Pulsatile cardiopulmonary bypass for patients with renal insufficiency

GORDON N OLINGER, LAURENCE D HUTCHINSON, LAWRENCE I BONCHEK

From the Department of Cardiothoracic Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin, USA

ABSTRACT Pulsatile cardiopulmonary bypass has been shown to preserve renal function and could therefore have considerable clinical value in patients undergoing cardiac surgery with preoperative renal insufficiency, by protecting them from further postoperative renal deterioration. Our three-year experience with pulsatile bypass in 29 patients with a preoperative serum creatinine concentration over 1.7 mg/100 ml (mean 2.9, range 1.8–6.1 mg/100 ml) ($>150 \mu\text{mol/l}$ (mean 256, range 159–539 $\mu\text{mol/l}$)) supports this premise. There were no renal deaths in the perioperative period and only two patients had irreversible postoperative deterioration in renal function; one died on day 3 of low-output syndrome and the other had rapidly progressive nephrosclerosis and died of that disease one year later. Postoperative oliguria occurred in the patient with low cardiac output and in only one other. This experience contrasts with our previous experience and that reported by others with non-pulsatile bypass in patients with renal insufficiency. We suggest that pulsatile bypass should be considered for cardiac surgery in patients with preoperative renal dysfunction.

Although the use of pulsatile cardiopulmonary bypass is increasing, many of its alleged benefits are unproved clinically and remain controversial.¹⁻³ Nevertheless, the kidney appears to respond favourably to pulsatile as opposed to non-pulsatile blood flow. Both in vitro and in vivo studies have shown that pulsation maintains renal perfusion and oxidative metabolism,⁴⁻⁷ augments urine flow,⁸⁻¹⁰ and mitigates stress responses in vasopressin and in the renin-angiotensin system that have been observed to occur with depulsation.¹¹⁻¹⁶ We reasoned that in patients with preoperative renal insufficiency who have reduced functional renal reserve, pulsatile bypass might offer the clinical advantage of preserving functioning nephron mass and in so doing might prevent postoperative oliguria, uraemia, and—in the worst cases—the need for temporary or even permanent dialysis. We are unaware of any reports of pulsatile cardiopulmonary bypass in patients with pre-existing renal insufficiency and therefore present our three-year experience at the Medical College of Wisconsin with pulsatile cardiopulmonary bypass in such patients.

Address for reprint requests: Dr Gordon N Olinger, Department of Cardiothoracic Surgery, The Medical College of Wisconsin, 8700 West Wisconsin Avenue, Milwaukee, Wisconsin 53226.

Accepted 16 March 1983

Patients and methods

Since November 1978, all patients undergoing cardiac surgery with a preoperative serum creatinine concentration repeatedly greater than 1.7 mg/100 ml (normal 0.8–1.2 $\pm$ SD 0.2 mg/100 ml) ($150 \mu\text{mol/l}$ (normal 71–106 $\pm$ SD 18 $\mu\text{mol/l}$)) have been selected for pulsatile perfusion. Twenty-nine patients, four women and 25 men, ranging in age from 25 to 78 years (mean 60 years) underwent cardiac operations for disabling symptoms. The mean preoperative creatinine concentration was 2.9 ± 1.2 mg/100 ml (median 2.3, range 1.8–6.1) ($256 \pm 106 \mu\text{mol/l}$ (median 203, range 159–539 $\mu\text{mol/l}$)); the mean preoperative blood urea nitrogen concentration was 49 ± 25 mg/100 ml (range 15–103) and the blood urea concentration was 105 ± 54 mg/100 ml (range 32–220) (17.5 ± 9.0 mmol/l (range 5.3–36.7)). Eleven patients were in New York Health Association (NYHA) functional class III and 18 were in class IV. The operations comprised 16 isolated coronary revascularisations, two revascularisations with elective aortic valve replacement, and one with emergency repair of a postinfarction ventricular septal defect. There was one elective mitral valve replacement and one emergency replacement for an infected porcine xenograft prosthesis. There were six isolated aortic

valve replacements; one was for a thrombosed Björk-Shiley prosthesis and five were urgent or emergency procedures for infective endocarditis. One aortic and mitral valve replacement was performed urgently for endocarditis.

