not influenced by aetiological factors distinct from those concerned with atherosclerosis in general is by no means justifiable. Bearing this in mind, it is possible to state a few generalisations about the prevalence of atherosclerosis. The relationship with age is clear; fully developed lesions are uncommon before the fourth decade. There is a more important link with sex, for in women the development of the lesions lags one or two decades behind or, to express it another way, women rarely show significant lesions until after the menopause. The roles of race and heredity are difficult to disentangle from those of diet and environment; there appears to be much less atherosclerosis in African and Asian countries than in Western Europe and North America, which have the highest rates (Keys 1956) but when the inhabitants of the former areas established
themselves in the latter they gradually acquire the higher rates of their new environment (Larsen 1957).

Diet and Fat Metabolism

It was in 1847 that Vogel, demonstrated the presence of cholesterol in atheromatous plaques, much attention has been focused on the problem of how it gets there. Antscho, in 1913 described the production of atheroma-like lesions in rabbits kept on a diet to which cholesterol had been added. In more recent years, atheroma-like lesions have been produced in other animals, including dogs (Steiner and Kendall, 1946) and chickens (Dauber and Katz, 1942) by procedures designed to maintain a high blood cholesterol over prolonged periods (Katz and Stamler, 1953). In considering the relation between these experimental lesions and human disease it is essential to answer two questions: 1. Are people whose blood cholesterol is raised as a result of other diseases especially prone to atherosclerosis? and 2. Do people with severe atherosclerosis have raised cholesterol level?

The conditions most characteristically associated with hypercholesterolaemia are diabetes, hypothyroidism, the nephrotic syndrome and certain types of familial xanthomatosis. Of the frequency and severity of atherosclerosis in diabetics there can be no doubt (Warren 1938) and the same seems now to be well established in the case of other conditions mentioned. The converse question, that of the occurrence of hypercholesterolaemia in patients with atherosclerosis, is more difficult to answer, their serum cholesterol usually falling within so-called "normal" limits, but as a group they tend to show slightly but significantly raised levels on comparison with presumptively normal people of the same age (Oliver and Boyd, 1953).
The Thrombogenic Theory

Duguid, (1946) studying serial sections of coronary arteries in which thrombi had formed, found transitions from thrombus to atheromatous plaque. He expressed his conclusions in these words "Many of the lesions we classify as atherosclerosis are arterial thrombi which, by the ordinary process of organisation, have been transformed into fibrous thickenings and he added that many of the, atheromatous, fatty patches resulted from softening occurring in the thrombi". Duguid's observations have now been confirmed by many observers (Morgan 1956) and the way in which fibrinous encrustations become incorporated as intimal thickening has been studied (Crawford and Levene, 1952). It seems clear now that the incorporation of fibrinous encrustations is an important element in the build-up of the fully developed atheromatous lesion (Woolf and Carstairs, 1967) although the earlier stages cannot be explained in this way.

Disturbances of Blood Coagulation. Even qualified acceptance of the thrombogenic theory outlined above leads one to seek a cause for the fibrinous encrustations of the intima. Such a cause might lie in increased sensitivity of the blood coagulation mechanism on the one hand or in diminished fibrinolytic power of the blood on the other. Study of the former aspect has again shown an interesting link with the fat content of the diet, for fatty meals cause significant shortening of clotting time (Fullerton and Anastasopoulos, 1949 - Fullerton, et al 1953).

Smooth muscle cell proliferation and the plaque

Without proliferation of the modified smooth muscle cell within the arterial intima it is unlikely that atherosclerotic plaque would develop at all. Not only do these cells form a significant proportion of the cell population of the plaque during the part of its natural history when
degenerative phenomena do not predominate. Studies of these cells using
in vitro culture systems have showed that they are capable of synthesising
the extracellular connective tissue matrix, which is such an important part
of plaque matrix.

Benditt and Benditt, (1973) suggested that smooth muscle cell
proliferation within fibrous plaques is monoclonal in type and that the
process is more clearly allied to what occurs in neoplasia than in the
repair phase of injury.

Hypertension and Physical Factors

Elevation of the blood pressure is not necessary for the development
of atherosclerosis, but there is no doubt that in the presence of
hypertension the lesions tend to develop earlier and to become more
severe. These general impressions were confirmed and placed on a
statistically firm basis as a result of a world-wide geographical and
racial survey (McGill 1968). In this connection it was concluded that
hypertension and diabetes, though not primary causes of atherosclerosis
accelerated the natural progression of the lesions in all populations
regardless of sex, age, race, and geographical locations (Robertson and
Strong, 1968). The participation of blood pressure in the pathogenesis of
atherosclerosis is further indicated by the limitation of lesions to those
parts of the arterial tree subjected to the higher arterial pressure, and
by the occurrence of lesions in the pulmonary arteries only in the
presence of pulmonary hypertension. This pressure factor seems to act by
inhibiting the organisation of fibrin deposits (Crawford and Lavene, 1952)
or by exaggerating developmental weaknesses in the elastic lamina (Lavene
1956) and thereby localising the disease process.
The Role of Endocrine Factors

The difference in sex incidence of atherosclerosis noted above suggests a protective action of oestrogens.

The role of smoking

The relation between smoking and coronary heart disease is well established (Smoking or Health, 1977). There is an even closer association between cigarette smoking and atherosclerotic disease of the aorta and arteries of the leg than there is between smoking and coronary heart disease. 97 per cent of patients with arterial disease of the legs are reported to be smokers (Greenhalgh, 1984). Moreover those who continue smoking are liable to late occlusion of by-pass grafts inserted for treatment of their occlusive arterial disease. Doll and Peto, (1976) showed that death rates from aortic aneurysms was more than six times higher in cigarette smokers and ten times higher in those smoking 25 or more cigarettes daily.

Frost, (1973) studied the effects of smoking on the aorta by exposing rabbits to cigarette smoke. This resulted in focal loss of endothelial cells with adherence of platelets to the underlying endothelial tissue. Asmussen and Hjeldsen, (1975) have also described abnormalities in the umbilical arteries of newborn infants born of mothers who smoked cigarettes.

Aneurysms

An aneurysm of an artery is a swelling formed by localised dilatation of the lumen. The wall of a true aneurysm is therefore formed by the stretched remnants of the arterial wall. The general shape of an aneurysm will depend on whether the stretching process affects the whole
circumference of the artery or only a small part. In the former case, a fusiform aneurysm results, in the latter case the result is a saccular aneurysm. Once aneurysmal dilatation has commenced it is likely to continue at a progressively increasing rate, for the strain on the wall of the vessel increases as the diameter increases. The tendency is therefore for an aneurysm to go on enlarging until rupture occurs. There is, however, the possibility of this progression being checked by the occurrence of thrombosis within the aneurysmal sac. There is the further possibility of thrombus formed in the aneurysm becoming detached and giving rise to embolism.

Atherosclerotic aneurysms are regarded today as the commonest variety. This is a disease of the elderly, being seldom seen under the age of 60 years. The abdominal aorta is the typical site but atherosclerotic aneurysms are common also in the iliac, femoral and popliteal arteries. Thrombus formation is particularly abundant in these aneurysms.

The hazards of these aneurysms are, thrombus may be detached and give rise to embolic closure of an artery or an important branch. There may be pressure effects on adjacent visceras, vessels, nerves or bones or the aneurysm may rupture, usually into the retroperitoneal tissues or into the peritoneal cavity.
CHAPTER ONE

1.6 Pathophysiology Of Renal Dysfunction

In Patients With Arterial Disease
Thurlbeck and Castleman, in 1957 attempted to assess the incidence and significance of embolisation by atheromatous material to the kidneys. They examined microscopically the kidneys of 22 patients who died in hospital after aortic surgery. The operation was performed for ruptured aneurysm in 11 patients; for elective aneurysm repair in 6 and for atherosclerotic occlusive disease of the abdominal aorta in 5. Also they examined kidneys from other autopsies used as a control group. The control group included 42 patients with aortic aneurysms not previously operated upon, 38 patients with severe atherosclerosis of the abdominal aorta with mural thrombosis and occlusion, and 44 patients over the age of fifty years with minimal aortic atherosclerosis and no intimal ulceration.

Findings in the post-operative group

Seventeen of the 22 patients who died post-operatively had acute emboli in their kidneys. In addition; 6 patients had old organised emboli in the arcuate and interlobular arteries. When embolisation was sever this was associated with multiple renal cortical infarcts. One of these cases with severe embolisation had other emboli to the spleen, pancreas, and the spinal cord.

The acute emboli seen in the post-operative group were of three types; which occurred alone or in combination with each other. Jagged fragments of almost acellular hyaline material containing cholesterol crystals were the most common. In the small arteries; there were occasional single cholesterol crystals, or several cholesterol crystals with a little adherent hyaline material. A second type consisted of jagged fragments of hyaline material only; with no cholesterol crystals. A third type of emboli consisted of an aggregate of lipid filled histiocytes.
These emboli were morphologically identical with fragments of an atheromatous plaque. Emboli were never seen in the glomeruli, and superimposed thrombosis was not a prominent feature. By step and serial sections; it was possible to show that the renal infarcts were related to the emboli. Furthermore, the infarcts could be dated to coincide with the interval between the operation and death.

Findings in control non-operative groups

42 cases of aneurysms of the abdominal aorta, 13 of which had ruptured; were examined. Emboli were found in 13 patients, 5 in cases with ruptured aneurysms, and 8 in cases without rupture. They were located in interlobular and arcuate arteries, were characteristically old, completely obliterating the interlobular arteries, and were related to small subcapsular scars.

38 patients with severe atherosclerosis occlusive disease of the aorta were studied. 6 had emboli to the renal vascular bed. All these emboli were occasional, small and old, and none were considered clinically significant.

44 cases with minimal atherosclerosis were also examined, there were no emboli to the renal vascular bed in them.

<table>
<thead>
<tr>
<th></th>
<th>No Of Cases</th>
<th>Emboli</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative</td>
<td>22</td>
<td>17</td>
<td>77</td>
</tr>
<tr>
<td>Non-operative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneurysm</td>
<td>42</td>
<td>13</td>
<td>31</td>
</tr>
<tr>
<td>Severe atherosclerosis</td>
<td>38</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>Minimal atherosclerosis</td>
<td>44</td>
<td>0</td>
<td>--</td>
</tr>
</tbody>
</table>

Incidence of Embolisation
It is postulated that clamping and manipulation of the aorta may fragment atheromatous plaques. Just proximal to the clamp, there is probably considerable turbulence, tending to churn up atheromatous material, which in turn is carried to the nearest vessels, the renal vessels.

It also proven beyond doubt that embolisation of the renal vascular bed occurs in patients with atherosclerotic aortic disease without having surgery.

Patients undergoing cardiovascular operations are running a risk of developing acute renal failure. This is not only due to the embolisation previously described, but also many other factors play a role the pathogenesis.

Causes of acute renal failure

1. *Acute tubular necrosis*, this may be toxic or ischaemic. Nephrotoxic agents lead characteristically to necrosis of the proximal part of the tubules. The effects of ischaemia depend on its severity and duration; if transient or mild there are no obvious microscopic changes in the tubules. More severe ischaemia leads to patchy tubular necrosis; affecting particularly the terminal portions of the proximal convoluted tubules and the distal convoluted tubules, and characteristically the basement membrane is disrupted. There is oedema of the interstitial tissue and sometimes an inflammatory infiltrate. Functionally the interstitial oedema probably aggravates the anuria by occluding the nephrons. Severe ischaemia leads to massive cortical necrosis, which involves destruction of glomeruli and therefore precludes recovery of renal function.
2. Renal vasoconstriction, a fall in arterial pressure will usually reduce the glomerular filtration rate and renal blood flow. Vasoconstriction of the renal vessels occurs in response to the drop in arterial pressure; leading to ischaemic damage to the kidneys. Renal vasoconstriction occurs following a sudden decrease in blood volume due to haemorrhage; or severe plasma and fluid loss. Cardiac failure is attended by a fall in renal blood flow sometimes to less than 500 ml per minute. Occasionally in myocardial infarction, there may be sudden severe renal vasoconstriction with anuria. This is of importance when patients with generalised arterial disease undergo major cardiovascular surgery.

3. Acute bilateral renal artery obstruction, the commonest cause of this is dissecting aneurysm of the aorta.

4. Acute renal diseases, e.g. polyarteritis nodosa, acute glomerulonephritis, and certain infections may occasionally be so fulminating that they lead to complete anuria.

5. Acute urinary tract obstruction, this may be due to a stone in the pelvis or ureter; sometimes a calculus in one ureter causes a reflex anuria on the other side.

6. Acute renal failure may be superimposed on chronic renal failure.

The most important type of acute renal failure is that following acute tubular necrosis. The functional effects are divided into an oliguric phase which corresponds to the period of necrosis, and a diuretic phase (provided the patient survives) in which there is epithelial regeneration.
In this study the renal functioned is examined accurately, before and after infrarenal aortic reconstruction. Also factors affecting this function e.g. cardiac status, degree of hydration, and operative parameters were all measured and related to the renal function immediately after the operation and also six months later.
CHAPTER TWO

Surgical Management & Patients
2.1 Surgical Management
of
Arterial Disease

The wounded surgeon piles the steel
That questions the distempered part,
Beneath the bleeding hands we feel
The sharp compassion of the healer's art
Resolving the enigma of the fever chart.

