

The Effects of Perfusion on Renal Function

Philip D. Beckley, B.S. and Joseph P. Mandl, M.S.

Circulation Technology Division, The Ohio State University, 1583 Perry Street,
Columbus, OH 43210.

INTRODUCTION

The incidence of acute renal failure as a result of open heart surgery is difficult to quantify (Table 1). Some investigators are reporting this complication as any renal impairment following the surgical procedures in which case the incidence approaches 40%.¹ Others report only those cases which involve severe renal failure, occurring less than 10%.²⁻⁵ The real importance, however, in the analysis of this data, is not the absolute incidence of this complication. Rather, the importance is that the mortality rate of patients with severe acute renal failure following open heart surgery approaches 100%, even though this is a theoretically reversible complication and that aggressive medical management is available.⁵ In addition, the incidence of acute renal failure is likely to be on the increase due to the increase of the high risk surgical patient population. This paper will review foundational physiological principles regarding this complication and summarize a number of considerations for the perfusionist.

PHYSIOLOGICAL PRINCIPLES

Vasoconstriction—A common denominator for factors leading to post perfusion acute renal failure will now be reviewed (Fig. 1).

In hypotension or hypovolemia—The kidney actively participates in what is termed “protective redistribution of blood flow.”⁶ When either hypovolemia (e.g., pre-operative dehydration) or hypotension (e.g., low perfusion pressure) begins to compromise blood flow to vital organs such as the heart and brain, the kidney will begin to sacrifice its blood flow by redistributing it to these more vital organs. It is difficult to say with precision at what point in the trend of declining blood pressure this redistribution begins. When mean perfusion pressure is maintained at or above 80 mmHg the incidence of subsequent renal impairment is less than 13%. However, when mean perfusion pressure is less than 80 mmHg for over 30 minutes the increase of incidence is quite significant at 35%.³ These facts would indicate that low pressure bypass time, i.e. the quantity of time perfusion pressure is below 80 mmHg, is an important factor in vasoconstriction and subsequent ischemia.²

An interesting mechanism has been described which explains a vicious cycle created when vasoconstrictive ischemia leads to additional vasoconstriction.⁷ A precise balance is normally maintained in each nephron between the amount of solute (mainly sodium)

TABLE I: INCIDENCES OF ACUTE RENAL FAILURE (ARF)
FOLLOWING OPEN HEART SURGERY

STUDY	NO. OF PATIENTS	ANY RENAL IMPAIRMENT	SEVERE ARF %
ABEL (1)	507	39	
BHAT (2)	490	26	4
DOBERNECK (4)	1000		3
McLEISH (5)	1542	02	
YEBOAH (3)	428	26	5

filtered into the tubule and the amount which is delivered to the distal parts of the nephron after initial tubular reabsorption. This is termed the "autoregulation of the kidney" and allows for precise filtration in spite of fluctuating renal perfusion pressure. If, for example, the amount of solute delivered to the distal nephron is higher due to increased perfusion pressure, the nephron will decrease the amount of solute filtered by vasoconstriction of the preglomerular arterioles. When renal ischemia occurs, the amount of energy available for the initial tubular reabsorption is diminished, which mimics the situation of increased solute load delivered to the distal nephron. The kidney, then, with this unfortunate misinformation, will vasoconstrict further. This in turn will additionally increase the ischemia and continues the vicious cycle.

In hemolysis and hemoglobinuria (Fig. 3)—Free hemoglobin is about the largest molecule that can pass through the "pores" of the glomeruli of the kidney (molecular weight approximately 68,000). Under normal circumstances, however, no hemoglobin is found in the urine because it is bound to plasma haptoglobin in a concentration of approximately 5 mg%. Generally, there is sufficient haptoglobin to bind free hemoglobin up to concentrations of 125 mg%, if that concentration should exist. Above this plasma concentration, hemoglobin is filtered into the tubule of the nephron and, except for a small amount that is reabsorbed, appears in the urine.

One study indicated that 85% of those patients with plasma free hemoglobin concentrations greater than 300 mg% developed acute renal failure and nearly all of those patients experienced a perfusion time in excess of four (4) hours.² Other analyses indicate that the incidence of acute renal failure significantly increases as bypass time exceeds 120 minutes.³ Therefore, these facts would indicate that high plasma free hemoglobin

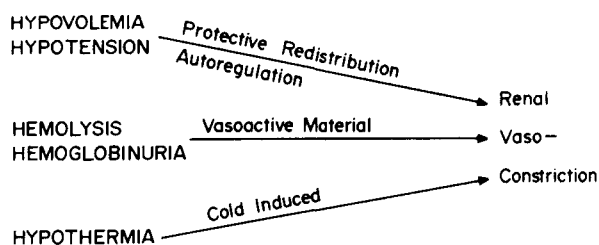


Figure 1. Factors of acute renal failure following open heart surgery.