The presumed or documented causes of preoperative renal insufficiency are listed in table 1. Patients are grouped according to the duration of renal failure. Table 2 correlates the operation performed with the cause of the renal insufficiency. In general,

Table 1 *Causes of the preoperative renal insufficiency in the 29 patients*

Cause	No of cases
Chronic	
Nephrosclerosis	15
Solitary kidney with nephrosclerosis	1
Solitary kidney—partially rejected transplant	1
Glomerulonephritis	1
Acute	
Prerenal	
Congestive heart failure or low cardiac output or both	2
Congestive heart failure or low cardiac output or both plus:	
immune complex nephritis	2
possible immune complex nephritis	3
aminoglycoside toxicity	1
Renal	
Immune complex nephritis	2
Chronic and acute	
Solitary kidney with nephrolithiasis plus congestive heart failure	1

chronic causes were associated with coronary disease and acute causes with particularly ill patients with valvular heart disease.

Complete left heart haemodynamic measurements were obtained before operation in 22 of the 29 patients. Table 3 shows these values with the more notably abnormal data of the subgroup of eight patients with a presumed prerenal component to their renal insufficiency.

Except for the addition of pulsation, cardiopulmonary bypass and operative techniques were performed in the standard fashion for our institution. The pump prime consisted of normal saline and a variable quantity of blood, depending on the preoperative haematocrit. Twenty-five grams of mannitol were added, as in all our patients, to promote diuresis. The average packed cell volume during cardiopulmonary bypass was 0.28 ± 0.004 . Systemic hypothermia ($28-30^{\circ}\text{C}$) was used in all patients. A commercial pulsatile assist device (either the Datascope PAD or the Shiley TKP Pulsator) was incorporated in-line. Conversion from non-pulsatile to pulsatile bypass always produced a phasic arterial pressure wave characterised by a more rapid fall than rise and associated with a rise in the mean pressure. The actual rate of rise and the duration of the pulse wave varied from patient to patient and for individual patients during bypass. An attempt was made to approximate the physiological waveform and size by pharmacological adjustment

Table 2 *Operations performed in relation to acute and chronic causes of renal failure*

Operation	Type of renal insufficiency				
	Chronic	Acute (prerenal)	Acute (prerenal + renal)	Acute (renal)	Chronic + acute (prerenal)
Coronary artery bypass	15	1			
Coronary artery bypass and aortic valve replacement	2				
Coronary artery bypass and ventral septal defect repair		1	4	2	1
Aortic valve replacement			1		
Mitral valve replacement	1				
Aortic valve replacement and mitral valve replacement			1		
Total (29)	18	2	6	2	1

Table 3 *Preoperative left ventricular haemodynamics*

		Pulmonary wedge pressure (mm Hg)	LVEDP (mm Hg)	Cardiac index (l/min/m ²)
All patients	Mean	21	23	2.4
	SD	10	14	0.7
	Range	6-38	4-54	1.3-3.9
Patients with prerenal azotaemia	Mean	27	35	2.1
	SD	7	14	0.5
	Range	20-38	20-54	1.3-2.6

LVEDP—left ventricular end-diastolic pressure.

of systemic vascular resistance and venous capacitance as necessary, with phenylephrine, nitroglycerine, and sodium nitroprusside. During pulsatile bypass the mean systemic diastolic pressure was 71 ± 11 (range 39–98) mm Hg and the mean pulse pressure 33 ± 13 (range 11–60) mm Hg. The mean pump flow was 4.3 ± 0.7 l/min (range 2.9–5.9 l/min) or 57 ± 11 (range 34–81) ml/kg/min. In most patients frusemide (20–100 mg) was given at the initiation of cardiopulmonary bypass to aid renal cortical blood flow distribution.^{17,18} Additional frusemide was given in some patients when urine flow was low. The mean dose for all patients during bypass was 67 mg (range 20–300 mg). The mean cardiopulmonary bypass time was 135 ± 34 minutes (range 86–209 min). Patients undergoing coronary artery bypass had all proximal and distal anastomoses done on cardiopulmonary bypass.

Renal function was followed after operation by measurements of electrolyte, daily blood urea, and serum creatinine concentrations.