T.S. Eliot
1888 - 1965
Patients with arterial insufficiency of the lower limbs fall into two categories; those suffering from intermittent claudication, or ischaemic pain in the lower limb precipitated by exercise, and those with more severe impairment of the circulation producing continuous pain in the lower limb at rest or critical ischaemia.

The important difference between these two groups; is that patients with intermittent claudication are often candidates for conservative rather than operative management, but patients with critical ischaemia are likely to lose the limb unless circulation is restored by surgery.

Claudication is not initially treated surgically. Many claudicants improve with the development of a collateral circulation, and because of this natural tendency to improve in the first 6 months after the onset of symptoms; patients are encouraged to wait several months before surgery is contemplated. During this period conservative management is pursued.

Medical management

Regular exercise is most important in improving the walking distance of claudicants, either by stimulating the development of the collateral circulation; or by promoting more efficient muscle metabolism. Claudicants in this study were advised to exercise as much as possible. Patients were also advised to stop smoking. Vasodilators were not used in these patients; there being no role in the treatment. Weight reduction was advised when necessary.

Treatment of associated conditions, for example control of cardiac failure and hypertension were carried out using the appropriate medication. Anaemia and polycythemia were treated accordingly.
These were the lines of conservative management applied to the control group. Patients with severe claudication, rest pain or gangrene due to aorto-iliac occlusion were offered surgery.

Patients with infrarenal aortic aneurysms were operated upon electively to avoid the risk of rupture. Due to the time consuming nature of the tests patients with ruptured aneurysms were not included in this study.
2.2 Patients In This Study

Though this be madness, yet there is a method in it.

Hamlet
By
William Shakespeare
1564 - 1616
The vascular patients in this study were operated upon by two vascular surgeons over a period of three years. All patients gave their informed consent for the study; which included two age matched control groups of patients. Patients having major colo-rectal surgery were studied to measure the effect of surgical trauma and general anaesthesia on renal function. A group of patients with intermittent claudication; under conservative management were investigated to see natural disease progression and its effect on the renal function.

76 patients were recruited. They were divided as follows:

1. 59 patients in the main study, with infrarenal aortic disease undergoing elective surgery.
2. 8 patients undergoing elective colo-rectal surgery in the first control group.
3. 10 patients suffering from peripheral vascular disease in the second control group.

<table>
<thead>
<tr>
<th></th>
<th>Mean age</th>
<th>Range</th>
<th>Males</th>
<th>Females</th>
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</thead>
<tbody>
<tr>
<td>Aortic patients</td>
<td>63</td>
<td>38 - 81</td>
<td>46</td>
<td>13</td>
</tr>
<tr>
<td>Colo-rectal patients</td>
<td>66</td>
<td>42 - 78</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Arteriopathic patients</td>
<td>61</td>
<td>55 - 67</td>
<td>6</td>
<td>4</td>
</tr>
</tbody>
</table>

The indications for surgery in the aortic patients were:

1. Repair of infrarenal aortic aneurysms. 26 patients.
2. Aorto-iliac occlusion causing severe claudication, rest pain or gangrene. 27 patients.
3. A combination of aneurysmal and occlusive disease. 4 patients.
4. Distal embolisation due to atherosclerotic ulcers or fragments of mural thrombus. 2 patients.
Renal function was tested pre-operatively, 10 - 14 days post-operatively and six months later. The colonic group had the same tests pre-operatively and two weeks post-operatively. The claudicants forming the second control group had the same tests twice with a six months period separating them.

Due to the profound effect of aortic clamping and declamping on haemodynamics and left ventricular function; it was essential to obtain an objective assessment of left ventricular function. Also this was important to ensure that cardiac function was not affected by the operation; as deterioration in cardiac function and consequently perfusion may lead to deterioration of renal function. Radionuclide ventriculography using blood pool offers measurement of left ventricular ejection fraction and also assessment of regional wall motion. This was carried out at the same time of the renal tests on all patients.

Patients in this age group have evidence of coronary artery disease. Left ventricular fraction offered an objective assessment of left ventricular function for pre-operative selection of the patients. Patients with a left ventricular ejection fraction of less than 30 per cent were not offered an aortic operation. Occlusive aortic disease with critical ischaemia in these patients was treated by axillo-bifemoral grafting. Two patients during the period of this study were considered unfit for direct aortic reconstruction, one had a successful axillo-bifemoral graft; he died of a myocardial infarction nine months later, the second patient had completely occluded vessels in both groins; he died in hospital after bilateral above knee amputation.
It was important to study the renal function in a group of patients undergoing major surgery using the same methods as the aortic patients; to confirm that the changes in the aortic patients are specific to this type of surgery. Colo-rectal cases were chosen, as a control group, the surgical procedure being of similar magnitude to the aortic operations; require blood and fluid transfusion; and also being of similar duration.

The indications of surgery in the colonic patients were

2. Carcinoma of the anal canal. One patient.

All patients had either anterior resection or abdomino-perineal excision of the rectum. There was no hospital mortality in this group.

Arterial disease is of a generalised nature; it affects many of the patients vital organs brain, heart, kidneys, and also the limbs. This disease is often progressive; a second control group of patients was included to find out if progression of arterial disease and its multisystem effects leads to any change in the renal function of these patients. The second control group of patients were 10 claudicans attending the vascular surgery clinic. All patients had clinical evidence of peripheral vascular disease, due to aorto-iliac occlusion (One patient had complete aortic occlusion), superficial femoral artery occlusion or a combination of both. These findings were confirmed with doppler waveform analysis. The patients were recruited randomly, and they had similar risk factors to the operative aortic group, hypertension, coronary artery disease, and carotid disease (One patient had a cerebro-vascular accident and did not attend for the follow up).
A medical history was obtained with particular reference to previous myocardial infarcts, cerebro-vascular accidents and previous renal problems. If patients were receiving diuretics pre-operatively, they were restarted on the same diuretic therapy and the same dose post-operatively to ensure that the renal function tests were performed under the same conditions.

Routine pre-operative investigations were also performed. These included ECG, chest X-rays, pulmonary function tests, haematological and biochemical tests.

Arteriography was performed on patients with occlusive vascular disease, on a separate admission prior to the pre-operative renal function tests. This was done to ensure that the pharmacological effect of the contrast medium on renal function did not interfere with renal function tests.

During the operative procedure the patients were continuously monitored. The systolic and diastolic arterial blood pressure and central venous pressures were traced on a chart, using a chart recorder, and this was continued for 24 hours post-operatively. This was done to ensure that renal perfusion was maintained. All patients were treated post-operatively by one surgeon. Post-operative parameters were also recorded.

In the aortic group of patients, 3 died post-operatively in hospital, and one patient died 6 months later at home. The hospital mortality rate was 5 per cent. These cases will be discussed later in chapter five.
CHAPTER TWO

2.3 The Operative Procedure
Endotracheal intubation and general anaesthesia were used for all patients. The abdomen was explored first through a midline incision. The transverse colon was retracted upwards, the small intestines were kept wet using swabs in a plastic bag outside the wound.

The posterior parietal peritoneum was divided longitudinally exposing the infrarenal aorta. The aorta was exposed from the bifurcation to the level of the left renal vein. The aorta was dissected just below the left renal vein on both sides to allow for clamping. If the operation was performed for occlusive disease the femoral vessels were exposed through bilateral longitudinal groin incisions. Common femoral, superficial femoral and profunda femoris arteries were exposed in each groin. Slings were placed around these vessels and branches were controlled with slings or small bulldog vascular clamps. All patients with occlusive disease were treated with aorto-bifemoral bifurcation grafts, if knitted grafts were used pre-clotting was done at this stage using 40mls of the patient's own blood. The patient was systemically heparinised, and the aorta clamped below the left renal vein. The distance from the left renal vein was noted. The proximal end of the graft was sutured end to end with closure of the distal aorta, or end to side to the aorta anteriorly using 3/0 prolene suture. The inferior mesenteric artery was divided between ligatures when necessary. Each limb of the dacron graft was tunneled extraperitoneally to the corresponding leg, the end to side anastomosis was carried out to the bifurcation of the common femoral artery. Vascular clamps were removed allowing the circulation to be restored to one leg first then both legs. Groin drains were used routinely and the incisions were closed in layers.
Infrarenal Aortic Aneurysm Before Clamping
If the operation was to repair an infrarenal aortic aneurysm the same exposure was performed. The inferior mesenteric artery was always ligated and divided. The inferior mesenteric vein was ligated separately when necessary. Depending on the condition of the common iliac vessels and the aortic bifurcation, either straight or bifurcated grafts were used (9 straight grafts and 29 bifurcated grafts). If bifurcated grafts were used either common iliac, external iliac, or femoral arteries were used for the distal anastomosis depending on the state of these vessels. If iliac aneurysms were present they were ligated both proximally and distally.

The inlay technique was always used, the lumbar artery orifices being oversewn inside the aorta after removal of the mural thrombus and at the end the aneurysm sac was sutured covering the graft.

The left renal vein was divided in some patients to facilitate safe cross clamping of the aorta when this was necessary. The left renal vein was divided as close as possible to the inferior vena cava and was not reconstructed at the end of the procedure.

Special attention was given to aberrant renal arteries. They were preserved and only clamped with a bulldog clamp when necessary.

During the operation the following data were recorded:

- Blood pressure
- Central venous pressure
- Urine output

Before aortic cross clamping
During aortic cross clamping
After aortic cross clamping

Volume and type of intravenous infusions.
Volume of blood transfusion and blood loss.

Volume of urine produced before during and after aortic cross clamping.

Distance of aortic clamp from the left renal vein was estimated. Duration of aortic cross clamping was noted. If a bifurcation graft was used the duration of cross clamping started from the point of application of the clamp until the circulation was restored to the first leg. If a straight graft was used the duration started from the application of the clamp to the restoration of the circulation to both legs.

If forced diuresis was used the type and volume of infusion was recorded. During the first post-operative day vital signs were monitored, blood pressure and central venous pressure were continuously traced. Volume and type of infusions were recorded as well as the urine output.
CHAPTER THREE

Methods
CHAPTER THREE

3.1 Renal Function tests
Renal function tests

1. Urine Concentration

The ability to concentrate urine is a valuable overall index of renal function. The specific gravity of urine is an index of the density of solutes. It is an expression of the difference between the weight of a given volume of urine and that of an equal quantity of distilled water at 4 degree C.

2. Proteinuria

Provided there is no urinary tract infection, more than 10 to 15 mg per 100 ml Proteinuria is significant. It is best to determine the total daily protein excretion since a brief period of high urinary flow can produce an unrepresentative, low concentration. A total daily leak in excess of 150 mg is significant.

3. Microscopy

Microscopic examination of the deposit of a fresh specimen of urine should also be carried out when the history and clinical examination suggest a disease of the urinary tract.

4. Blood Urea

Urea is the major end product of protein metabolism. Since it is excreted by the kidneys it is a valuable indirect index of renal function. The blood urea level depends upon the rate of its production and the rate of urinary flow. It is not likely to be elevated unless the GFR is reduced to 50 per cent of normal, and not therefore suitable for monitoring small changes in renal function.
5. Endogenous Serum Creatinine

Endogenous creatinine concentration in the serum is preferable to blood urea as a test of renal function despite the fact that the methods available for its determination also measure certain non-creatinine compounds present in the serum.

6. Renal blood flow

Renal blood flow can be determined by introducing into the circulation substances such as para-amin hippurate (PAH) which is removed, virtually completely, in a single circulation through the kidney. A predetermined amount of PAH is administered by continuous intravenous infusion so as to achieve a constant plasma concentration. By determining the rate of excretion of the injected substance, and the difference between the arterial and venous concentrations, the renal plasma flow and hence the blood flow can be calculated.

7. Radioisotopes

Investigations of renal function by radioisotope techniques began when contrast media were first labelled with radioactive iodine. Since then a number of substances have come into use in the study of glomerular filtration rate (GFR), effective renal plasma flow (ERPF), renal morphology, and the functioning mass of the kidney. The use of radioisotope materials in the precise measurement of GFR and ERPF have now replaced laborious chemical methods.

In summary, Urine concentration is only used as a bedside test. Proteinuria could be physiological due to increased protein excretion which occurs with heavy exertion, heart failure, fever, and operative trauma without any known changes in renal structure or permanent change in renal
function; (Kerr and Davison, 1975) and is therefore unsuitable for monitoring small post-operative changes in renal function. Blood urea and endogenous serum creatinine reflect the overall renal function but they are not affected by small changes in renal function. It is not widely appreciated that when the serum creatinine concentration is only just above the normal range then the patient has functionally lost one kidney (Gabriel, 1986).