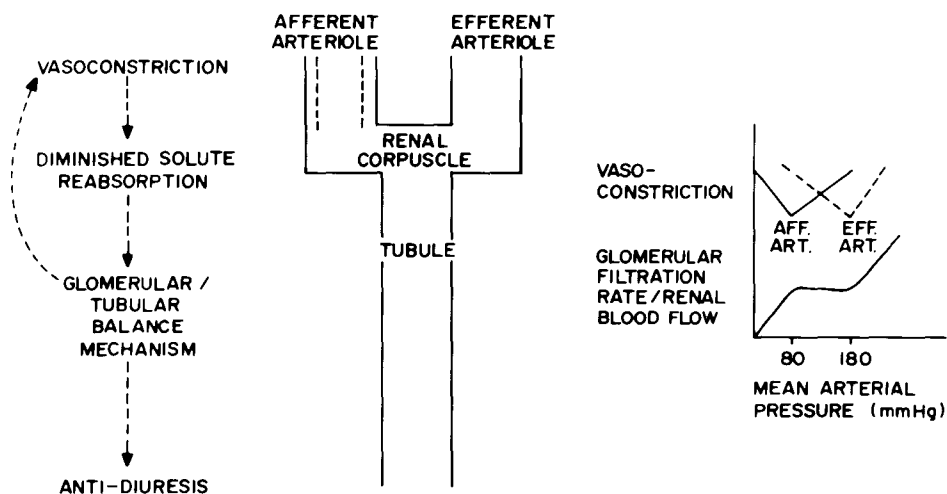


Figure 2. Vasoconstrictive physiology due to hypotension and/or hypovolemia.

due to mechanical red cell destruction is a product of long bypass time and contributes significantly to acute renal failure.

Pre-glomerular vasoconstriction has been implicated as a causative factor in acute renal failure as a result of hemolysis.⁸ This may be related to the release of vasoactive substances such as catecholamines and serotonin from mechanically destroyed cellular elements.⁷ Renal failure due to hemoglobinuria can be potentiated by hypotension and hypovolemia. It is difficult to produce acute renal failure in an experimental animal by infusing high concentrations of hemoglobin when the animal is well hydrated and nor-

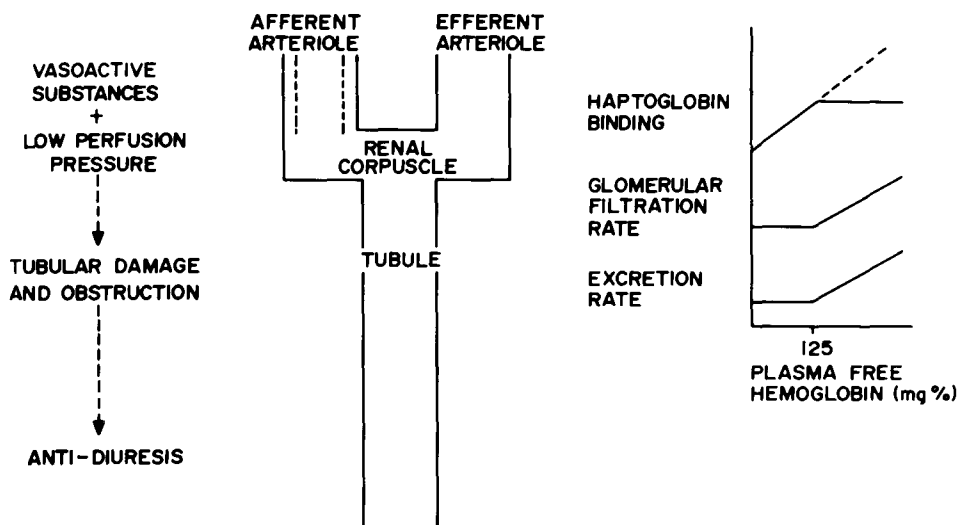


Figure 3. Vasoconstrictive physiology due to hemolysis and hemoglobinuria.