Results

MORTALITY

There were four hospital deaths. The first was in a 71-year-old man (patient 1) who had an emergency coronary artery bypass complicated by severe arteriosclerotic aortic disease, which caused difficulty in performing the proximal anastomoses. A large extracoronary collateral flow—undoubtedly enhanced by pulsatile perfusion—contributed to inadequate myocardial protection with cold hyperkalaemic cardioplegia. He died on day 3 of ischaemic low cardiac output and was the only patient in the series to require positive inotropic cardiac support after operation. There was satisfactory urine flow during operation, but urine output declined and then ceased within 24 hours. This patient also suffered a major postoperative cerebrovascular accident that was shown at postmortem examination to have been caused by atheromatous emboli. That examination also showed one shrunken kidney destroyed by nephrosclerosis and renal artery occlusion and the other kidney severely affected by nephrosclerosis and supplied by a tightly stenotic renal artery.

The three other hospital deaths occurred at five, six and eight weeks after operation. The first was from respiratory failure and *Serratia marcescens* sepsis in a chronically debilitated, immunologically deficient man who underwent aortic valve replacement for what was thought to be marantic endocarditis. After a respiratory arrest during the second postoperative week, his renal function deteriorated and he was haemodialysed thereafter until his death.

The second death was from hepatic and respiratory failure with sepsis in a man operated on in a moribund state for Gram-negative porcine mitral valve prosthetic endocarditis. Renal function remained stable despite his decline. The third death was also from sepsis with empyema and mediastinitis in a man operated on for a thrombosed Björk-Shiley aortic prosthesis. His renal function also remained stable. Both deaths from sepsis infection occurred during an epidemic of sepsis that occurred in late 1978 at our hospital.

Two late deaths occurred—one from respiratory failure with pneumonitis six months after operation in a patient who had an aortic valve replacement for bacterial endocarditis and one from progressive renal failure at 12 months in patient 7.

NON-RENAL MORBIDITY

Cardiac morbidity was restricted to patient 1. There were two focal, apparently embolic, cerebrovascular episodes. One occurred in patient 1, as already discussed. The second was a very localised and reversible, non-dominant event that followed coronary artery bypass in an elderly woman who had a very diseased ascending aorta. A third episode occurred in a 67-year-old man, who suffered diffuse bilateral posterior hemispherical injury of uncertain aetiology after an uneventful coronary artery bypass. He remains comatose. As discussed below, this might be attributable to pulsation with the technique we used. There was no other morbidity or technical complication associated directly with pulsatile as opposed to non-pulsatile bypass. Infective complications were restricted to the patients discussed above.

RENAL FUNCTION

The patients as a group showed no appreciable overall postoperative deterioration in renal function. Notable exceptions are discussed below. Urine output during cardiopulmonary bypass was acceptable (≥ 1 ml/min) or brisk in virtually all patients. The mean urine output was 460 ± 430 ml (range 60–2000 ml), or 3.8 ± 3.8 ml/min. The mean urine output during anaesthesia was 1150 ± 670 ml and for the subsequent three 24-hour periods 1900 ± 800 , 1600 ± 700 , and 1500 ± 700 ml. Only two patients (Nos 1 and 2—see below) were oliguric during the first 72 postoperative hours and one of these (No 2) was also oliguric during operation (urine output < 1 ml/min).

The postoperative blood urea and serum creatinine concentrations are summarised in table 4 for the entire group and certain subgroups. While there are no statistically significant alterations in these indices of renal function within the total series and subgroups or between subgroups, certain trends

Table 4 Mean ($\pm$ SD) serum creatinine and blood urea nitrogen concentrations in the patients

	Serum creatinine (mg/dl)				Blood urea (mg/dl)			
	Preop	POD 1	POD 2	POD 3	Preop	POD 1	POD 2	POD 3
All patients	2.9 ± 1.2	2.8 1.2	3.1 1.7	3.2 2.2	105 ± 54	94 45	105 54	103 54
Chronic subgroup	2.8 ± 1.4	2.9 1.5	3.2 1.9	3.6 2.5	94 ± 58	92 45	101 56	109 64
Acute prerenal subgroup	2.9 ± 0.8	2.7 0.7	3.1 1.5	2.7 1.5	113 ± 47	103 51	118 62	105 45
Acute renal subgroup	3.2 ± 0.9	2.8 0.5	3.0 1.3	3.0 1.3	116 ± 39	94 30	103 39	103 34

Preop—preoperative state; POD 1, 2, 3—postoperative days 1, 2, 3.

