EFFECTS OF ANAESTHESIA AND SURGERY ON RENAL HAEMODYNAMICS

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Changes in renal function during anaesthesia and surgery have been noted since the beginning of this century. These changes occasionally are severe and may progress to acute renal failure. This paper reviews these alterations in renal function and attempts to analyze the various mechanisms involved, with special attention to the role of the renal circulation.

RENAL CIRCULATION

The kidneys are the most vascular organs, receiving approximately 25 per cent of the cardiac output although they constitute only 0.4 per cent of body weight. Almost all of the blood supplied to a kidney flows through the afferent arterioles of the glomeruli, the residual minute quantity entering hilar fat and renal capsule. After flowing through the capillary bed of the glomerulus the blood may take either of two routes, depending on whether the glomerulus is situated in the cortex or juxtamedullary region. Eighty-five per cent of the glomeruli are situated in the cortex. The blood from these glomeruli passes through the glomerular efferent arteriole which then subdivides into a capillary network in close contact with the tubule of that glomerulus. The efferent arteriole of the 15 per cent of glomeruli situated in the juxtamedullary region branches repeatedly, giving rise to straight capillary channels which plunge directly into the inner medulla, turn a hairpin bend at the tip of the papilla to return to the juxtamedullary region and join the venous system. These straight capillary channels are called vasa recta and play important roles in the countercurrent system of concentration of urine. There are, therefore, four different anatomical and functional parts of the kidney—cortex, juxtamedullary region, medulla and perirenal fat. Each part has its own special type of vasculature intimately related to function. Alterations in renal function could thus occur either by changes in total renal blood flow or by a redistribution of flow within the kidney in the presence of unaltered total flow.

Constriction of the afferent glomerular arteriole results in both decreased renal blood flow and glomerular filtration. Constriction of the efferent glomerular arteriole also results in decreased renal blood flow but in addition increases the fraction of flow being filtered at the glomerulus—the filtration fraction.

Glomerular arterioles are innervated through the sympathetic nervous system (Mitchell, 1951) with stimulation resulting in constriction. Under basal conditions there is very little stimulation of the renal vasculature and renal blood flow is probably near maximum value. Any effect on the renal circulation tends to produce a reduction in renal blood flow.

MEASUREMENT OF RENAL HAEMODYNAMICS

Renal Plasma Flow (RPF)

Clearance of para-aminohippuric acid.

The most frequently utilized method involves the clearance of para-aminohippuric acid (PAH) by the kidney. Under specific circumstances it can be shown that PAH clearance equates with renal plasma flow.

The clearance of a substance by the kidney is

\[
UV/P \text{ ml per min}
\]

where \( U \) = urinary concentration of the substance;
\( V \) = volume of urine per minute;
\( P \) = plasma concentration of the substance.

The Fick principle states that the blood flow (F) through an organ can be calculated by measuring the concentration of a substance in the artery (A) and vein (R) and determining the quantity (Q) of that substance removed by the organ per minute. According to Fick,

\[
F = Q/(A - R) \text{ ml per min}
\]

The clearance of a substance is not removed by lymph and not stored in the organ; therefore

\[
F = (U \times V)/(A - R)
\]

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When metabolism of the renal tubules is normal, then \( R \) is negligible and
\[
F = U \times V/A \quad (iv)
\]
Since PAH is not metabolized in the peripheral tissues, the arterial and peripheral venous concentration \( (P) \) is equal and
\[
F = U \times V/P = \text{PAH clearance} \quad (v)
\]
Therefore, when PAH clearance is equated with renal plasma flow the following assumptions have been made.

1. The convoluted tubules involved in PAH secretion have undisturbed metabolism.
2. PAH is not stored in the kidney.
3. Volume of urine formed is adequate to allow accurate measurement over the period under study.
4. Blood flow through the kidney is not diverted to areas incapable of secreting PAH such as the medulla.