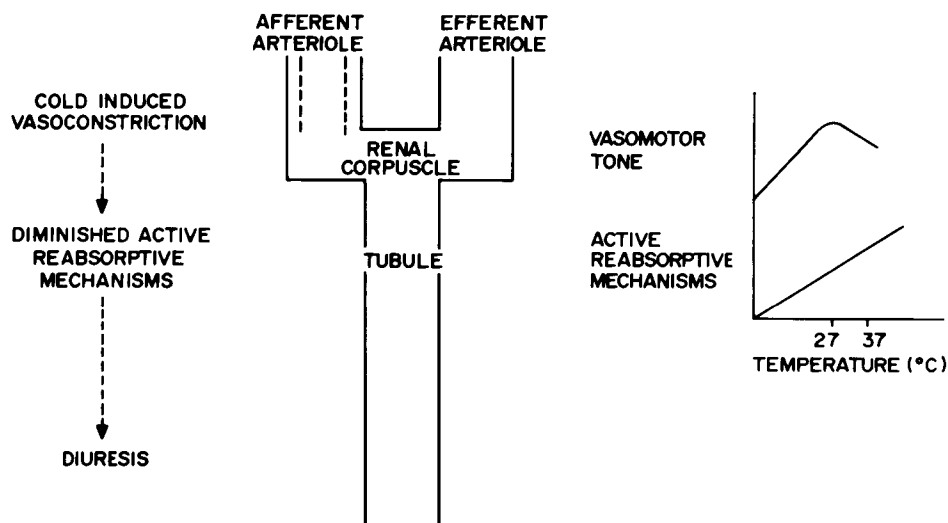


Figure 4. Vasoconstrictive physiology due to hypothermia.

motensive.⁵ A lesion which occurs in hemoglobinuria and lends itself to renal failure, in part, depends on this state of reduced hydration and increasing vascular tone.² In this situation, the hemoglobin in the tubule becomes highly concentrated and precipitates thus leading to tubular obstruction and damage.

In hypothermia (Fig. 4)—Renal vasoconstriction also plays a part in hypothermia.⁹ At 27°C there is a cold induced vasoconstrictor response in the kidney which occurs most selectively in the inner portions of kidney parenchyma. At this temperature the active mechanisms which are responsible for the reabsorption of electrolytes (with water following passively) are depressed. Although renal vasoconstriction is occurring, this means that the hypothermia is accompanied by a diuresis and electrolyte excretion. Further cooling does not produce additional vasoconstriction but rather a renal vascular dilation due to the difficulty of the contraction of vascular smooth muscle. This is particularly the case at temperatures below 18°C. Additionally, active reabsorptive mechanisms

ELEVATED CHEMISTRIES

UREA > 50 mg %

CREATININE > 5 mg %

URINE ANALYSIS

PROTEINURIA > 90 mg / DAY

HEMATURIA > 5 RBC / mm³

RADIOGRAPHY

RENAL FUNCTION TESTS

HISTORY OF UREMIA, URINARY TRACT INFECTION,
HYPERTENSION, EDEMA, POLYURIA,
OLIGURIA

PULMONARY ARTERY WEDGE PRESSURE

NORMAL = 9-12 mm Hg

OPTIMAL USE = 14-16 mm Hg

USE SOLUTIONS COMPATIBLE WITH
ELECTROLYTE BALANCE/OSMOLAR
BALANCE

Figure 5. Review of the patient's history.

Figure 6. Ensure adequate patient hydration.

become further inhibited and the urine volume and its electrolyte content can increase. It is imperative during this period of hypothermia that the perfusionist keep the patient adequately hydrated and monitor electrolyte deficits.

In non-pulsatile flow—Non-pulsatile flow may diminish renal blood flow and urinary output. Mavroudis¹⁰ makes reference to renal vasoconstriction to explain diminished renal blood flow and urinary output associated with non-pulsatile flow. Another study,¹¹ on the other hand, produced data which failed to show that renal vascular resistance significantly differed when pulsatile and non-pulsatile flow were compared. It may be of significance, however, that current kidney preservation techniques for organ transplantation utilize pulsatile flow.¹²

PREVENTIVE MEASURES FOR THE PERFUSIONIST

Based on an understanding of the various physiological factors causing renal complications, the perfusionist can then practice these four preventive measures:

(1) *Review the patient's history* prior to the surgical session with particular attention to those clues which may indicate suboptimal preoperative renal function (Fig. 5). Open heart patients who do develop post-operative renal impairment have significantly higher mean pre-operative blood urea values when compared to those who did not develop post-operative renal impairment.³ A similar study by Bhat and associates indicated that patients undergoing coronary artery grafting have a higher incidence of acute renal failure when compared to other groups of open heart patients.² The perfusionist should review blood chemistries for elevated blood urea or creatinine and urine analysis for proteinuria or hematuria. Also, radiography and specific renal function tests will yield valuable information which can make the perfusionist keenly aware of the suboptimal renal function of the patient. It would be the perfusionist's responsibility to pay particular attention to the precautions which follow.