Conversion: Traditional to SI units—Creatinine: 1 mg/dl = 88.4 μ mol/l; blood urea: 1 mg/dl = 0.166 mmol/l.

are noteworthy. The eight patients with *acute* prerenal azotaemia (in isolation or combined with a renal cause) tended to improve after operation. One patient in this subgroup showed appreciable early worsening of renal function and skewed the mean data accordingly. Trend lines of serum creatinine for this patient (No 3) and the other seven in this subgroup are seen in figure 1. Patients with *acute* renal insufficiency of renal aetiology (alone or in combination) also tended to improve during the first three postoperative days. Trend lines for serum creatinine concentrations in these patients are seen in figure 2. Improvement was most striking in patient 4, who was being haemodialysed before operation for isolated immune-complex nephritis. Again patient 3, with combined prerenal and renal factors, skewed the group data.

On the other hand, patients with *chronic* renal insufficiency appeared far more vulnerable to insult by operation and to postoperative deterioration in function. Trend lines for all 29 patients are seen in figure 3. Of the seven patients who showed apparent deterioration in function from the preoperative state to day 3, as defined by a rise in serum creatinine concentration of ≥ 1 mg/dl (88 μ mol/l) (bold lines), six had chronic insufficiency. The seventh was patient 3, noted previously. Detailed examination of these seven patients reveals several relevant points.

Patients 5 and 6 had the poorest preoperative renal function of all the patients, No 5 from previous glomerulonephritis and No 6 from hypertensive nephrosclerosis. Both had longstanding renal failure with a preoperative creatinine clearance of 7.6 and 13.0 ml/min respectively. Creatinine clearances in both remained stable during their entire postoperative courses. The transient rises in serum creatinine concentration noted reflected the normal postoperative increase in creatinine load and not a deterioration in clearance capacity.

Patient 1, as described previously, suffered acute renal failure secondary to a low cardiac output syn-

Fig 1 Preoperative and postoperative serum creatinine concentrations for individuals in the subgroup of patients with acute renal insufficiency contributed to by prerenal factors. Preop—before operation (op); POD 1, 2, 3—postoperative days 1, 2, 3. Conversion: traditional to SI units—Creatinine: 1 mg/dl = 88.4 μ mol/l.

drome. Renal failure in such a setting has been well documented.¹⁹

Patient 3, who underwent aortic valve replacement for endocarditis with concomitant triple coronary artery bypass and had staphylococcal

Fig 2 Preoperative and postoperative serum creatinine concentrations for individuals in the subgroup of patients with acute renal insufficiency contributed to by primary renal disease. (Abbreviations as in fig 1.) Conversion: traditional to SI units—Creatinine: 1 mg/dl = 88.4 μ mol/l.

immune-complex nephritis with a preoperative low cardiac output (1.3 l/min/m²), and patient 2, who had generalised arteriosclerotic vascular disease and hypertensive nephrosclerosis, both had postoperative exacerbation of renal insufficiency. They were two of six patients in the series who had cardiac catheterisation with angiography within 24 hours of operation. Angiographic contrast nephrotoxicity may have contributed to temporary worsening of their renal function. Renal function in patient 3 returned to normal in two weeks. Patient 2 was the only patient other than patient 1 who was oliguric after operation. She responded well to dopamine, begun 36 hours after operation at a dose of 2 μ g/kg/min to increase renal cortical blood flow.²⁰ Serum creatinine returned to baseline before she was discharged.

Patient 7 had rapidly progressive nephrosclerosis with a preoperative creatinine clearance of 22 ml/min. Mitral valve replacement was accomplished

Fig 3 Preoperative and postoperative serum creatinine concentrations for all patients. (Abbreviations as in fig 1.) Conversion: traditional to SI units—Creatinine: 1 mg/dl = 88.4 μ mol/l.

uneventfully, but despite excellent perfusion values she manifested further non-oliguric renal failure, which did not reverse and led to her death one year later. She was the only survivor to show permanent postoperative deterioration of renal function.