In conditions of antidiuresis and oliguria it is incorrect to make any of these assumptions and this is recognized by renaming PAH clearance "effective" renal plasma flow.

\[ \text{Renal Blood Flow (RBF)} \]
\[
\text{RBF} = \frac{\text{Renal plasma flow}}{1-\text{Haematocrit}}.
\]

\[ \text{Glomerular Filtration Rate (GFR)} \]
\[ \text{Creatinine clearance or inulin clearance} \]

If a substance is filtered at the glomerulus and is neither reabsorbed nor secreted by the tubule, then the clearance of that substance equals the glomerular filtration rate. These criteria apply to inulin under all conditions and also to creatinine in man unless there is very poor renal function or the nephrotic syndrome is present.

\[ \text{Filtration Fraction (FF)} \]
This is the fraction of renal plasma filtered.
\[
\text{FF} = \frac{\text{GFR}}{\text{RPF}}
\]
Filtration fraction is increased if there is efferent glomerular arteriolar constriction.

\[ \text{Renal Vascular Resistance (RVR)} \]
This is measured by
\[
\frac{\text{Mean arterial pressure}}{\text{Renal blood flow}}
\]

**Intrarenal Distribution of Blood Flow**

Inert gas washout technique.

A bolus of xenon-133 dissolved in saline solution is injected through a catheter placed in the renal artery. The gas equilibrates immediately with the renal parenchyma. The rate of washout of the gas from the parenchyma is monitored by an external scintillation counter. This washout curve is analyzed as the sum of four exponential components. The components represent the rate of washout of the gas from the cortex, juxtamedullary region, medulla and hilar fat (Thorburn et al., 1963). The percentage of renal blood flow supplied to each of these areas is proportional to the size of the component. The flow per unit mass of tissue in each of these areas can be calculated from the slope of each component using the Kety application of the Fick principle (Rosen et al., 1968).

**EFFECT OF PREMEDICATION**

The antidiuretic effect of morphine has been recognized for more than half a century and has been investigated extensively. Attempts to define the precise mechanisms responsible in patients have been complicated by many factors. These include the difficulties inherent in applying data obtained in animals to the circumstances pertaining in patients. Difficulties also arise in comparison of the relatively large doses on a body weight basis used in animals to the doses given in man. Interpretation is further aggravated in many of the studies in patients because of the background of discomfort, variable degrees of hydration and electrolyte balance, infection and emotional stress. Theories concerning the decrease in urine volume following morphine administration have centred on either an increase in secretion of antidiuretic hormone or an alteration in renal haemodynamics, or a combination of both of these factors.

**Results of Animal Experiments**

Antidiuretic hormone.

Morphine has been observed by many workers to cause a decrease in urine volume in well-hydrated dogs and also to depress the renal response of normal dogs to administered water. The dosage of morphine used varied from 0.08 to 5 mg/kg body weight (Debodo, 1944; Duke et al., 1951). Evidence for a role for antidiuretic hormone in this urinary response was obtained when Duke and co-workers (1951) noted that morphine inhibited water diuresis when only 4-32 μg were injected into the supra-optic
nuclei during water diuresis. This evidence is strengthened by the finding of an antidiuretic substance in the urine of dogs undergoing antidiuresis following injection of morphine (Lipschitz and Stokey, 1947). This antidiuretic substance in the urine was not morphine since it was not inhibited by nalorphine (Winter, Gaffney and Flataker, 1954), and in several characteristics it resembled vasopressin (Giarman, Mattie and Stephenson, 1953).

Renal haemodynamics.

Doses of morphine in excess of 2 mg/kg body weight administered to dogs cause a decrease in creatinine clearance and PAH clearance. This implies that altered renal haemodynamics are at least partly responsible for the antidiuresis. Additional evidence for a mechanism other than ADH is also suggested by data from dogs in which diabetes insipidus has been caused by division of the hypophyseal stalk (Handley and Keller, 1950). An antidiuresis still appeared on administration of morphine, but the renal haemodynamic data in the dogs with diabetes insipidus are particularly difficult to interpret because a section of the hypophyseal stalk per se caused a reduction of 50 per cent in both the creatinine clearance and PAH clearance.