Radioisotopes are used in clearance studies for measurement of GFR and ERPF. The reproducibility of GFR using this method is within 5 per cent (Kerr and Davison, 1975). Radioisotopes are also used for renography and renal scanning. A renogram is a measure of renal function and can provide a comparison of function of the two kidneys. It will also reveal the presence of an obstruction. Renal scanning enables the shape, size, and the position of the functioning mass of each kidney to be defined. Also it yields useful information concerning relative renal function (Kerr and Davison, 1975). So the radioisotopic methods are particularly useful in the measurement of relative renal function.
CHAPTER THREE

3.2 Radiopharmaceuticals
A radiopharmaceutical is a radioactive compound used in medicine for the purpose of diagnosis or therapy. Its composition should be constant and it should be radioisotopically and radiochemically pure. It must also be non-toxic and specific for the organ or system under study. Ideally the radionuclide employed should have a short physical half-life and emit monoenergetic gamma rays in the range of 100 - 200 KeV. Its biological half-life should be long enough to permit completion of the test and short enough to avoid giving an unnecessary high radiation dose to the patient.

A wide variety of radiopharmaceuticals are available for study of the kidneys and urinary tract. Their use in conjunction with suitable equipment permits the evaluation of functional parameters such as renal perfusion, glomerular filtration rate, and the effective renal plasma flow.

Glomerular filtration rate (GFR)

The chelating agent Ethylenediaminetetraacetic acid (EDTA) has been labelled with a number of radionuclides, and the success for measurement of GFR would appear to rest on the stability of the compound in vivo.

\(^{51}\text{Cr-EDTA}\) is used in this study for GFR measurement and is currently probably the most widely used for this purpose. Its clearance has been shown to correlate well with, but slightly less than, that of Inulin (Garrett, et al 1967) and its stability and lack of extrarenal clearance make it eminently suitable for plasma clearance analysis (Chantler, et al 1969).

Effective renal plasma flow (ERPF)

It has not been possible to produce a gamma-emitting labelled form of para-aminohippuric acid, and by far the most widely used radioactive
analogue is ortho-iodohippuric acid labelled with $^{131}$I. Its lower extraction efficiency (66% compared with 80% for PAH) could be a result of its considerably greater degree of plasma protein binding (67% compared with 26% for PAH) (Gässer, et al 1971) but it currently represents the agent of choice for determination of the effective renal plasma flow.

Radiopharmaceuticals used for renal imaging

$^{99m}$Tc compounds

$^{99m}$Tc is now easily obtained by means of a 'generator', which consists of the parent radionuclide, molybdenum-99, absorbed onto an alumina column and contained within a radiation shield. The elution of this column with saline produces a solution containing the daughter, technetium-99, as pertechnetate ion. The half-life of $^{99m}$Tc itself is only 6 hours and this, combined with its monoenergetic gamma radiation of 140 KeV and its lack of particulate emission, makes it an excellent choice of radionuclide. It can be used in its pertechnetate form, as eluted from the generator or as a label for other chemical compounds.

$^{99m}$Tc-Dimercaptosuccinic acid (DMSA)

Dimercaptosuccinic acid (DMSA) is an ideal radiopharmaceutical for renal cortical imaging. Because of its high level of renal fixation, it is possible to measure the activity trapped by the individual kidney by a similar technique to that used by Raymond (1974) with $^{197}$Hg-chlormerodrin. After intravenous injection the compound is strongly bound to plasma proteins; as a consequence, glomerular filtration is prevented and the clearance from blood occurs through tubular secretion. At one hour 50% can be found in the kidneys and eventually up to 70% concentrates in these organs. Best cortical images are obtained 2 - 3 hours after injection (Vanlic-Razumetic and Goric, 1976).
This is a chelate in which the DTPA is in its pure form. It is completely filtered by the glomeruli and is not reabsorbed by the renal tubules. The fact that DTPA is purely filtered makes imaging with this agent truly functional. Best images are obtained during the first 15 minutes after injection (Arnold, et al 1975). The derivation of activity time curves from the renal area using $^{99m}$Tc-DTPA as reported by (Hemson, et al 1977) allows the renographic curves to be performed.

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Half-life</th>
<th>Principal emissions (Kev)</th>
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<tbody>
<tr>
<td>$^{51}$Cr</td>
<td>27.7 days</td>
<td>320</td>
</tr>
<tr>
<td>$^{99m}$Tc</td>
<td>6.02 hours</td>
<td>141</td>
</tr>
<tr>
<td>$^{99}$Tc</td>
<td>2.13 x 10$^6$ years</td>
<td>None</td>
</tr>
<tr>
<td>$^{131}$I</td>
<td>60.14 days</td>
<td>35</td>
</tr>
</tbody>
</table>

Properties of isotopes
CHAPTER THREE

3.3 Clearance Studies
The accurate diagnosis of disorders of renal function is greatly facilitated by the interpretation of the various functional tests of renal activity. The understanding of the concept of renal clearance is important. Radionuclide techniques of clearance are simple laboratory procedures and have the advantage over classical methods in that the assessment of clearance by individual kidneys can be calculated at the same time.

**Theory and Terminology**

Any substance may be found to have a concentration \( P \) in the plasma of a renal artery and to appear in the urine with a concentration \( U \). If the urine is being produced at a rate \( V \), it can be calculated that the substance is excreted at a rate \( UV/\text{min} \). In each minute, therefore, the volume of plasma from which all the substance might have been cleared is equal to \( UV/P \), and this quantity is known as the renal clearance of that specific substance.

\[
\text{Clearance} = \frac{UV}{P}
\]

If the substance is filtered by the glomerulus as efficiently as water and if it subsequently passes through the tubular system without further exchange with plasma, then its clearance is a measurement of the glomerular filtration rate (GFR). These conditions imply that the substance is neither reabsorbed nor secreted by the tubules, that it remains free of plasma protein binding, and that it is not metabolised within the kidney. Normal values of GFR are \( 124 \pm 26\text{ml/min} \) for adult males and \( 109 \pm 13\text{ml/min} \) for adult females (Smith, 1951). Although these figures vary with age.
If the substance is not metabolised by the kidney, we may deduce that any amount passing through the renal artery must, under equilibrium conditions, be equal to the total amount leaving via the renal vein and the urine (The Fick principle). If the total renal plasma flow be \( F \), the renal arterial concentration \( PA \) and the renal venous concentration be \( PV \), then

\[
FPA = FPV + UV
\]

or \( F = UV / (PA - PV) \)

A substance which is completely eliminated from the plasma in one pass (for which \( PV \) would be zero) would, therefore, have a clearance equal to the renal plasma flow. This would imply elimination by tubular secretion in addition to or instead of glomerular filtration.

**Traditional methods of measuring renal clearance**

In the 1930s inulin - a Fructose polysaccharide - was found to satisfy the conditions outlined above for an indicator of glomerular filtration rate. Inulin concentration can be measured in samples of plasma and urine and it can safely be infused intravenously. The clearance of inulin, as measured from plasma and urine samples taken while a constant plasma concentration is maintained by continuous infusion has therefore become a reference standard for measurement of glomerular filtration rate.

Endogenous creatinine may be analysed chemically in plasma and urine samples, and its clearance is also used as a measure of GFR. This has been criticised (Berlyne, 1965 - Kla, et al 1969) because of suspicion of significant tubular secretion and non-specificity of the chromogen test used, but the variability of results probably reflects true variations in a
patient's GFR and the method has been shown to correlate well with inulin clearance (Bennett and Porter, 1971).

The classical substance used for measurement of ERPF is p-aminohippuric acid (PAH) and the normal clearance values obtained are 623 ± 112 ml/min (Smith, 1951). The classical methods of measurement of clearance of inulin or PAH involve continuous intravenous infusion, multiple venous sampling, bladder catheterization in order to obtain complete urine collections during successive time intervals, and difficult chemical determinations. They are too time consuming for routine diagnostic tests and they do not lend themselves to simplification. The ease and sensitivity with which samples of gamma emitting radionuclide may be measured in a scintillation well counter has enabled the continuous infusion method to be replaced by simpler techniques, all of which have been validated by correlation with the classical chemical methods.

Radionuclide techniques for measuring renal clearance

A number of measurement techniques may be employed, and these may be classified as follows
1. Constant infusion methods.
4. External monitoring (a) vascular; (b) vesical; (c) renal.
5. Approximations from volume of dilution measurements.

The single injection method with plasma sampling only, is the technique used in this study and is the only one that will be discussed here.
The procedures for determining the clearance of $^{51}$Cr labelled EDTA, for the assessment of glomerular filtration rate, and $^{123}$I labelled ortho-iodohippurate, for the assessment of the effective renal plasma flow, were performed at the same time as the DMSA renal study. This results in fewer visits for the patients with a considerable saving in time. Because of the overlap in the times that the blood samples are taken there is a saving in the number of samples taken as well.

A bolus injection of $^{51}$Cr-EDTA and $^{123}$I-Hippuran were injected intravenously into two separate arm veins. Blood samples were taken at regular intervals. The activity in each of the blood samples was measured using a standard counter. The time activity curve is drawn; this allows the activity at time zero to be calculated. The slope of the graph allows the GFR and the ERPF to be calculated.
3.4 Renography & Renal Scanning

Come, come, and sit you down. You shall not budge!

You go not till I set you up a glass, where you may see the inmost part of you.

_Hamlet_

_by_

_William Shakespeare_

1564 - 1616
Renography

This is a method of monitoring the arrival, uptake and elimination of a radiopharmaceutical by the kidneys to give an assessment of individual renal function and clearance. The radiopharmaceutical contains a gamma-emitting nuclide in order that external detection can be accomplished with a gamma camera. The most widely used agents for this purpose are \(^{131}\)I labelled ortho-iodohippurate, hippuran, (Blaufux, 1972) and more recently \(^{99m}\)Tc-DTPA, diethylenetriaminepenta-acetic acid, (Nelson, et al 1977).

Method

Detecting and recording the renal handling of the radiopharmaceutical is done using a gamma camera computer system. The computer stores a sequence of images of the renal handling of DTPA. It is then possible to define the areas of the kidneys as regions of interest and derive a renogram curve from the series of counts from the area of interest stored in the computer memory. The test is usually performed with the patient sitting, because this is a more common posture in day to day activity. Provided they are comfortable, patients do not appear to have any difficulty in maintaining this position for the duration of the test (20 minutes). The patient requires no preparation other than that he should be well hydrated. In practice this means giving the patient a pint of fluid orally in the hour preceding the test. This amount of fluid makes it unnecessary to empty the bladder immediately before the test and again at the end of it for urine collection to measure the flow rate during the renography. The urine flow rate should be in the range of 1-3 mls/min. There should be no fluid deprivation before the test, as it is important to avoid an oliguric state, since the resultant renogram can mimic an obstructive pattern.
This is due to the low flow rate of the radiopharmaceutical through each kidney and may give rise to misinterpretation of the test results.

Once the patient is positioned, 125 MBq of the $^{99m}$Tc-DTPA is injected into a suitable superficial vein. The injection should be completely intravenous, since any extravasation will produce a distorted curve due to diffusion of tracer from the subcutaneous tissue into the vascular system.

**Interpretation**

The normal renogram performed in this way shows three typical phases originally termed vascular, secretory, and excretory, but better termed simply the first, second and third phases.

*The first phase* of the curve is a rapid rise corresponding to the increase in radioactivity within the regions of interest drawn around the kidneys, produced by the intravenous injection of radiopharmaceutical. It reflects the rapidity of injection and vascular supply to the kidney. The radioactivity detected within the region of interest is that in blood, kidney and external tissues. After a few seconds this gives way to a more gradual slope, the second phase.

*The second phase* corresponds to the renal handling of the DTPA as it is filtered by the glomerulus and passes through the lumen of the nephron. The shape and duration of this part of the curve are dependant on several factors: supply rate, filtration efficiency, intraluminal transit, and excretion. This rising curve is due to the fact that more DTPA is arriving at the kidney through recirculation while none has yet left the renal pelvis. If no activity were to leave the pelvis because of an obstructive process, this second phase would continue to rise and this pattern is
POSTERIOR VIEW

* 100. COUNTS

RIGHT

HEART

LEFT

Normal Renogram
usually found in obstructive uropathy. In the normal kidney, however, after between 2% and 4% minutes, gamma activity starts to leave the renal pelvis and at that point there is a fall in total gamma activity seen within the kidney region of interest. This corresponds to the beginning of phase three. This point also corresponds to the time at which activity first appears in the bladder. The peak of phase two can be delayed by a variety of conditions, such as an obstructive pathology preventing excretion of tracer, renal artery stenosis causing a more prolonged gradual supply of tracer to the kidney, low urine flow rate or parenchymal disease, and these can similarly affect the slope of both phase two and phase three.

The third phase of the curve is predominantly but not exclusively excretory, for it reflects the amount of DTPA arriving at the kidney, the amount leaving it, and the continuing fall in activity in the blood and background tissues.