Patient 8 had a transient non-oliguric rise in serum creatinine after an uneventful coronary artery bypass. This deterioration was not readily explained by any factor mentioned previously, although it is of interest that he was one of only two patients who did not receive frusemide at initiation of bypass.

Discussion

The pathogenesis of renal failure in patients undergoing non-pulsatile cardiopulmonary bypass has not been fully explained, although decreased renal perfusion with increased vascular resistance appear to be primary aetiological factors.^{16 21 22} With diminution in renal cortical blood flow and in sodium reab-

sorption in the proximal tubule, the macula densa of the juxtaglomerular apparatus increases renin secretion. Production of angiotensin ensues, followed by preglomerular arteriolar constriction and an associated further fall in glomerular filtration. Vascular resistance within the kidney rises and blood flow is shifted from cortex to medulla. The potential value of pulsation in preventing this sequence of events has been suggested by several studies,⁴⁻¹⁶ the overall results of which imply that the addition of pulsation to standard cardiopulmonary bypass might help to maintain normal intrarenal haemodynamics and nephron perfusion and mitigate the potential for the postulated sequence of events that leads to renal failure.

The results in this series of 29 patients with moderate-to-severe preoperative renal insufficiency support this premise. Only two patients had irreversible postoperative deterioration in renal function. One suffered irremediable low output syndrome with its expected consequences. The other had an unusually active nephrosclerotic process, from which she died one year later. Her renal failure while she was in hospital was nevertheless non-oliguric and did not prevent successful convalescence from her mitral valve replacement. Each of the other 27 patients showed postoperative preservation of preoperative nephron mass and function. In 22 cases postoperative serum creatinine concentrations were stable or improved, while five patients had a considerable rise in postoperative serum creatinine concentration but subsequently returned to preoperative levels or below. When renal function did worsen after operation, it was mostly in patients with chronic renal disease—a logical sequel to insult to a fixed, limited nephron mass incapable of the recovery expected with prerenal azotaemia or acute glomerular or tubular injury.

The protective effects of pulsatile bypass are likely to have been lessened in two of the six patients who received angiographic contrast shortly before operation (patients 2 and 3). Whenever possible the patient with underlying renal disease should be allowed a period of at least 24 and preferably 72 hours after contrast injection for clearance of contrast and for equilibration of renal function. An elective operation should be postponed to allow recovery from further tubular dysfunction.

Because of the very precarious clinical condition of patients with limited renal reserve, we believe they should be offered the potential benefit of other supportive measures besides pulsatile bypass. Frusemide to enhance renal cortical blood flow is one such adjunct. Another is dopamine, which, while not given to any patient during operation, was used effectively in low dose afterwards in one

patient to improve urine output. There may be a role for intraoperative low-dose dopamine to supplement pulsatile bypass in patients with renal insufficiency. We have no experience with this technique and would use it reluctantly whenever the increase in cardiac contractile state and oxygen demand might impair myocardial protection.

The possible morbidity associated with pulsatile bypass with an in-line pulsator must be weighed against its intended benefits. Cerebrovascular damage is clearly the major hazard. There were three such episodes in this series, a rate of 10%. Two were probably related to atheromatous emboli generated by aortic clamping or by disruption of visible atheroma at the site of proximal vein graft anastomoses. Aortic cannulation in both patients was opposite was chosen because in each instance this was with the cannula directed distal to the brachiocephalic vessels. This very distal cannulation site was chosen because in each instance this was the only segment of aorta that by palpation seemed suitably soft and gave sufficient room for proximal vein graft anastomoses. Femoral arterial perfusion was impossible because of extensive peripheral vascular disease. If pulsation should dislodge atheromatous material in such circumstances the emboli should be directed away from the cerebral circulation. Of more concern is the third, more global, ischaemic injury. It has been suggested that vigorous vacuum collapse of in-line pulsatile devices can generate microbubbles and thereby cause cerebral air emboli.³ We have consciously avoided excessively vigorous pulsation because of this risk. Since mean pulse pressure during this particular operation was only 21 mm Hg, this phenomenon was an unlikely, although not inconceivable, cause of the injury. Pulsation achieved by acceleration-deceleration of the roller pump head, a technique now commercially available, and with which Taylor *et al* have had substantial clinical experience,²³ would obviate this potential complication. An additional possible disadvantage of pulsatile bypass when cardioplegic arrest is being used for myocardial protection is the augmentation of extracoronary collateral myocardial blood flow that may result from higher aortic pressures.²⁴ Indeed, this may have contributed to our solitary cardiac death.