Results of Investigation in Human Subjects

The effect of 10–16 mg morphine administered intramuscularly has been investigated. Diuresis was stimulated by an infusion of 5 per cent dextrose. Each subject served as her own control. Morphine diminished the urine volume without increasing urinary specific gravity or chloride concentration. This suggested that an influence other than ADH was producing the antidiuresis (Kraushaar et al., 1949). Administration of morphine, by the same authors, to women with diabetes insipidus has been followed by a decrease in diuresis, although this was less than that in normal persons. The urine specific gravity and chloride concentration of the urine again failed to rise, providing an answer to the criticism that these patients may have had a small residual degree of posterior pituitary function.

More direct evidence for the action of morphine on the renal haemodynamics of man has been obtained by measurement of PAH and inulin clearance. Several groups have concluded that antidiuresis is accompanied by decreased glomerular filtration rate and “effective” renal plasma flow (Brown, Hodges and Bradbury, 1949). Thus all the evidence in man suggests a renal haemodynamic mechanism for the antidiuresis of morphine.

METABOLIC EFFECTS OCCURRING DURING SURGERY

During surgery metabolic changes may occur. Most of these changes may be due to the effects of the primary illness or be secondary to the stimuli and complications of surgery, but side effects of anaesthetic drugs may also make a contribution. The effects of some of these changes on the renal circulation have been investigated.

Hypotension

The classical model for the investigation of the effects of hypotension on the renal circulation has been produced in the dog. A cannula from the femoral artery allowed bleeding into a reservoir so that the hypotension could be maintained at a stable level. At a mean blood pressure of 70 mm Hg there are profound changes in renal haemodynamics. Renal blood flow measured by PAH clearance falls dramatically and this has been confirmed by using an electromagnetic flowmeter. This reduction in renal blood flow is accompanied by an intrarenal redistribution of blood flow as measured by the inert gas washout technique. The redistribution of blood flow is due to a decrease in percentage of total renal blood flow being supplied to the cortex. Autoradiography of the kidney in these circumstances shows patchy areas of cortex perfused at a grossly diminished rate (Rosen, 1968).

Serial measurements of intrarenal distribution of blood flow in this study showed that as the duration of hypotension increased there was a progressive reduction in percentage of total renal blood flow supplied to the cortex. This redistribution was not prevented by completely denervating the kidney nor by the administration of mannitol before or during the hypotension. Injection of papaverine and acetylcholine into the renal artery did not modify the patchy cortical hypoperfusion but alpha-adrenergic blockade completely prevented or corrected it (Truniger et al., 1971). This evidence indicated that the cortical ischaemia under these conditions was due to circulating catecholamines.

Activation of the Sympathetic Nervous System

There are many reports indicating that increased quantities of catecholamines may be liberated from sympathetic nerve endings, the adrenal medullae and
possibly the central nervous system during anaesthesia and surgery (Price et al., 1959). The effect of such catecholamines on renal haemodynamics could be profound. Continuous infusion of adrenaline and noradrenaline (Moyer and Handley, 1952) caused a decrease in creatinine clearance and PAH extraction which was inversely proportional to the dose infused and also to the resultant elevation in systemic blood pressure. Filtration fraction increased indicating efferent arteriolar constriction. This effect of noradrenaline is exaggerated when blood volume is diminished (Nelson, Henry and Lyman, 1961).

Stimulation of the sympathetic system may be caused by multiple factors. It may be due to anaesthetic drugs such as diethyl ether and cyclopropane. Hypotension as a cause of stimulation of the sympathetic nervous system has already been discussed. The trauma of surgery per se could be a potent cause. In the latter circumstances the noradrenaline may be liberated at the nerve ending in the renal vasculature itself since renal cortical ischaemia induced by exploration of the peritoneal cavity can be prevented by denervation of the kidney (Rosen et al., 1967).