Because the final shape of the curve is affected by these multiple factors, it is unwise to attempt to derive quantitative physiological parameters on renal function from visual analysis of the curve shapes. Deconvolution of the renographic curves was not performed in this study. Nevertheless, unlike conventional radiography, the renogram is a truly functional rather than anatomical assessment of renal status. It can provide a considerable amount of functional information in bilateral problems and more particularly in unilateral disease where the normal kidney can be seen as a control for comparison with the abnormal one. Renography is simple, rapid and safe. It requires little preparation and gives a low radiation dose. (see tab 3.1).
Renal Imaging

Several radiopharmaceuticals can be used for renal imaging. The 99mTc labelled agents are the most widely used because of the excellent physical properties of the radionuclide (half-life 6 hours, gamma energy 140 KeV). DTPA "Diethylenetriaminepentaaetic acid" and DMSA "Dimercaptosuccinic acid" are used in this study. 99mTc-DTPA is predominantly filtered with little cortical retention, while 99mTc-DMSA is retained in the cells of the proximal tubules allowing good cortical pictures to be obtained.

Radiation Doses

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Chemical form</th>
<th>Administered</th>
<th>Whole body activity (MBq)</th>
<th>Dose (μg)</th>
<th>Kidney dose (μg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>51Cr</td>
<td>EDTA</td>
<td>4</td>
<td>0.02</td>
<td></td>
<td>0.006</td>
</tr>
<tr>
<td>99mTc</td>
<td>DTPA</td>
<td>125</td>
<td>0.2</td>
<td></td>
<td>0.825</td>
</tr>
<tr>
<td>99mTc</td>
<td>DMSA</td>
<td>60</td>
<td>0.2</td>
<td></td>
<td>13.8</td>
</tr>
</tbody>
</table>

(Tab 3.1)

Absorbed doses when renal function is normal: these figures are calculated on the assumption that the patient voids only once every 3½ hours. A diuresis with voiding every 30 minutes would reduce the absorbed dose to the bladder and ovaries by more than 75 per cent. There would be a small effect on the absorbed dose to other organs (Garrich, 1984).
CHAPTER THREE

3.5 Ventriculography
Ventriculography

Ventriculography can be performed ultrasonically, angiographically or with the use of radioisotopes. Either ventricle can be examined. The angiographic method is the most invasive and carries a significant morbidity and mortality. It is generally regarded as the reference technique against which other methods must be judged. It gives better anatomical detail than any other method but functional studies obtained during angiographic ventriculography must be treated with some caution as the rapid administration of a volume of hypertonic contrast comparable with the normal end systolic volume is not without haemodynamic effects.

Ultrasound in experienced hands is capable of providing excellent anatomical detail and accurate measurements of all chambers of the heart. It is completely non-invasive and safe, and takes relatively little time. This should therefore always be employed as the initial screening procedure. However with increasing age of the patient it becomes progressively more difficult to obtain studies of adequate quality. Chronic lung disease, especially emphysema, restricts the ultrasonic window, and in many subjects the heart cannot be adequately visualised by this technique (Merrick, 1984).

In these patients radionuclide ventriculography is the investigation of choice. Radionuclide ventriculography is also indicated in patients with abnormal ventricular function, particularly if there is distortion of the shape of the ventricle as this is the only method which does not make assumptions about ventricular geometry.

$^{99m}$Tc-labelled autologous erythrocytes have entirely superseded all other technetium labelled radiopharmaceuticals for this purpose.
Labelling can be achieved with high efficiency using a combined in vivo and in vitro method. The in vivo method is used in this study. 1 mg of stannous tin in the form of stannous chloride solution is injected intravenously + 2.2 mg of medronate. 15 to 30 minutes later 700 MBq of \textsuperscript{99m}Tc as pertechnetate is injected intravenously. During this period about 85 per cent of radioactivity becomes attached to the red cells.

**Multigated studies**

After labelling the erythrocytes with \textsuperscript{99m}Tc, the heart is readily identified. The left ventricle can be visualised in the right anterior oblique projection at equilibrium, but is partially overlapped by activity in the chamber of the right ventricle. Only in the 20 degree left anterior oblique projection, preferably with the camera angled 10 degrees towards the feet, is the left ventricle unobscured by any other chamber. This angulation should be adjusted to obtain the best visualisation of the left ventricle in the particular patient. The acquisition is controlled by the patients ECG signal to add frames corresponding in time to equivalent phases in the cardiac cycle. In this way counts can be accumulated over several hundred cycles to obtain a series of frames containing adequate statistics for further analysis. Although often unsuitable for calculation of ejection fraction because of overlap of the right and left ventricles, a second projection does enable anterior wall abnormalities to be distinguished from those involving the posterior wall.

**Processing of Results**

In order to calculate the ejection fraction it is first necessary to estimate and subtract those counts originating from extracardiac regions. Background subtraction does not alter the shape of the time activity curve, only its vertical height.
The ejection fraction is

\[
\frac{\text{nett end diastolic counts} - \text{systolic counts}}{\text{nett end diastolic counts}}
\]

The consecutive frames can be displayed in a rapid sequence to obtain a display of regional wall motion. By repeating the cycle of frames a continuous display may be obtained which may be speeded up or slowed down to facilitate visual interpretation.
CHAPTER THREE

3.6 Protocols Of Procedures
Used In This Study
Clearance Procedures

The procedures for determining the clearance of $^{51}$Cr labelled EDTA for the assessment of glomerular filtration rate, and $^{125}$I labelled ortho-iodohippurate for the assessment of the effective renal plasma flow, were performed at the same time as the DMSA renal scan. This resulted in two fewer visits for the patients and also a considerable saving in time for the performance of these procedures. Because of the overlap in the times that the blood samples are taken there is a saving in the number of samples taken as well.

The various steps of these procedures are as follows:

1. For the $^{51}$Cr-EDTA clearance a 2 ml disposable syringe is weighed complete with 21G needle and guard.

2. The stock solution of $^{51}$Cr-EDTA as supplied by Amersham International is checked for quantity of material in vial and its date of expiry.

3. Approximately 0.6 ml of solution is drawn up into the syringe.

4. The syringe is reweighed complete with the same needle and guard and both weights are recorded on the data sheet, together with the batch number of the material and its reference date.

5. A 1 ml syringe is weighed complete with 21G needle and guard.

6. The stock solution of $^{125}$I ortho-iodohippurate as supplied by Amersham International is checked for quantity of material in vial and its date of expiry.

7. Approximately 0.2 ml of solution is drawn up into the syringe.

8. The syringe is reweighed complete with the same needle and guard and both weights are recorded on the data sheet together with the batch number of the material and its reference date.

9. The contents of both syringes are injected into the patient at two different sites taking great care that there is no extravasation of the injected material.
10. The times at which these injections are done is noted on the data sheet to the nearest minute.

11. Both syringes are flushed with water into the same volumetric flask as well as the needles used in the drawing up and administration of the injections. This flask is known as the residue flask and labelled with the patients name and date of the investigation.

12. 5 ml blood samples are taken from the patient at 1, 15, 2, 3, and 4 hours into a standard full blood count vial. The times at which these samples are taken is noted on the data sheet to the nearest minute.

13. The height and weight of the patient are recorded on the data sheet.

14. The third blood sample is used for the determination of the packed cell volume and the haemoglobin level before being processed further.

15. After the last blood sample has been taken and the DMSA scan has been performed the patient is allowed home.

16. The patient blood samples are centrifuged to separate the plasma from the erythrocytes and an aliquot of plasma is withdrawn from the sample bottle using Eppendorf pipette with disposable tips. The aliquot is placed into a counting tube labelled with the patients name and the position of the sample in the sequence of samples from the patient.

17. An aliquot of 2 ml is withdrawn from the residue flask and placed into a counting tube labelled with the patients name and the word residue.

18. All the tubes are capped and placed in a rack together with standard tubes for the $^{51}$Cr-EDTA and $^{131}$I-Hippuran.

The following procedures are only performed for the first use of a new batch of material:

1. For the $^{51}$Cr-EDTA a 2 ml syringe complete with needle and guard is weighed and the weight is recorded in the investigation record book and the patient data sheet.
2. Approximately 0.3 ml of the $^{51}$Cr-EDTA solution is drawn up into the syringe, and the syringe complete with needle and guard is reweighed. The weight is recorded in the investigation record book and on the patient data sheet together with the batch number and reference date.

3. The contents of the syringe are flushed into a clean volumetric flask and both syringe and needle are repeatedly flushed with water to remove as much of the radioactivity as possible from the syringe, needle, and needle guard. The contents of the flask are made up to the correct calibration level and the flask is labelled as the standard flask for that batch of material. The volume of the flask is also recorded in the investigation record book and the patient data sheet.

4. For the $^{123}$I-Hippuran a 1 ml syringe is weighed complete with 21G needle and guard, the weight is recorded in the investigation book and on the patient data sheet.

5. Approximately 0.1 ml of the $^{123}$I-Hippuran solution is drawn up into the syringe, the syringe complete with needle and guard is reweighed. This is recorded in the investigation record book and the patient data sheet, together with the batch number and reference date.

6. The contents of the syringe are flushed into a clean volumetric flask and the syringe and needle are repeatedly flushed with water together with the guard if it is suspected of being contaminated with radioactivity. The contents of the flask are made up to a calibration volume mark and the flask is labelled the standard flask for that batch and the volume of the flask is recorded in the investigation record book and on the patient data sheet.

7. A 2 ml aliquot is withdrawn from both standard flasks and each is put into a counting tube labelled with the standard batch number which is then capped and used for the counting of all patients samples containing material from that batch.
Because of the presence of a third radioactive isotope $^{99m}$Tc in these samples with only two channels on the automatic gamma ray sample counter it is necessary to wait for the $^{99m}$Tc to decay away.

$^{99m}$Tc has a half life of 6 hours, while the half lives of $^{61}$Cr and $^{128}$I are 27.3 days and 60.2 days respectively, thus the wait for the decay of the $^{99m}$Tc has a very small effect on the quantities of $^{61}$Cr and $^{128}$I present in the sample. As the quantity of each substance injected and used for the standard is determined by weight rather than activity any decay in counting is irrelevant provided sufficient radioactivity remains for satisfactory assessment of the quantities present in each sample.

In practice if the procedures are performed on a Monday or Tuesday then the samples are put on to count on the following Friday afternoon and for Wednesday, Thursday or Friday procedures the samples are put on to count the following Monday afternoon. All the samples, standards, residue and associated background samples are counted for 50 minutes each or 800000 counts whichever occurs first.

The figures obtained by counting all these samples are entered into a specially written program on a Commodore PET microcomputer. The program takes the data from the data sheets as well as patient identification data and the data from the automatic sample counter. Procedures have been written into the program to enable verification and any necessary correction of data to be made at various stages of data entry before processing it.

The program then converts the counts recorded to counts per unit time and then removes the appropriate background count rate from each of the samples, standards and residue for each counting channel. After this
is done the program calculates the fractional spillover of each isotope into the other isotopes counting channel from the standard sample figure. These ratios are then used to correct the count in each channel for the spillover from the count rate in the other channel.

The total amounts of $^{51}$Cr-EDTA and $^{125}$I-Hippuran injected into the patient are calculated in the following way.

\[
\text{(1) dose} = \frac{\text{net weight of injection}}{\text{volume of standard flask}} \times \frac{\text{net weight of standard aliquot counted}}{\text{aliquot counted}} = Z
\]

\[
\text{(2) dose} = Z \times \text{net standard count rate} = Y
\]

\[
\text{(3) dose} = Y - \frac{\text{volume of residue flask aliquot counted}}{\text{net residue count rate}}
\]

The clearance constant (slope if plotted on a graph) of $^{51}$Cr-EDTA is obtained by taking the logarithm of the count rates for the last three samples taken from the patient and performing a least squares fit for log count rate against time. The program checks that the earliest sample used for the GFR calculation was not taken less than 90 minutes after the injection of the $^{51}$Cr-EDTA. If there should be less than three samples taken more than 90 minutes post injection the program halts for confirmation to proceed with the calculation using the sample immediately prior to the samples already being used. From the clearance constant the count rate is extrapolated back to the time of injection. The GFR is then calculated then from the formula,

\[
\text{GFR} = \frac{\text{dose counts injected} \times \text{clearance constant}}{\text{counts / minute / ml at } t=0}
\]

Similarly for $^{125}$I-Hippuran the total dose counts are calculated from the weights and counts of the standard and residue. The clearance rate is calculated in a similar manner to that of $^{51}$Cr-EDTA except that only those samples taken less than two hours post injection of the $^{125}$I-Hippuran are used.
Again the program halts for confirmation to proceed if there are less than three samples, and uses that sample taken immediately after the samples already being used. The hippuran clearance is calculated from the formula,

\[
ERPF = \frac{\text{dose counts injected \times clearance constant}}{\text{plasma counts / ml / minute at } t = 0}
\]

The results of glomerular filtration rate (GFR), and the Effective renal plasma flow (ERPF) are presented in ML/Min. in this study.

To verify the reproducibility and accuracy of the glomerular filtration rate and the effective renal plasma flow measurements we tested six healthy volunteers twice with a three weeks period inbetween the two measurements.