The evidence for the efficacy of pulsatile bypass in this series is circumstantial. We are nevertheless convinced of its benefit because experience with the patients reported in this paper contrasts strikingly with our own previous anecdotal experience with similar patients on whom it was not used. Furthermore, the systematically analysed and frequently cited reports of Abel *et al*,²⁵ Porter *et al*,²⁶ Yeboah *et al*,²⁷ and Bhat *et al*,²⁸ each of which examined the

incidence and causes of renal failure after cardiac surgery performed with *pulseless perfusion*, showed unequivocally that preoperative renal insufficiency carried with it an excessive postoperative incidence of renal morbidity and mortality that was proportional to the degree of renal insufficiency present at the time of operation. Typifying these findings was Abel *et al*'s worst subgroup of 18 patients with a mean preoperative creatinine concentration of 2.03 mg/dl (179.5 μ mol/l), compared with our mean of 2.9 mg/dl (256 μ mol/l). Postoperative creatinine levels in all patients rose to 5 mg/dl (442 μ mol/l), 15 patients required dialysis, and mortality was 88.8%. Of additional significance in these reports was that the duration of non-pulsatile cardiopulmonary bypass contributed independently and directly to the incidence of postoperative renal failure. The duration of bypass in our series, a mean of 135 minutes, bore no relation to postoperative renal function.

Our own practice now is to use pulsatile bypass in all patients with preoperative renal insufficiency, a policy that seems physiologically sound and worthy of consideration and further evaluation by others. We realise that the credibility of our data on the value of pulsation rests on uncontrolled comparison with other series and on the personal experience of surgeons who, like us, have been dissatisfied with the use of non-pulsatile flow in the presence of established renal insufficiency. Controlled studies of pulsatile versus non-pulsatile perfusion in patients with poor renal function are clearly required, though they may be difficult to perform in view of the many perioperative variables which may influence renal function.