Electrolyte and Acid-base Disturbances
Alterations in electrolyte and acid-base balance can be due to many causes. Insufficient preoperative preparation of an ill patient, poor choice of replacement fluids, chest infections, inadequate ventilation, etc. All these abnormalities are associated with changes in the renal circulation. Specifically, hyponatraemia and acidosis have been shown to be associated with decreased blood flow and decreased glomerular filtration rate.

Hypothermia
Decrease of PAH secretion correlates with the degree of cooling reaching an estimated zero at 23°C (Page, 1955).

EFFECTS OF ANAESTHETICS
Many reports stress the adverse effects of diverse anaesthetic agents on the renal circulation (Habif et al., 1951; Blackmore et al., 1960; Deutsch, Pierce and Vandam, 1967; Westermark, 1969). Creatinine clearance and PAH clearance are reduced with cyclopropane, diethyl ether, thiopentone, and halothane. The effect on general vascular resistance varies with the type of anaesthetic, being increased with cyclopropane and indicating efferent arteriolar constriction, whilst it is decreased with halothane.

The relative contribution made by the drug to changes in renal haemodynamics in a specific clinical situation is difficult to assess because of varying dosage regimens in the reports and possible differences in the reactivity of the renal circulations in the animals studied. In clinical practice it may also be a problem to divorce the direct effect of the drug on the renal vasculature from the effect of other factors previously discussed and shown to exert an intrarenal vasoconstrictor effect. Attempts have, however, been made to dissect these various facets.

Dosage.
Blackmore et al. (1960) described changes in the renal circulation of dogs given 2 per cent halothane. During anaesthesia with 1.5 per cent halothane the measurements of renal haemodynamics returned toward control volumes although urinary volume and electrolyte excretion remained abnormal. In man, changes in the renal circulation occur at both levels of dosage but there is a greater percentage fall at the higher dosage (Mazze et al., 1963).

Morris and co-workers (1959) using cyclopropane and ether claimed that there was no significant alteration of glomerular filtration rate and renal blood flow if the dosage was considerably reduced and surgery conducted under light anaesthesia with the assistance of suxamethonium.

Hydration.
Mazze et al. (1963) suggested that renal circulatory changes can be prevented by adequate hydration prior to anaesthesia and Barry, Mazze and Schwarz (1964) provide supportive evidence. However, this is not corroborated by Deutsch and co-workers (1966) who measured the effect of 1.5 per cent halothane in oxygen in thirteen hydrated normal human volunteers without preanaesthetic medication or operation. Infusions of ethyl alcohol were used to reverse the antidiuresis associated with anaesthesia and to obtain urine volumes greater than 2 ml/min to allow the application of inulin and PAH clearance techniques. Glomerular filtration decreased by 19 per cent and renal blood flow decreased by 38 per cent during anaesthesia. The same workers found under similar conditions of diuresis that cyclopropane reduced GFR by 39 per cent and renal blood flow by 42 per cent (Deutsch, Pierce and Vandam, 1967). Considerable research has revealed some of the mechanisms by which anaesthetics exert their effect on renal blood flow.
Sympathetic nervous system.

Price and co-workers (1959) described the effects of cyclopropane, thiopentone, diethyl ether and halothane on the concentration of plasma catecholamines. Noradrenaline concentration significantly increased by more than 0.5 μg/l in most of the normal subjects receiving cyclopropane or diethyl ether. The amount of increase was significantly related to the concentration of anaesthetic in blood during cyclopropane but not during ether anaesthesia. The source of the noradrenaline was probably from the nervous system since plasma noradrenaline concentration did not rise in two bilaterally adrenalectomized patients and in one patient who concomitantly received a high spinal anaesthetic. Halothane and thiopentone anaesthesia were not associated with significant changes in plasma noradrenaline concentration.

The vascular response to increased plasma concentration of noradrenaline was investigated by studying the haemodynamic changes brought about by infusion of the substance during anaesthesia. It was concluded that the response in systemic blood pressure to infusion was normal in cyclopropane and diethyl ether anaesthesia but reduced during halothane and thiopentone administration.