**Glomerular filtration rate in volunteers**

<table>
<thead>
<tr>
<th>First measurement</th>
<th>Second measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>143</td>
<td>127</td>
</tr>
<tr>
<td>124</td>
<td>115</td>
</tr>
<tr>
<td>138</td>
<td>138</td>
</tr>
<tr>
<td>109</td>
<td>118</td>
</tr>
<tr>
<td>86</td>
<td>83</td>
</tr>
<tr>
<td>101</td>
<td>109</td>
</tr>
</tbody>
</table>

Mean first GFR 117 ML/Min.  Mean second GFR 115 ML/Min.

S.D. 22            S.D. 19
Effective renal plasma flow in volunteers

First measurement       Second measurement

1475                    1197
720                     696
1332                    1468
716                     400
658                     702
630                     921

Mean first ERPF 922 ML/Min.  Mean second ERPF 901 ML/Min.
S.D. 377                S.D. 391

These results show our measurements of total GFR and ERPF to be reproducible. This is especially true for the GFR measurement where the mean difference for the two measurements was 7.3 with a standard deviation of 5.7. This indicates that the error in a single GFR measurement is 8 ML/Min. and that a difference of 11 ML/Min. is significant (0.05) (Young and Bailton, 1980). For ERPF the mean difference was 185 ML/Min. with a standard deviation of 129. This would indicate the error in a single measurement of ERPF is 180 ML/Min. (0.05) and that a difference of 258 ML/Min. is significant (0.05) (Young and Bailton, 1980).
NORMAL GFR
AGE RELATED

Total GFR (ml/min)

AGE (YEARS)
1. Prepare a dose of $^{99m}$Tc-DTPA. The adult dose is 125 MBq.
2. Set the gamma camera for dynamic study acquisition
3. Position the patient for the renogram, PA view, in the sitting position. Ideally, the kidneys should be in the centre of the field of view, with the lower part of the heart just at the top of the picture. With a modern 40 cm large field of view gamma camera the bladder may also be included.
4. Store a dynamic study of 100 frames, each of 15 sec. duration (i.e. 25 min. of data in total), starting immediately after the injection.
5. Right marker is positioned in the early frames.
6. For assessment of renal function, the program first produced a summed picture on which the regions are to be assigned with the joystick or keyboard. Assign the right kidney and the left kidney, a background region between the kidneys and above the ureters, and a blood region over the heart or the liver. The program then produces the curves. These curves are the renal curves corrected for blood background activity.

All renographic curves in this study will be assessed by one experienced observer. A score will be allocated to the function and the clearance in each curve.
Renal Scan Procedure

1. 60 MBq of $^{99m}$Tc labelled DMSA is drawn up into a syringe and assayed for radioactive content.

2. The $^{99m}$Tc-DMSA is injected intravenously at a separate site to the $^{51}$Cr-EDTA and $^{125}$I-Hippuran injections given at the same occasion. Care being taken to avoid extravasation as there is very little diffusion of extravasated material back into the intravascular compartment.

3. Three hours later (range 2½-4 hours) imaging was carried out using a standard gamma camera. Images of the patients kidneys were obtained from the anterior view, the posterior view, and in the patients first visit both lateral projections as well. The anterior and posterior images are accumulated until 400000 counts have been obtained over the whole image. For the lateral views only 200000 counts were obtained.

4. The images were recorded onto an X ray film for reporting purposes to assess the distribution of radioactivity within each kidney and the detection of any filling defects.

5. Regions of interest were drawn around both kidneys in the posterior and the anterior views together with another region to assess background radioactivity in those other tissues included within the renal regions of interest.

6. The relative radioactive content of each kidney is calculated in the following way

\[
Ra = \frac{\text{Counts R, kidney ant} - \text{Area R, kidney ant, ROI}}{\text{Area background ant, ROI}} 
\times \frac{\text{X Background counts}}{}
\]

\[
Rb = \frac{\text{Counts R, kidney post} - \text{Area R, kidney post, ROI}}{\text{Area background post, ROI}} 
\times \frac{\text{X Background counts}}{}
\]
Similarly for both projections of the left kidney. The relative function of each kidney is given by

\[
R\% = \frac{(Ra \times Rb)^{Y} \times 100}{(Ra \times Rb)^{Y} + (La \times Lb)^{Y}}
\]

Accuracy and reproducibility

What level of change in the percentage of function measured should be considered significant? Peters, et al (1986) considered this question, they showed 95 per cent confidence limit for a change of 4.5.
CHAPTER FOUR

Results
4.1 Changes In Total
Glomerular Filtration Rate

I am ...... most fearful of committing myself when I lack evidence.
But on the contrary, no consideration can keep me from defending what I
hold as true when I rely on solid scientific proof.

Rene J. Dubos

In

Louis Pasteur, Free Lance Of Science
Aortic patients (n = 59)

The total glomerular filtration rate (Total GFR) results were available on 57 patients pre-operatively, 56 patients immediately post-operatively, and on 53 patients six months later (late results).

Mean Pre-Op Total GFR = 82 Ml/Min S.D.= 27 Range 18 - 155
Mean Post-Op Total GFR = 84 Ml/Min S.D.= 23 Range 21 - 134
Mean Late Total GFR = 73 Ml/Min S.D.= 23 Range 29 - 130

When the total GFR pre-operatively and early post-operatively were compared using the Wilcoxon test, there was no significant difference P>0.05. Comparing the total GFR pre-operatively and six months following surgery using the Wilcoxon test, there was a significant decrease in total GFR P=0.007.

These results suggest that infrarenal aortic surgery had no immediate effect on the total glomerular filtration rate. Six months later the total GFR of the same patients showed a significant decrease. There was a mean decrease in total GFR of 9Ml/Min or 11 per cent of the pre-operative value.

The results of the total glomerular filtration rate of the aortic patients are shown in the appendix.

Colonic patients (Control group, n = 8)

The results of total glomerular filtration rate were available on eight colonic patients pre-operatively and two weeks post-operatively.
Mean Total GFR
Aortic Patients

ML/Min

100
90
80
70
60
50
40
30
20
10
0

SD=27
P>0.05

SD=23
P=0.0001

SD=23

PreOp  PostOp  Late
Mean Pre-Op Total GFR = 74 ml/min  
S.D. = 19  
Range 47 - 101

Mean Post-Op Total GFR = 81 ml/min  
S.D. = 27  
Range 51 - 132

When the total GFR in this group of patients were compared pre-operatively and post-operatively using the Wilcoxon test, there was no significant difference \( P>0.05 \). The results show that colonic surgery had no effect on total glomerular filtration rate.

The results of the total glomerular filtration rate of the colonic patients are shown in the appendix.

Non operative patients (Control group, \( n = 10 \))

The first total glomerular filtration rate results were available on ten patients. The second total GFR results measured six months later were available on nine patients, as the tenth patient developed a cerebro-vascular accident and failed to attend for follow up.

Mean first Total GFR = 85 ml/min  
S.D. = 7  
Range 77 - 97

Mean second Total GFR = 81 ml/min  
S.D. = 10  
Range 55 - 87

The total GFR was measured in the non operative arteriopathic patients twice within a period of six months. When the results were compared using the Wilcoxon test there was no significant difference \( P>0.05 \). The results show that arterial disease in these patients did not have an effect on the total GFR within a period of six months.

The results of total glomerular filtration rate of the non operative patients are shown in the appendix.
The results suggest that colonic surgery had no effect on the total glomerular filtration rate. The results from the non-operative arteriopathic patients show that arterial disease within a period of six months did not have an effect on total glomerular filtration rate. In the group of patients having aortic surgery there was no change in total glomerular filtration rate immediately post-operatively, but the total GFR decreased when measured again after six months. This late decrease in total GFR does not appear to be due to progression of arterial disease but is most likely to be the effect of aortic reconstruction. Also it was not evident in the immediate post-operative period; when statistically examining the results of all patients, due to the fact that an increased GFR in 31 patients masked the deterioration in the rest.

The immediate post-operative results can be divided into two groups, firstly patients who showed an increase in total GFR, second patients who showed a decrease in total GFR. Then if for each of these two groups of patients the pre-operative GFR is compared to the late GFR measured 6 months later. Analysis of the results in this way allow us to find out if the changes in total GFR in the immediate post-operative period were the same at six months time.

Patients showing immediate increase in total GFR (n = 31)

<table>
<thead>
<tr>
<th></th>
<th>Mean Pre Op Total GFR</th>
<th>S.D.</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>71 ml/min</td>
<td>22</td>
<td>18 - 113</td>
</tr>
<tr>
<td>Mean Post Op Total GFR</td>
<td>89 ml/min</td>
<td>25</td>
<td>21 - 134</td>
</tr>
<tr>
<td>Mean Late Total GFR</td>
<td>73 ml/min</td>
<td>23</td>
<td>29 - 116</td>
</tr>
</tbody>
</table>

When the the total pre-operative GFR in this group of patients was compared to the GFR six months later, there was no significant difference ($P>0.05$ (Wilcoxon test). patient No. 52 is a typical example of this.
This suggests that an increased GFR immediately post-operatively is a temporary phenomenon. It was this increase in the GFR in this group of patients that statistically masked the decrease in the remaining patients.

Patients showing immediate decrease in total GFR (n = 26)

<table>
<thead>
<tr>
<th></th>
<th>Mean Pre Op Total GFR</th>
<th>S.D.</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>94 Ml/Min.</td>
<td>28</td>
<td>52 – 155</td>
</tr>
<tr>
<td>Mean Post Op Total GFR</td>
<td>80 Ml/Min.</td>
<td>20</td>
<td>51 – 119</td>
</tr>
<tr>
<td>Mean Late Total GFR</td>
<td>75 Ml/Min.</td>
<td>24</td>
<td>37 – 130</td>
</tr>
</tbody>
</table>

When the total pre-operative GFR in this group of patients was compared to GFR six months later, there was a significant decrease in total GFR P=0.003 (Wilcoxon test). When the total GFR in this group post-operatively was compared to that six months later, no significant difference was found, P>0.05 (Wilcoxon test). Patient No. 14 is a typical example of this.

It can be seen that when the total GFR showed an increase in the immediate post-operative period, it had returned to the pre-operative level by six months later. When the total GFR showed a decrease immediately post-operatively this was maintained when measured six months later. This decrease was probably due to the operative procedure as there was no difference between the post-operative and late total GFR.

When the pre-operative total GFR was compared to the GFR measured six months later, it was found that 35 patients showed a decrease in total GFR and 17 patients show an increase. The results for the two groups will be analysed separately.
G.F.R. IN AORTIC PATIENTS

Immediate Post Op. Changes

GFR Ml/Min

00.00

POST-OP DECREASE

POST-OP INCREASE

P>0.05

P=0.003

Post Op. decrease deteriorated further
Post Op. increase returned to normal

PreOp  PostOp  Late
Patients showing late increase in total GFR (n = 17)

Mean Pre Op Total GFR = 72 Ml/Min.  S.D.= 23  Range 18 - 112
Mean Post Op Total GFR = 80 Ml/Min.  S.D.= 21  Range 21 - 113
Mean Late Total GFR = 85 Ml/Min.  S.D.= 22  Range 29 - 130

When the pre-operative and the immediate post-operative total GFR of this group of patients was compared using the Wilcoxon test, there was no significant difference P>0.05. Patient No. 44 is an example of this.

Patients showing late decrease in total GFR (n = 35)

Mean Pre Op Total GFR = 89 Ml/Min.  S.D.= 27  Range 36 - 155
Mean Post Op Total GFR = 87 Ml/Min.  S.D.= 22  Range 51 - 134
Mean Late Total GFR = 69 Ml/Min.  S.D.= 21  Range 29 - 113

When the pre-operative and the immediate post-operative total GFR in this group of patients were compared, there was no significant difference P>0.05 (Wilcoxon test). Patient No. 14 is an example of this.

35 patients having aortic surgery (69 per cent) showed long term decrease of the total GFR, the mean decrease was 20 Ml/Min. (22 per cent of the pre-operative value). The long term change in GFR could not be predicted from the immediate post-operative measurements, except that if there is an early post-operative decrease in total GFR it is unlikely to improve.
G.F.R. IN AORTIC PATIENTS

Late Changes

GFR Ml/Min

00.00

Late Decrease
Late Increase

P>0.05

P>0.05

P>0.05

P<0.0001

No difference between Pre & Post operative values

PreOp  PostOp  Late
CHAPTER FOUR

4.2 Changes In
Effective Renal Plasma Flow
Aortic patients: n = 38

The effective renal plasma flow (ERPF) results were available on 36 patients pre-operatively, 35 patients post-operatively, and 33 patients six months later (late results).

Mean Pre Op ERPF = 524 ml/min.  S.D.= 212  Range 88 - 1137
Mean Post Op ERPF = 509 ml/min.  S.D.= 226  Range 111 - 1177
Mean Late ERPF = 450 ml/min.  S.D.= 218  Range 142 - 909

When the pre-operative ERPF was compared to the immediate post-operative effective renal plasma flow (ERPF) using the Wilcoxon test, there was no significant difference between those two sets of results P>0.05.

When the pre-operative ERPF was compared to the late effective renal plasma flow (ERPF) measured 6 months later, again there was no significant difference P=0.05 (Wilcoxon test).

Comparing the ERPF immediately post-operatively to the ERPF measured six months later, there was no significant difference P>0.05 (Wilcoxon test).