(2) *Insure adequate patient hydration* pre and post-operatively (Fig. 6). Norman¹³ mentions that often overzealous pre-operative use of diuretics may initially compromise the patient's renal function. The pulmonary artery wedge pressure (PAWP) can yield useful information in regards to the hydration of the patient. In patients with heart disease it is advisable to maintain the PAWP between 14 and 16 mmHg,¹⁴ which will allow for optimal left ventricular filling and cardiac output. Pressures in excess of this range will cause dyspnea and eventually pulmonary edema without any increase in cardiac output. Lower pressures (12 mmHg and below) will compromise cardiac output with subsequent depression of renal function. PAWP should be maintained with solutions appropriate to electrolyte and osmolar balance.

(3) *Maintain patient perfusion pressure* during bypass and monitor the peripheral resistance to be confident you are not perfusing in the face of a systemic vasoconstriction (Fig. 7). Renal autoregulation, or the ability of the kidney to maintain a constant filtration rate over a range of perfusion pressures, is functional from 80 mmHg to 180 mmHg¹⁵ (Fig. 2). Throughout this range of pressures, when independent of other variables, the renal glomerular beds selectively constrict or dilate to maintain a constant renal blood flow and filtration rate. Below 80 mmHg both renal blood flow and filtration rate decrease linearly to approximately 15 mmHg, the minimum pressure necessary to initiate any blood flow whatsoever. In view of these well established physiological principles and the

**UTILIZE THE RENAL AUTOREGULATORY RANGE
(80–180 mmHg)**

Patient's Urinary Output (ml/min) Perfused Below Mean Pre-Op Arterial Pressure (mmHg)	Patient's Urinary Output (ml/min) Perfused At or Above Mean Pre-Op Arterial Pressure (mmHg)
n = 27	n = 7
$\bar{x}$ = 5.46	$\bar{x}$ = 17.64
S.D. = 3.84	S.D. = 12.42

$p < .005$

Figure 7. Maintain patient perfusion pressure.

MANNITOL (12.5–25 Gm)

LASIX (40 mg)

**URINARY OUTPUT < 1.25 ml/min WITH
HEMODILUTION**

MONITOR ELECTROLYTES

Figure 8. Utilize hemodilution and diuretics.

literature previously mentioned, it is reasonable that the perfusion pressure should be maintained above 80 mmHg.

A recent study performed by our group ($n = 34$) indicates that patients perfused at or above pre-operative mean arterial pressures had significantly greater urinary output ($p < .005$) than the group perfused below pre-operative mean arterial pressures.

(4) *Use hemodilution and diuretics* to maintain a diuresis during the bypass procedure (Fig. 8). Although there is no apparent relationship between the use of mannitol and/or furosemide (Lasix) and the incidence and/or severity of renal failure following cardiopulmonary bypass³, their use is advocated to maintain some urinary output during the bypass.² The critical time period from the initial insult to the point where the agents are not effective, as well as the dosages which are necessary for effectiveness, are not known. Some predictors of therapeutic response for diuretics have been calculated but are applicable only if well established renal failure is questioned. The perfusionist may be reasonably sure that both mannitol and furosemide will be effective in the typical duration of the bypass procedure.

Mannitol acts as an osmotic diuretic. It is freely filtered from the vasculature into the renal tubules and establishes an osmotic gradient within the tubular lumen preventing water and solute reabsorption thus producing diuresis. Furosemide is an extremely potent agent which has a rapid onset of action (within minutes) with peak effect at approximately one-half hour. It acts to inhibit the reabsorption of sodium (or possibly chloride) in the "Loop" of the nephron. This establishes an osmotic gradient preventing water reabsorption with subsequent diuresis.

Guidelines for diuretic administration are available for management of acute renal failure in the nephrology setting but are difficult to apply to the bypass procedure. The typical dose of mannitol is 12.5–25 gm administered over a 5–15 minute period. Lasix is administered as a 40 mg dose over a 15 minute period. Both of these agents are usually administered when urine flow drops below 0.5 ml/min. Normal urine flow under normal hydration conditions is approximately 1.25 ml/min.¹⁵ Under conditions of overhydration the urine flow can approach 20 ml/min. The perfusionist should expect the urine flow to be greater than 1.25 ml/min with a well perfused kidney. Agents such as mannitol and furosemide can be administered when urine flow drops below that point. Serum electrolytes should be monitored since diuresis will increase their excretion.

SUMMARY

A number of basic principles of renal physiology have been presented, emphasizing those areas under the direct control of the perfusionist. The areas are hypotension, hypovolemia, hemolysis, hemoglobinuria and hypothermia. It is obviously very difficult to integrate all of these parameters and determine the precise functional state of the kidney at any one time during the perfusion. However, it is possible to make recommendations to optimize renal perfusion during the bypass procedure. Those recommendations include: 1) an applied knowledge of the patient's medical history prior to bypass, 2) ensuring adequate patient hydration, 3) maintaining perfusion pressures within normal autoregulatory range, and, 4) appropriate use of diuretics.

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