Hypotension.

Price and co-workers (1959) indicated that the blood pressure in man was better maintained in patients receiving cyclopropane and diethyl ether anaesthesia. The fall in blood pressure was not proportional to the dose of anaesthetic but hypotension could usually be increased by increasing the dose of anaesthetic (except with cyclopropane). Westermark (1969) concluded that hypotension was a major cause of the renal circulatory response to halothane in cats although the fall in renal blood flow was proportionately less than the fall in blood pressure.

EFFECT OF CHANGES IN RENAL HAEMODYNAMICS

Sodium Retention

During and following anaesthesia there is retention of sodium with consequent fluid retention. Out of this phenomenon grew the practice of restricting fluid prior to anaesthesia. It has, however, been claimed that this fluid retention can be prevented by taking prophylactic precautions against stimuli known to cause intrarenal vasoconstriction; and these measures include adequate preoperative hydration (Barry, Mazze and Schwartz, 1964). There are two major mechanisms by which sodium retention occurs during renal vasoconstriction.

Glomerular filtration.

Sodium is filtered at the glomerulus and decreased amounts would be available for excretion when there is a reduction of glomerular filtration rate. The latter has invariably occurred whenever renal blood flow is diminished. Reduced glomerular filtration of sodium could theoretically be counterbalanced by reduced tubular reabsorption, but the opposite effect probably occurs as described below and accentuates the problem.

Tubular reabsorption.

Sodium is usually reabsorbed in the proximal tubule in isotonic concentration but speculation has recently occurred concerning active reabsorption at this site. However, very little is known about the mechanisms for sodium reabsorption in the proximal tubule in clinical states. At the distal tubule, sodium is reabsorbed under the influence of aldosterone. Increased production of aldosterone following surgery is indicated by the presence of increased quantities of salt-retaining hormone in the urine of such patients (Llaurado, 1955). The stimulus for the increased aldosterone production could be preoperative dehydration or increased renin secretion or a combination of both. The trigger for the aldosterone release could be via the renin-angiotensin system or via baroceptors in the right atrium. Renin is produced in the juxtaglomerular apparatus which is associated with theafferent glomerular arteriole. Release of renin is precipitated by several mechanisms occurring during anaesthesia and surgery. Liberation of renin has been reported following the infusion of catecholamines (Wathen et al., 1965; Vander, 1965). Sympathetic innervation as found in the juxtaglomerular apparatus (Barajas, 1964) may play a role in the function of the juxtaglomerular apparatus as a renal baroceptor responding to changes in blood pressure (Skinner, McCubbin and Page, 1963).

The renin secreted acts on a plasma alpha-2-globulin to produce the decapeptide angiotensin I. This is then converted to the active octapeptide, angiotensin II by plasma enzymes. Angiotensin II is a stimulus to the adrenal cortex to secrete aldosterone. Thus stimulation of renin associated with decreased renal blood flow could cause salt retention through the agency of aldosterone. This
chain of events probably does occur following surgery since increased concentration of renin has been found in peripheral venous blood following surgery (Deutsch, Pierce and Vandam, 1967). Angiotensin II is itself a powerful vasoconstrictor agent and when produced within the renal circulation may further aggravate existing intrarenal vasoconstriction (Schmid, 1962; Thureau, 1964).