These results indicate that infrarenal aortic reconstruction appears to have no effect on the effective renal plasma flow.

The results of the effective renal plasma flow of the aortic patients are shown in the appendix.
Mean ERPF
Aortic Patients

Ml/Min

SD=212  SD=226  SD=218

P>0.05  P>0.05  

PreOp  PostOp  Late
Colonic patients (Control group, N = 8)

The results of ERPF were available on 8 patients both pre-operatively and two weeks post-operatively.

Mean Pre Op ERPF = 445 Ml/Min.  S.D.= 234  Range 134 - 878
Mean Post Op ERPF = 479 Ml/Min.  S.D.= 270  Range 97 - 900

Comparing the ERPF pre-operatively and post-operatively in this group of patients using the Wilcoxon test, there was no significant difference between the two sets of results P>0.05.

The results show that colonic surgery does not appear to alter the effective renal plasma flow.

The results of the effective renal plasma flow of the colonic patients are shown in the appendix.

Non operative patients (Control group, N = 10)

The first ERPF results are available on 10 patients. The second ERPF results, six months later, are available on 9 patients.

Mean first ERPF = 549 Ml/Min.  S.D.= 170  Range 349 - 862
Mean second ERPF = 509 Ml/Min.  S.D.= 88  Range 397 - 645

Comparing the two sets of results in this group of patients, there was no significant difference between them P>0.05 (Wilcoxon test).

The results indicate that generalised arteriopathy does not appear to affect the effective renal plasma flow within a period of six months.
In the three groups of patients aortic, colonic, and non operative there was no significant change in the ERPF. This suggests that infrarenal aortic reconstruction, colonic surgery, and arterial disease all have no effect on the effective renal plasma flow.

The glomerular filtration rate and the effective renal plasma flow physiologically have a close relation. GFR / ERPF = Filtration Fraction, this is normally 0.2. To find out if the changes in GFR were also reflected on the ERPF, and also to confirm that these changes were due to to the effect of the operation on the renal blood flow; I will analyse the changes in ERPF in the same groups of patients discussed in the GFR section.

Changes in ERPF in aortic patients showing an immediate post-operative increase in the total GFR.

Mean Pre Op ERPF = 420 Ml/Min. S.D.= 145 Range 88 - 703
Mean Post Op ERPF = 528 Ml/Min. S.D.= 278 Range 111 - 1177
Mean Late ERPF = 409 Ml/Min. S.D.= 235 Range 142 - 909

Comparing the pre-operative and post-operative ERPF in this group of patients using the Wilcoxon test, there was no significant difference P>0.05. When the ERPF measured pre-operatively was compared to that six months after the operation, there was no significant difference P>0.05 (Wilcoxon test).

There was a significant difference between the immediate post-operative ERPF and the ERPF measured six months later. (Wilcoxon test) P=0.03.
E.R.P.F. CHANGES CORRESPONDING TO G.F.R. CHANGES

Ml/Min

P=0.01

P=0.003

PreOp PostOp Late
The results suggest the effective renal plasma flow in patients showing an immediate post-operative increase in the total GFR did not change post-operatively. ERPF measured six months later showed no change from the pre-operative value, but it showed a mean decrease of 119 Ml/Min. (23 per cent) when compared to the post-operative result.

Changes in ERPF in patients showing an immediate post-operative decrease in the total GFR.

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
<th>S.D.</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Pre Op ERPF</td>
<td>602 Ml/Min.</td>
<td>234</td>
<td>352 - 1137</td>
</tr>
<tr>
<td>Mean Post Op ERPF</td>
<td>496 Ml/Min.</td>
<td>153</td>
<td>279 - 802</td>
</tr>
<tr>
<td>Mean Late ERPF</td>
<td>534 Ml/Min.</td>
<td>206</td>
<td>224 - 909</td>
</tr>
</tbody>
</table>

Comparing the pre-operative and the post-operative ERPF in this group of patients, there was a significant decrease P=0.01 (Wilcoxon test). The mean decrease was 106 Ml/Min. (18 per cent)

Using the same test to compare the pre-operative and the late ERPF, and also the immediate post-operative and the late ERPF, there was no significant difference P>0.05.

In conclusion, the effective renal plasma flow in patients showing an immediate post-operative decrease in total GFR has also decreased. The ERPF measured six months later showed no change from the pre-operative value or the immediate post-operative value. When patients showed an immediate post-operative decrease in total GFR, this was associated with a decrease in the effective renal plasma flow, most probably due to micro-embolisation of the renal vascular bed during the operative procedure.
Changes in ERPF in aortic patients showing long term decrease in total GFR.

Mean Pre Op ERPF = 561 Ml/Min. S.D.= 222 Range 210 - 1137
Mean Post Op ERPF = 514 Ml/Min. S.D.= 220 Range 182 - 1177
Mean Late ERPF = 486 Ml/Min. S.D.= 221 Range 142 - 909

Comparing the ERPF pre-operatively and six months later in this group of patients using the Wilcoxon test, there was a significant decrease \( P=0.04 \). The mean decrease is 75 Ml/Min. (13 per cent of the pre-operative value).

When total glomerular rate showed a long term decrease this was associated with a decrease in the effective renal plasma flow.

Changes in ERPF in aortic patients showing a late increase in the total GFR.

Mean Pre Op ERPF = 465 Ml/Min. S.D.= 156 Range 88 - 702
Mean Post Op ERPF = 522 Ml/Min. S.D.= 218 Range 111 - 917
Mean Late ERPF = 406 Ml/Min. S.D.= 253 Range 142 - 909

Comparing the ERPF pre-operatively and six months later in this group of patients, there was no significant change \( P>0.05 \) (Wilcoxon test).

A late increase in total glomerular filtration rate was not associated with a similar increase in the effective renal plasma flow.
E.R.P.F. CHANGES CORRESPONDING TO LATE G.F.R. CHANGES

Late decrease in ERPF in patients showing decreased GFR

Ml/Min

- Decreased GFR
- Increased GFR

PreOp PostOp Late

P > 0.05

P = 0.04

P > 0.05

P > 0.05

P > 0.05

P > 0.05
CHAPTER FOUR

4.3 Changes In Individual Kidney
Glomerular Filtration Rate
It was important to test the individual kidney function in this study. Individual kidneys did not always contribute by 50 per cent of the function. The percentage of function of individual kidneys was obtained by DMSA renal scanning, this scan relies on both glomerular and tubular function. The total glomerular filtration rate measurements relies entirely on glomerular function, this test measure the combined renal function of both kidneys. McAfee, et al, 1986 showed an excellent correlation between DMSA renal uptake and DTPA clearance, the latter is glomerulary filtered. This allows us to divide the total glomerular filtration rate by the percentage of function of individual kidney in each patient to obtain individual kidney glomerular filtration rate.

1. Right kidney

When the pre-operative and post-operative GFR of the right kidney was compared using the Wilcoxon test, there was no significant difference \( P > 0.05 \).

Using the same test to compare the pre-operative and the late GFR of the right kidney, there was a significant decrease \( P = 0.04 \).

\[
\begin{align*}
\text{Mean Pre Op GFR} & = 42 \text{ Ml/Min.} & \text{S.D.} & = 15 & \text{Range} & = 0 - 81 \\
\text{Mean Post Op GFR} & = 45 \text{ Ml/Min.} & \text{S.D.} & = 16 & \text{Range} & = 0 - 89 \\
\text{Mean Late GFR} & = 38 \text{ Ml/Min.} & \text{S.D.} & = 14 & \text{Range} & = 0 - 66
\end{align*}
\]

The results suggest that the right kidney showed no change in its GFR immediately post-operatively, but six months later the GFR decreased. The mean decrease was 4 Ml/Min. (10 per cent of the pre-operative value).
2. Left kidney

When the pre-operative and post-operative GFR of the left kidney was compared using the Wilcoxon test, there was no significant difference $P>0.05$.

Using the same test to compare the pre-operative and the late GFR of the left kidney, we find a statistically significant decrease $P=0.007$

\[
\begin{align*}
\text{Mean Pre Op GFR} & = 40 \text{ Ml/Mn.} & \text{S.D.=} & 15 & \text{Range} & 11 - 74 \\
\text{Mean Post Op GFR} & = 40 \text{ Ml/Min.} & \text{S.D.=} & 13 & \text{Range} & 0 - 62 \\
\text{Mean Late GFR} & = 35 \text{ Ml/Min.} & \text{S.D.=} & 13 & \text{Range} & 0 - 65 \\
\end{align*}
\]

The results suggest that the left kidney showed no change in its GFR immediately post-operatively, but six months later the GFR decreased. The mean decrease was 5 Ml/Min. (13 per cent of the pre-operative value).

Although both kidneys seem to behave in the same way when analysing the results statistically. This was not strictly true in all of the patients. Some patients e.g. No 4 and 9 showed a decrease in function in one kidney this was associated with a compensatory increase in function by the opposite side. In one patient, No 59, the left kidney stopped functioning completely post-operatively and the renal function was maintained entirely by the right kidney.
CHAPTER FOUR

4.4 Renographic Changes
Renography is a perfusion study; it offers the assessment of individual kidney function relying entirely on the glomerular filtration of DTPA. It also shows the outflow tract and indicates any obstruction in it.

Renography was used to confirm the previous findings of individual kidney function. The renographic curve of each kidney was given a score regarding the function and clearance. This scoring was done by only one experienced observer who was unaware of the clinical details to achieve an unbiased result.

The Score:

++ = 5 Definitely normal
+ = 4 Probably normal
0 = 3 Equivocal
- = 2 Probably abnormal
-- = 1 Definitely abnormal

Aortic patients

Both the right and left kidney function was compared pre-operatively and post-operatively using the Wilcoxon test, there was no significant difference P>0.05, on either side.

The right kidney clearance showed no significant change P>0.05, when the pre-operative and post-operative scores were compared (Wilcoxon test). Five left kidneys showed a significant deterioration in their clearance, when the pre-operative and the post-operative scores were compared using the Wilcoxon test P<0.03.
Post-operative Renogram showing Bilateral Obstruction
When comparing the renographic scores pre-operatively and six months later using the Wilcoxon test, the function of the right kidney showed no significant change \( P>0.05 \), the left kidney showed a significant deterioration \( P=0.03 \). Both right and left kidneys showed no significant change in their clearance \( P>0.05 \).

**Control patients: colonic and non operative**

Both groups showed no significant change in function or clearance.

The results show that five left kidneys showed deterioration in their clearance in the immediate post-operative period, this was a temporary finding and was not present at six months. This is most likely to be due to the effect of surgery on the regional blood supply of the ureter. Four left kidneys six months later showed a decrease in their function. It is interesting that the renographic studies showed that the effects of surgery were mainly on the left kidney. The individual kidney GFR analysis discussed in the previous section suggested that both kidneys are affected in the same way, but as the scoring in the renographic work was done subjectively it is difficult to expect it to yield exactly the same result.
CHAPTER FIVE

Discussion
5.1 Changes In Total Glomerular Filtration Rate
G.F.R.

The aim of argument, or of discussion, should not be victory, but progress.

Joseph Joubert
Total glomerular filtration rate (GFR) was measured in this study as it reflects the overall total renal function. Small changes in total GFR are not reflected on the level of blood urea or serum creatinine. When serum creatinine concentration is only just above the normal range then the patient has functionally lost one kidney (Gabriel, 1986).

Changes in renal function following aortic surgery have been recognised for a long time. Earlier studies in this field (tab 1.1) showed that renal impairment occurred frequently. These studies relied mainly on biochemical testing of renal function. Nielsen and Engell in 1986 showed an increase in total glomerular filtration rate in the immediate post-operative period in patients undergoing elective infrarenal aortic surgery.

In this study total glomerular filtration rate was measured three times in each patient. Pre-operatively, 10 - 14 days post-operatively and six months later. The whole group of patients did not show a change in the GFR in the immediate post-operative period. Six months later the mean GFR decreased by 9 Ml/Min. comparing it with the mean pre-operative value. Examining the results of the whole group, the mean decrease in GFR was not evident in the immediate post-operative testing due to the an increased GFR in some patients. Dividing the patients into subgroups revealed that 26 patients have sustained a decrease in their GFR immediately post-operatively, this was associated with a decrease in the effective renal plasma flow. This immediate post-operative decrease in GFR was maintained on further testing 6 months later. The decrease in the ERPF suggests that the operative procedure led to a decrease in the renal blood flow, and consequently a reduction in the renal function.
If we take into consideration the reproducibility of GFR measurements and the fact that small changes are clinically insignificant, we find that a change of 11 ml/min. (10 per cent) is clinically significant. Examining the results taking this into consideration shows that in the immediate post-operative period 14 patients (26 per cent) increased their GFR, and 10 patients (19 per cent) decreased their GFR, the remainder were unchanged. Looking at the results at six months time taking the same factors into consideration, we find that 6 patients (12 per cent) showed an increased GFR, 21 patients (41 per cent) decreased their GFR, the remaining patients were unchanged.