References

- 1 Frater RWM, Wakayama S, Oka Y, *et al*. Pulsatile cardiopulmonary bypass: failure to influence hemodynamics or hormones. *Circulation* 1980;**62**, suppl 1:19–25.
- 2 Trinkle JK, Hleton NE, Bryant LR, Griffen WO. Pulsatile bypass: clinical evaluation. *Surgery* 1970;**68**: 1074–8.
- 3 Zumbro GL, Shearer G, Fishback ME, Galloway RF. A prospective evaluation of the pulsatile assist device. *Ann Thorac Surg* 1978;**28**:269–73.
- 4 German JC, Chalmers GS, Hirc J, Mukherjee ND, Wakabayashi A, Connolly JE. Comparison of nonpulsatile and pulsatile extracorporeal circulation on renal tissue perfusion. *Chest* 1972;**61**:65–9.
- 5 Agishi T, Pierce EC II, Kent BB. A comparison of pulsatile and nonpulsatile pumping for ex vivo renal perfusion. *J Surg Res* 1969;**9**:623–34.
- 6 Paquet KJ. Hemodynamic studies on normothermic perfusion of the isolated pig kidney with pulsatile and nonpulsatile flows. *J Cardiovasc Surg* 1969;**1**:45–53.
- 7 Mukherjee ND, Beran AV, Hirc J, *et al*. In vivo determination of renal tissue exogenation during pulsatile and nonpulsatile left heart bypass. *Ann Thorac Surg* 1973;**15**:354–63.
- 8 Boucher JK, Rudy LW jun, Edmunds LH jun. Organ blood flow during pulsatile cardiopulmonary bypass. *J Appl Physiol* 1974;**36**:86–90.
- 9 Bregman DB, Bowman FO, Parodi EN, *et al*. An improved method of myocardial protection with pulsation during cardiopulmonary bypass. *Circulation* 1976;**56**, suppl 2:157–60.
- 10 Philbin DM, Levine FH, Emerson CW, Coggins CH, Buckley MJ, Austen WG. Plasma vasopressin levels and urinary flow during cardiopulmonary bypass in patients with valvular heart disease. Effect of pulsatile flow. *J Thorac Cardiovasc Surg* 1979;**78**:779–83.
- 11 Landymore RW, Murphy DA, Kinley CE, *et al*. Does pulsatile flow influence the incidence of postoperative hypertension? *Ann Thorac Surg* 1979;**28**:261–8.
- 12 Taylor KM, Brannan JJ, Bain WH, Caves PK, Morton IJ. Role of angiotensin II in the development of peripheral vasoconstriction during cardiopulmonary bypass. *Cardiovasc Res* 1979;**13**:269–73.
- 13 Watkins L jun, Lucas SK, Gardner TJ, Potter A, Walker WG, Gott VL. Angiotensin II levels during cardiopulmonary bypass: a comparison of pulsatile and nonpulsatile flow. *Surg Forum* 1979;**30**:229–30.
- 14 Philbin DM, Levine FH, Kono K, *et al*. Attenuation of the stress response to cardiopulmonary bypass by the addition of pulsatile flow. *Circulation* 1981;**64**:808–12.
- 15 Many M, Giron F, Birtwell WC, Deterling RA jun, Sorooff HS. Effects of depulsation of renal blood flow upon renal function and renin secretion. *Surgery* 1969;**66**:242–9.
- 16 Goodman TA, Gerard DF, Bernstein EF, Dilley RB. The effects of pulseless perfusion on the distribution of renal cortical blood flow and on renin release. *Surgery* 1979;**80**:31–9.
- 17 Engleman RM, Gouge TH, Smith SJ, Stahl WM, Gombos EA, Boyd AD. The effect of diuretics on renal hemodynamics during cardiopulmonary bypass. *J Surg Res* 1974;**16**:268–76.
- 18 Nuutinen L, Hollmen A. The effect of prophylactic use of furosemide on renal function during open heart surgery. *Ann Chir Gynaecol Fenn* 1976;**65**:258–66.
- 19 Hilberman M, Derby GC, Spencer RJ, Stinson EB. Sequential pathophysiological changes characterizing the progression from renal dysfunction to acute renal failure following cardiac operation. *J Thorac Cardiovasc Surg* 1980;**79**:838–44.
- 20 Goldberg LI. Dopamine—clinical uses of an endogenous catecholamine. *N Engl J Med* 1974;**291**:707–10.
- 21 Patek RV, Lifschitz MD, Stein JH. Acute renal failure: clinical aspects and pathophysiology. *Cardiovasc Med* 1979;**4**:19–38.
- 22 Krian A. Incidence, prevention, and treatment of acute renal failure following cardiopulmonary bypass. *Int Anesthesiol Clin* 1976;**14**:87–101.
- 23 Taylor KM, Bain WH, Davidson KG, Turner MA. Comparative clinical study of pulsatile and nonpulsatile perfusion in 350 consecutive patients. *Thorax* 1982;**37**:324–30.
- 24 Olinger GN, Bonchek LI, Geiss DM. Non-coronary collateral distribution in coronary artery disease. *Ann Thorac Surg* 1981;**32**:554–7.
- 25 Abel RM, Buckley MJ, Austen WG, Barnett GO, Beck

- CH jun, Fischer JE. Etiology, incidence, and prognosis of renal failure following cardiac operations. *J Thorac Cardiovasc Surg* 1976;**71**:323–33.
- ²⁶Porter GA, Kloster FE, Herr RJ, Starr A, Griswold HE, Kimsey J. Renal complications associated with valve replacement surgery. *J Thorac Cardiovasc Surg* 1967;**53**:145–52.
- ²⁷Yeboah ED, Petrie A, Pead JL. Acute renal failure and open heart surgery. *Br Med J* 1972;i:415–8.
- ²⁸Bhat JG, Gluck MC, Lowenstein J, Baldwin DS. Renal failure after open heart surgery. *Ann Intern Med* 1976;**84**:677–82.