**Acute Intrinsic Renal Failure**

Factors causing intrarenal vasoconstriction result in decreased urine flow and abnormal electrolyte excretion. When these factors are removed the vasoconstriction usually quickly reverses and urine formation reverts to normal. Occasionally return of normal urine formation is considerably delayed and this particularly occurs when there is coexistent sepsis, jaundice, crush injury, pregnancy or mismatched transfusion. This resultant condition is then called acute intrinsic renal failure and is more likely to occur when an illness requires anaesthesia and surgery. During acute intrinsic renal failure there is persistence of renal vasoconstriction following removal of the original vascular stimulus. Early studies on renal blood flow using PAH excretion and clearance indicated that blood flow was reduced at 3 per cent of control values, and it was concluded that the kidney was severely ischaemic (Bull, Joekes and Lowe, 1950). Because of the basic problems inherent in measuring blood flow in the oliguric kidney using PAH, this conclusion regarding the extreme severity of the ischaemia cannot now be justified. Techniques suitable for such occasions show that blood flow was 39 per cent of control value during the oliguric phase, rising to 70 per cent of control value during the recovery phase (Shaldon et al., 1964). The persistence of oliguria in acute intrinsic renal failure cannot be explained only by a reduction in total renal blood flow since patients with chronic renal failure maintain reasonable function with flow reduced to 40 per cent of normal. A possible explanation for the oliguria is that the blood supplied to the kidney is distributed to areas not predominantly concerned with filtration (Shaldon et al., 1964) since there is evidence for heterogeneity of nephron function (Coehelo and Bradley, 1964). This explanation is supported by observations of altered red cell transit time through the kidney (Shaldon et al., 1964) and has been confirmed by measurement of the intrarenal distribution of blood flow using the inert gas washout technique (Hollenberg et al., 1968).

The reason for the persistence of an abnormal intrarenal distribution of blood flow following removal of the vasoconstrictor influences may be related to the blockage of parts of the intrarenal vasculature with fibrin deposits (Clarkson et al., 1970).

**REFERENCES**


BOOK REVIEW


Mr Roberts is consultant cardiothoracic surgeon and Dr Edwards is consultant anaesthetist at Birmingham Children's Hospital. They describe this book as a manual for resident doctors and senior nurses to whom they aim to make clear the basic principles underlying the care of the critically ill child. They have deliberately adopted a pragmatic approach and only a few references are given.

The first three chapters are concerned with the concept of intensive patient care, design features of the unit and the control of cross-infection. Most people will agree with their statement that there is really no place for the specialist "intensivist" who takes over the care of a patient completely. They go on to state that an "intensivist" cannot have the knowledge in depth of all problems likely to arise and it is better for the director of the unit to act as a co-ordinator of the various disciplines that may be concerned in the care of an individual patient.

They also correctly stress that an ITU is not a means of remedying an overall nurse shortage nor is it economical to run in terms of trained nursing staff.

Chapters 4 deals with "Fluid, electrolyte and metabolic balance". This is the longest chapter in the book and this difficult and often controversial subject is presented lucidly. It will be extremely useful to residents concerned intensive therapy. Chapters on "Acid/base balance and blood gas studies", "Respiratory physiology" and "Cardiovascular physiology" then follow. These chapters are quite comprehensive and orthodox. Dr Hall Davies, consultant anaesthetist, has written the chapter on "Patient monitoring". He stresses the need for a bedside nurse irrespective of the amount of monitoring equipment being used. The difficulties of various methods of measuring blood pressure and central venous pressure in infants are described. The dangers of too great a reliance on the electrocardiogram as a means of respiratory monitoring are also emphasized. The chapters on "Radiological investigations", "The nurse in the ICU" and "Acute renal failure" have been contributed by a radiologist, the sister-in-charge of the ITU and a paediatrician respectively. These add considera-bly to the range of subjects covered in this book.

Most of the remaining chapters are orientated, as one might expect, towards respiratory and cardiovascular management with chapters on "Ventilators", "Care of respiratory problems", "Post-operative thoracic surgical care" and "Cardiovascular management". The final chapters are devoted to "Special problems of neonates", "Convulsive states and the unconscious patient" and "Emergency resuscitation". Then follows an appendix which deals with doses of over thirty drugs commonly used in the ITU. Brief comments are made on each drug.

The authors have succeeded very well in their aims and this book will be extremely useful to the two groups mentioned earlier, namely, resident doctors and senior nurses. In addition it will also be useful to more senior specialists who may wish to find concise answers to problems in intensive care outside their own particular field.

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