The colonic group of patients showed no change in the GFR post-operatively indicating that the changes in the aortic patients are true changes due to the aortic reconstruction itself. The non-operative patients showed no change in the GFR within a period of six months. The decrease in GFR in the aortic patients six months post-operatively is likely to be due to the aortic reconstruction and not due to the progression of the arterial disease.

Melsen and Engell related the increased GFR in their patients to an increase in the extracellular fluid volume. This study showed no immediate change in GFR in the whole group of aortic patients. To obtain an index of the degree of hydration of the patients the Packed Cell Volume and haemoglobin estimation were carried out on the second blood sample used for every GFR estimation. No statistical correlation could be found between the GFR and the packed cell volume. Physiologically the changes in the degree of hydration will lead to changing the level of the antidiuretic hormone secreted by the pituitary gland, this in turn acts on the collecting tubules of the nephron controlling the urine concentration, and
should have no significant effect on the glomerular filtration rate. In our patients hydration did not affect the glomerular filtration rate.

Why should some patients show increased GFR post-operatively? Reduction of renal mass leads to structural and functional hypertrophy of the residual nephrons, with marked increases in the perfusion and filtration of remaining nephron units (Hayslett, 1979). Hyperfiltration in remnant nephrons has generally been regarded as beneficial; since it minimizes the reduction in total glomerular filtration rate that would otherwise ensue. Recent experimental observation, however, suggests that these changes are in fact maladaptive, in that sustained glomerular hypertension and hyperperfusion cause progressive glomerular structural damage. The price of this high glomerular pressure and flow, contributes in turn to the eventual destruction of the remaining glomeruli. These changes are morphologically identical to those seen in the aging kidney, the only difference is the speed of glomerular structural deterioration (Anderson and Brenner 1986).

Thurlbeck, in 1957 showed that embolisation of the renal vascular bed occurs frequently during infrarenal aortic reconstruction, most probably during the dissection of the aorta and clamping it. In this case the embolized glomeruli will stop functioning and the remaining non embolised glomeruli will show hyperfiltration. This hyperfiltration may or may not be accompanied by an increase in the renal blood flow, these changes start in the first 24 hours after nephrectomy (Hayslett, 1979). It is interesting to note that patients showing a decrease in GFR immediately post-operatively or after six months started at a higher GFR in comparison to those who showed an increase. It is likely that the patients who showed a decrease had no renal reserve to increase their GFR.
A total of 35 patients showed a decrease in GFR when tested six months post-operatively. As there was no change in the GFR of the arteriopathic control patients, the deterioration in function in the operative group is due to the effect of the aortic operation itself. There is currently no literature evidence to support the idea of the long term deterioration in the renal function as reflected by the glomerular filtration rate measurements. The theory of the maladaptive hyperfiltration effect may be the main contributing effect to this late deterioration. Continuous monitoring of arterial blood pressure, central venous pressure during the operation and in the post-operative period, and measurements of the left ventricular ejection fraction suggest that the pre-renal factors were unchanged in our patients during the study.

Four patients died post-operatively, three during their hospital stay and one 4 months later after his discharge.

Patient No. 13 had a repair of an inflammatory aneurysm. A bifurcated woven dacron graft was used. During the procedure his left renal vein was ligated and divided. Immediately post-operatively he was hypotensive, this was not due to hypovolaemia, his blood pressure remained low during the whole post-operative period. He regained consciousness after the operation, and on the third post-operative day developed a cerebro-vascular accident. He died on the 8th post-operative day. A postmortem examination showed that the left kidney was paler than the right, congested left suprarenal gland, and the stump of the left renal vein was not thrombosed. Histological examination showed no difference between left and right kidneys. The congested left suprarenal gland must be due to increased venous drainage through the left suprarenal vein after division of the left renal vein.
Patient No. 24 had a repair of an aortic aneurysm using a bifurcated woven dacron graft. He was known to have nephrotic syndrome and myxoedema. In the second post-operative day he lost consciousness and seemed biochemically to be in renal failure, also he appeared to have left hemiplegia. On pre-operative testing his GFR was 52 ml/min., ERPF was 426 ml/min., and both kidneys were equally functioning. During the operation blood pressure and central venous pressure were maintained, his urine output was 70 ml. Postmortem examination did not show histologically evidence of recent renal damage, a recent cerebral infarct was found to be the cause of death. This patient is the only one in the whole study to show biochemical evidence of renal failure post-operatively.

Patient No. 25 had a repair of an inflammatory aortic aneurysm using a bifurcated woven dacron graft. During the procedure the left renal vein was ligated and divided to allow access to the aneurysm neck. His past history included cerebro-vascular disease, myocardial infarction, and also fibrosing alveolitis. He died suddenly on the third post-operative day. Postmortem examination revealed that the cause of death was cardiac failure also he was found to have a bronchial carcinoma; although his pre-operative chest X ray was normal. The left kidney was paler than the right; both kidneys appeared normal histologically with no evidence of damage.

Patient No. 9 had an aorto-bifemoral knitted dacron graft inserted. He was admitted with rest pain in the right leg due to severe aorto-iliac occlusion. He had a myocardial infarction in the past. During the operation the left renal vein was ligated and divided to allow access to the aorta that very heavily calcified. Immediately post-operatively he suffered with high blood pressure that was very difficult to control.
He sustained a myocardial infarction 12 hours post-operatively. Before discharge from hospital his left ventricular ejection fraction was 20 per cent, a drop of 41 per cent from the pre-operative value due to his recent infarct. Also his GFR decreased by 17 Ml/Min., ERPF decreased by 108 Ml/Min., and the left kidney function decreased by 23 per cent. He died of a third myocardial infarction 4 months later at home; postmortem examination was not carried out.

Only one of our patients showed post-operatively biochemical evidence of renal failure, he had nephrotic syndrome for years before his operation. There was no evidence of renal impairment clinically or biochemically in the rest of the patients. This low incidence is perhaps due to accurate monitoring and adequate intravenous fluid therapy. This indicates that the changes in renal function in our patients were pre-clinical.
CHAPTER FIVE

5.2 Effect Of Pre Operative and Operative Parameters On the Outcome Of Renal Function
In this section various factors related to the patients and to the operative procedure are analysed to find out if any of them contributed to the changes in the renal function. The statistical analysis relate to either increases or decreases in the total GFR which is an index of the overall renal function. The analysis of the results are performed twice, first for the immediate post-operative period, second at six months after surgery. Operative details are available on 38 patients in this study.

The immediate post-operative period

1. Age

There was no difference in age between patients showing an increase or a decrease in GFR P>0.05 (Mann-Whitney U)

30 patients decreased GFR Mean age 63 years S.D. 10
29 patients increased GFR Mean age 63 years S.D. 9

It might be argued that older patients who have lower renal reserve would show more decrease in GFR. They did not.

2. Sex

There was no difference between males and females in this study as far as the outcome of the renal function is concerned P>0.05 (Chi Square)

30 decreased GFR 26 males 4 females
29 increased GFR 20 males 9 females

3. Indication

There was no difference in the outcome of renal function if the patient had aortic aneurysm repair or a bypass aorto-bifemoral grafting for occlusive aortic disease P>0.05 (Chi Square)
If the mechanism of renal damage was micro-embolisation, it might be argued that patients undergoing aneurysm repair, as they have a mural thrombus are liable to embolic complications, should show more renal deterioration than patients undergoing bypass procedures for occlusive disease. They did not.

4. Volume of Intravenous Infusions

The total volume of intravenous infusions during the operation had no effect on the renal function $P>0.05$ (Mann-Whitney U).

22 decreased GFR  Mean volume 4432 Ml.  S.D. 1363
16 increased GFR  Mean volume 3884 Ml.  S.D. 1482

5. Volume of blood loss

The volume of blood loss had no effect on the outcome of renal function in aortic patients $P>0.05$ (Mann-Whitney U).

22 decreased GFR  Mean volume 2191 Ml.  S.D. 1231
16 increased GFR  Mean volume 2169 Ml.  S.D. 1355

6. Volume of blood transfusion

The volume of blood transfusion had no effect on the renal function of the aortic patients $P>0.05$ (Mann-Whitney U).

22 decreased GFR  Mean volume 2159 Ml.  S.D. 692
16 increased GFR  Mean volume 2031 Ml.  S.D. 1161

7. Volume of urine output during the operation

The total urine output during the operation did not predict the future renal function of the aortic patients, there was no difference between
patients showing an increased GFR and patients showing decreased GFR
\[ P > 0.05 \text{ (Mann-Whitney U).} \]

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Volume (ml)</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased GFR</td>
<td>433</td>
<td>446</td>
</tr>
<tr>
<td>Decreased GFR</td>
<td>371</td>
<td>401</td>
</tr>
</tbody>
</table>

8. Volume of urine output during aortic cross clamping

This also was not an indicator of the future renal function of these patients and there was no difference between the two groups of patients \[ P > 0.05 \text{ (Mann-Whitney U).} \]

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Volume (ml)</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased GFR</td>
<td>60</td>
<td>115</td>
</tr>
<tr>
<td>Decreased GFR</td>
<td>40</td>
<td>53</td>
</tr>
</tbody>
</table>

During the operation particularly while the aorta is cross clamped and also in the post-operative period, maintaining a good urine output is an important clinical evidence that the kidneys are perfused and functioning well. The volume of urine output during the operation or during aortic cross clamping did not predict the post-operative renal function in our patients. This is confirmed by the work of Alpert, et al., (1984) found that intra-operative urinary output was not predictive of post-operative renal insufficiency in patients undergoing aortic reconstruction.

9. Duration of aortic cross clamping

The duration of aortic cross clamping was measured in minutes. There was no difference in the length of aortic cross clamping between the two groups of patients \[ P > 0.05 \text{ (Mann-Whitney U).} \]

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Duration (min)</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased GFR</td>
<td>64</td>
<td>19</td>
</tr>
<tr>
<td>Increased GFR</td>
<td>59</td>
<td>13</td>
</tr>
</tbody>
</table>

It is surprising that the duration of aortic cross clamping had no effect on the outcome of renal function. Although aortic clamps are
usually applied just below the left renal vein below the origin of the renal arteries, in theory they should not alter the renal blood flow. In practice these clamps may lead to kinking of the renal arteries or distorting their orifices, also the may occlude polar vessels that may be suppling these kidneys.

10. Forced diuresis

Forced diuresis was used in 15 patients using Frusamide, Mannitol or a combination of both. It did not offer any protection to the renal function. There was no difference between the two groups of patients $P>0.05$ (Chi Square).

<table>
<thead>
<tr>
<th>Increased GFR</th>
<th>Diuresis</th>
<th>No Diuresis</th>
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<td>16</td>
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<td>10</td>
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<td>22</td>
<td>9</td>
<td>13</td>
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</tbody>
</table>

It is believed by many surgeons and anaesthetists that forced diuresis particularly using mannitol has a protective effect on the renal function during aortic surgery. This was not the case in our patients as the results indicate that renal damage may occur with or without forced diuresis. Baird, et al, (1963) concluded that patients treated with mannitol during aortic reconstruction; showed an increased operative and post-operative urinary output, but there was no conclusive proof that the increased urine volume protected against post-operative renal dysfunction.

11. Type of aortic anastomosis

5 patients had the graft inserted end to side to the aorta, the rest were inserted end to end. This made no difference to the outcome of renal function in the aortic patients $P>0.05$ (Chi Square).

<table>
<thead>
<tr>
<th>Increased GFR</th>
<th>End to End</th>
<th>End to Side</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
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<td>4</td>
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<tr>
<td>16</td>
<td>15</td>
<td>1</td>
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</table>
12. Ligation and division of the left renal vein

Ligation and division of the left renal vein was not performed routinely in this study. The left renal vein was divided as close as possible to the inferior vena cava in six difficult cases to facilitate the cross clamping of the aorta. The left renal vein has three large tributaries, a large lumbar vein, the left supra renal vein, and the left testicular vein. The three tributaries allow the venous drainage of the left kidney to continue. Three deaths occurred in these patients, postmortem examination of those patients showed that the stump of the left renal vein was not thrombosed indicating that venous drainage continued after division, also both kidneys looked the same during naked eye and microscopic examination. One patient had a very congested left supra-renal gland, he suffered from hypotension immediately post-operatively. This hypotension was not due to hypovolaemia or haemorrhage.

There was a significant difference in the post-operative total glomerular filtration rate between the patients who had ligation and division of the left renal vein and the patients in whom the left renal vein was left intact. Patients who had ligation and division of the left renal vein showed a decrease in their GFR. $P=0.02$ (Fisher Exact). Perhaps this reflects the technical difficulty in these cases or a true effect, no conclusions could be drawn due to the small numbers.

<table>
<thead>
<tr>
<th>GFR Decreased</th>
<th>Intact Vein</th>
<th>Divided Vein</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>16</td>
<td>6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GFR Increased</th>
<th>Intact Vein</th>
<th>Divided Vein</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>16</td>
<td>0</td>
</tr>
</tbody>
</table>

All these previous factors with the exception of the division of the left renal vein seem to have no effect on the outcome of the renal function in the immediate post-operative period. The changes in the renal function measured immediately post-operatively seem to be unrelated to the
operative technique and the results do not suggest that any changes in the surgical procedure would offer these patients less damage to their renal function.

Changes in GFR six months post-operatively

1. Age

Six months post-operatively there was no difference in age between patients an increase or decrease in GFR $P>0.05$ (Mann-Whitney U).

<table>
<thead>
<tr>
<th></th>
<th>Decreased GFR</th>
<th>Increased GFR</th>
</tr>
</thead>
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<tr>
<td>43</td>
<td>Mean age 62 years</td>
<td>S.D. 10</td>
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<tr>
<td>16</td>
<td>Mean age 65 years</td>
<td>S.D. 9</td>
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</tbody>
</table>

Surprisingly patients showing a decrease in the GFR six months after surgery are younger than the patients showing an increase.

2. Sex

Six months post-operatively there was no difference between males and females as far as the outcome of the renal function is concerned $P>0.05$ (Chi Square).

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<thead>
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<th></th>
<th>Decreased GFR</th>
<th>Increased GFR</th>
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</thead>
<tbody>
<tr>
<td>43</td>
<td>36 males</td>
<td>7 females</td>
</tr>
<tr>
<td>16</td>
<td>10 males</td>
<td>6 females</td>
</tr>
</tbody>
</table>

3. Indication

Six months post-operatively there was no difference in the outcome of renal function if patients had aortic aneurysm repair or aorto-bifemoral grafting for occlusive disease $P>0.05$ (Chi Square).

<table>
<thead>
<tr>
<th></th>
<th>Decreased GFR</th>
<th>Increased GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>20 aneurysms</td>
<td>23 occlusive</td>
</tr>
<tr>
<td>16</td>
<td>10 aneurysms</td>
<td>6 occlusive</td>
</tr>
</tbody>
</table>
It is the clinical impression of many surgeons the aneurysm repair has more risks than bypass procedures. Our results show that the risk of renal damage in the long term in aneurysm cases is not higher than the occlusive ones.

4. Volume of Intravenous Infusions
Six months post-operatively the total volume of intravenous infusions during the operation had no long term effect on the renal function P>0.05 (Mann-Whitney U).

28 decreased GFR Mean volume 4350 Ml. S.D. 1510
10 increased GFR Mean volume 3785 Ml. S.D. 1152

5. Volume of blood loss
Six months post-operatively the renal function was not affected by the volume of blood loss during the operation P>0.05 (Mann-Whitney U).

28 decreased GFR Mean volume 2282 Ml. S.D. 1356
10 increased GFR Mean volume 1900 Ml. S.D. 980

6. Volume of blood transfusion
The volume of blood transfusion during the operation had no effect on the outcome of the renal function when that was measured 6 months post-operatively P>0.05 (Mann-Whitney U).

28 decreased GFR Mean volume 2161 Ml. S.D. 1063
10 increased GFR Mean volume 1950 Ml. S.D. 832

7. Volume of urine output during the operation
The total urine output during the operation did not indicate the renal function of the aortic patients when that was measured six months post-operatively P>0.05 (Mann-Whitney U).
8. Volume of urine output during aortic cross clamping
This also did not predict the renal function of the aortic patients when that was measured six months post-operatively P>0.05 (Mann-Whitney U).

- Decreased GFR: Mean volume 448 mL, S.D. 476
- Increased GFR: Mean volume 294 mL, S.D. 193

The urine output of the patients during the operation or during the period of cross aortic clamping did not predict the long term renal function when this was assessed by the glomerular filtration rate six months post-operatively.

9. Duration of aortic cross clamping
The duration of aortic cross clamping was measured in minutes. The length of the duration of aortic cross clamping had no effect on the renal function when that was measured six months post-operatively P>0.05 (Mann-Whitney U).

- Decreased GFR: Mean duration 64 Min., S.D. 17
- Increased GFR: Mean duration 56 Min., S.D. 15

I previously discussed the importance of the duration of aortic cross clamping. The results show that this had no effect on the outcome of renal function of aortic patients when that was assessed six months post-operatively.

10. Forced diuresis
Forced diuresis was used in 15 patients using Frusemide, Mannitol or a combination of both. This did not protect the renal function of the
patients when that was measured six months post-operatively P>0.05 (Chi Square).

26 decreased GFR diuresis 9 no diuresis 19
10 increased GFR diuresis 6 no diuresis 4

The results here show that forced diuresis had no protective effect on the long term renal function of aortic cases. Implying that the use of forced diuresis during the operation is unnecessary.

11. Type of aortic anastomosis

5 patients had the graft inserted end to side to the aorta, the rest were inserted end to end. This made no difference to the outcome of the renal function of these patients when that was measured six months post-operatively P>0.05 (Chi Square)

26 decreased GFR end to end 24 end to side 4
10 increased GFR end to end 9 end to side 1

12. Ligation and division of the left renal vein

Six months post-operatively there was no significant difference in the renal function between patients who had their left renal vein ligated and the others in whom the left renal vein was left intact P>0.05 (Fisher Exact).

28 decreased GFR intact vein 22 divided vein 6
10 increased GFR intact vein 10 divided vein 0

The effect of dividing the left renal vein on renal function seems to be only temporary in the immediate post-operative period. The effect of division of the left renal vein could be easily seen in the immediate post-operative period on renography, but six months later the renographic appearance returned to normal indicating that the effect was only temporary.
When the GFR was measured six months post-operatively 35 patients (69 per cent) showed a decrease, in only 21 patients (41 per cent) this decrease is of clinical significance. The data suggest that none of the factors analysed had an effect on the renal function of these patients. The effect of ligation and division of the left renal vein need further studies using a larger number of patients.
CHAPTER FIVE

5.3 Changes In The Effective Renal Plasma Flow
E.R.P.F.
The effective renal plasma flow (ERPF) in the aortic group of patients took a very similar course to the glomerular filtration rate (GFR). In the immediate post-operative period the mean ERPF decreased but this was not of statistical significance. Six months later the ERPF was 74 ml. (14 per cent) less than the pre-operative value, this just reached statistical significance P=0.05. These results indicate that the decrease in the GFR occurring at six months post-operatively was associated with a concurrent decrease in the renal blood flow.

When the glomerular filtration rate decreased in the immediate post-operative period or at six months, these changes were associated in both cases with a decrease in the effective renal plasma flow. This indicates that the decrease was due to a decrease in the renal blood flow most probably due to embolisation of a part of the renal vascular bed.

Patients showing an immediate increase in the glomerular filtration rate showed no corresponding increase in the effective renal plasma flow, this had significantly decreased six months later. At six months the effective renal plasma flow was not different from the pre-operative value. Patients showing an increased glomerular filtration rate at six months time showed no change in the effective renal plasma flow. Whether the patients showed an increase in the glomerular filtration rate in the immediate post-operative period or at six months this was not generally associated with a change in the effective renal plasma flow. This shows that the functioning glomeruli are exposed to the same volume of renal blood flow, and the increased glomerular filtration rate is perhaps a true hyperfiltration effect.
5.4 Changes in Individual Kidney Function
The percentage of function of each kidney was obtained using the DMSA renal scanning. The glomerular filtration rate which reflects the function of both kidneys was then divided by the percentage of function of each kidney to obtain the single kidney GFR which was used for the statistical analysis. The individual kidney function was also assessed from the renographic examination.

Immediately post-operatively there was no change in function in either right or left kidney. Six months later the right kidneys show a drop in function of 10 per cent (P=0.04), the left kidney also showed a decrease in function of 13 per cent (P=0.007). Renography also confirmed that in immediate post-operative period there was no change in either right or left kidney function, but six months later there was a decrease in function only on the left side.

Immediately post-operatively five left kidneys showed evidence of deterioration in their clearance. Six months later there was no change in the clearance of each side when that compared with the pre-operative findings. The immediate post-operative hold up may be due to interference with the blood supply of the ureter rendering parts of it ischaemic. The blood supply of the ureter is segmental. The beginning of the ureter it is mainly supplied by branches from the renal arteries and the aorta. Dissection of the aorta to allow for clamping may interfere with the ureteric blood supply. The changes are temporary as they recovered six months post-operatively.

Left kidneys that had ligation and division of the renal vein showed a decrease in function in the immediate post-operative period, six months later they returned to normal. The numbers are very small to allow for
statistical analysis but it seems that the dividing the left renal vein has a temporary effect on the left kidney function. In this group of patients ligation of the left renal vein led to decrease in the total GFR in the immediate post-operative period, perhaps indicating the technical difficulties in these cases and also the higher level of clamping. Division of the left renal vein had a dramatic effect on the renograms of these kidneys. Renography shows that there is a temporary decrease in the function of the left kidney and also decrease in the clearance. These changes returned to normal after 6 months.

DaLaurentis and McGowen, in 1979 studied left kidney function after division of the left renal vein using stump pressure measurement and left spermatic venograms. They concluded that ligation and division of the left renal vein is a reasonably safe procedure in selected patients when exposure of the perirenal aorta is crucial. This manipulation is possible because of extensive venous collateralization from the left kidney. Anatomic studies confirm the consistency of collateral venous channels to the left renal vein. These collaterals descend from the inferior phrenic and adrenal tributaries and ascend from the gonadal, capsular, lumbar, and ascending lumbar tributaries. Communication with major central veins occurs through the hemiazygos and azygos veins and through the rich network of external and internal vertebral plexi. Reanastomosis of the vein is not necessary for preservation of renal function, although transient left renal dysfunction may occur. Contraindications to division of the left renal vein are infrequent, they include uncertainty about the presence of function of the right kidney and if a significant depression of the function of the left kidney already exists. This clearly shows the importance of obtaining pre-operatively the individual kidney function.
Post-operative Renogram Showing The Effect Of Division

Of The Left Renal Vein
5.5 Conclusion
The data from this study indicates that more than 41 per cent of patients undergoing elective infrarenal aortic surgery sustain a clinically significant decrease in their renal function when assessed six months post-operatively. These changes were not apparent in the immediate post-operative period in all the patients. These changes may be preclinical in a lot of patients due to the presence of a large renal reserve. A total of 69 per cent of patients showed a decrease in the glomerular filtration rate, but half of the patients had very small changes that are considered insignificant.

It is important to obtain pre-operatively an accurate evaluation of the renal function in patients undergoing aortic reconstruction. This should include evaluation of individual kidney function. Patients with pre-operative renal impairment should not be considered unfit for this type of surgery, as the effects on the renal function are small and also it is interesting to note that patients who showed evidence of damage to their renal function had a pre-operative mean GFR higher than those who did not sustain damage. Patients with pre-operative impairment of the renal function were not excluded from surgery in this study, patient No 37 had a pre-operative GFR of 18 Ml/Min. She recovered uneventfully from her aortic aneurysm repair.

With the exception of one patient there was no clinical or biochemical evidence of renal failure in our patients, perhaps this is due to invasive monitoring and adequate intravenous fluid therapy.

The associated changes in the ERPF suggest that the underlying mechanism of decreased GFR is most likely to a decrease in the renal blood
flow. Pre-renal factors played no part in affecting the outcome of renal function in this study.

Both kidneys showed statistically equal evidence of damage. This was not clinically true in all patients. Patient No. 59 sustained a 100 percent loss to the left kidney function, he consequently developed severe uncontrollable hypertension that was attributed to his renal ischaemia.

Aortic surgery had no effect on the clearance on each side, six months post-operatively. Renography indicated that temporary decrease in clearance occurred in some left kidneys, but returned to normal 6 months later.

The parameters measured during the operation showed no effect on the long term renal function of these patients. Ligation and division of the left renal was the only parameter associated with with damage of the left renal function immediately post-operatively. Forced diuresis in this study did not offer any protection to the renal function. The changes in the renal function seem to be unrelated to the operative technique with the exception of ligation and division of the left renal vein which should be avoided if possible.

Further work is needed to study the renal function post-operatively after a period more than six months. Also an accurate study in cases of ruptured aortic aneurysms could be helpful as renal failure remains to be an frequent cause of death in these patients.

The effect of aortic cross clamping on the renal blood flow need further work in human beings. This is because we found no effect of
aortic cross clamping on the renal function of aortic patients, while some animal experiments showed changes in renal blood flow during aortic cross clamping in dogs.

Elective infrarenal aortic reconstruction has a preclinical effect on the renal function in the majority of patient. Accurate pre-operative evaluation of the renal function including the function of individual kidneys is essential before embarking on this type of surgery. The presence of renal impairment pre-operatively should not contraindicate aortic reconstruction provided that careful attention is given to the fluid balance in these patients. No changes in the operative technique are recommended to protect the renal function in those patients. Forced diuresis seems to be unnecessary during the operation as the results suggest that it did not affect the outcome of the renal function in our patients, and finally the urine output during the operation did not reflect the changes in renal function immediately post-operatively or 6 months later.
APPENDIX
APPENDIX

Total G.F.R.
Operative Group
MI/Min.
<table>
<thead>
<tr>
<th>Patient No</th>
<th>PreOp GFR</th>
<th>PostOp GFR</th>
<th>Late GFR</th>
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APPENDIX

E.R.P.F.,
Operative Group
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The effect of aortic clamping and declamping on renal blood flow distribution.

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