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Cardiac performance in various stages of renal failure

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SUMMARY Cardiac catheterisation was performed to evaluate cardiac function in 12 patients with various stages of renal failure. All patients were studied at rest and during supine exercise to subjective exhaustion. Eight patients had a normal arteriovenous oxygen difference at rest and during exercise whereas three had a low arteriovenous oxygen difference and one a high arteriovenous oxygen difference. Left ventricular stroke work did not increase normally at transition from rest to exercise in most patients with serum creatinine concentrations >500 μmol/l. The left ventricular end diastolic pressure was abnormally raised during exercise in all patients (range 20–42 mm Hg) and also at rest in most of them (range 8–36 mm Hg), indicating myocardial dysfunction. These observations suggest that patients have abnormal cardiac performance at a relatively early stage of renal failure.

Cardiovascular complications are the most frequent causes of death in uraemic patients, accounting for more than 40% of the total mortality.[1–3] Congestive heart failure is common in end stage renal disease. Most published reports of cardiac performance in uraemic patients are based on non-invasive techniques, such as echocardiography,[4–10] measurement of systolic time intervals,[4 11–13] and radionuclide angiocardiography.[14] Cardiac catheterisation, which yields more exact information on cardiac function, has been carried out in a few studies[15–17] but not to our knowledge in the early stages of renal failure before dialysis is initiated.

The aim of the present study was to investigate cardiac performance as assessed at cardiac catheterisation at rest and during exercise in patients with various stages of renal failure.

Patients and methods

The study comprised six men and six women (mean age 46·8 (range 26–59) years). Table 1 shows some clinical data. The patients had various degrees of kidney function determined according to the serum creatinine concentrations. Three patients (cases 10, 11, and 12) were undergoing maintenance haemodialysis. No patient had signs or a history of ischaemic heart disease, pericarditis, or valvar heart disease. Only one patient (case 8) had clinical signs of congestive heart failure, rales and dilated neck veins. None had electrolyte imbalance at the time of the study. Severe anaemia (haemoglobin concentration <7·0 g/dl) was present in three patients. Seven were hypertensive with resting supine blood pressures >150/90 mm Hg or were receiving antihypertensive treatment. The diastolic pressure was recorded in Korotkoff phase 5. Informed consent was obtained and the study approved by the committee of ethics at the Karolinska Hospital.

All the patients underwent exercise stress tests sitting on a bicycle ergometer with an automatic device for increasing the continuous workload by 10 W each minute.[18] A 12 lead electrocardiogram was recorded in the supine position before the test. A six lead chest electrocardiogram was used for monitoring with the indifferent electrode placed on the forehead. All the patients exercised to symptom limited maximum tolerance. The relative heart volume was determined on chest *x* ray films in the erect position.

The patients were catheterised in the morning, in the fasting state, after premedication with 5 mg diazepam intramuscularly. A Swan-Ganz thermodilution catheter (Edward Laboratories, Model 93-113-F) was inserted percutaneously under local anaesthesia into an antecubital vein and was advanced to the pulmonary artery. A radio-opaque Teflon catheter was introduced percutaneously into the right brachial artery and guided into the left ventricle. In two

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Table 1 *Clinical and laboratory data*

Case No	*Sex/age (yr)*	*BSA (m^2)*	*Renal disease*	*Serum creatinine concentration (μmol/l)*	*Hb concentration (g/d)*	*Blood volume (l)*	*Relative heart volume (ml/m^2)*	*Blood pressure*	*ECG at rest/ on exercise*	*Medication*
1	F/54	1·57	CPN	400	12·1	3·5	320	NT	N/N	Frusemide 40 mg×1
2	M/44	1·82	CGN	450	11·5	4·5	410	HT	N/N	Alprenolol 200 mg×2 Hydralazine 80 mg×2
3	M/35	1·99	PK	450	16·0	4·8	310	HT	N/N	Metoprolol 100 mg×2 Frusemide 40 mg×1
4	M/55	2·12	CGN	500	11·7	5·6	450	HT	LAFB/LAFB	Metroprolol 100 mg×2 Hydralazine 25 mg×3
5	F/52	1·52	PK	550	7·5	4·4	520	NT	N/N	—
6	F/53	1·64	RD	670	10·3	3·3	490	HT	ST-T/ST-T	Alpenolol 200 mg×1 Hydralazine 15 mg×3 Frusemide 40 mg×1
7	M/41	2·28	CGN	800	13·6	—	400	HT	N/N	Metoprolol 100 mg×2 Hydralazine 50 mg×1 Frusemide 40 mg×2
8	F/53	1·55	PK	950	7·7	4·0	420	NT	N/N	Frusemide 40 mg×3
9	F/46	1·45	RD	1000	7·5	4·2	450	NT	ST-T/ST-T	Digitoxin 0·1 mg×1 Frusemide 80 mg×2
10	M/42	1·81	CGH	1245 (HD)	6·4	5·8	640	HT	LVH/LVH	Digitoxin 0·1 mg×1 Frusemide 250 mg×2 Hydralazine 25 mg×4
11	M/26	1·95	CGN	1440 (HD)	6·8	5·9	710	HT	LVH/LVH	Digitoxin 0·1 mg×1 Frusemide 250 mg×3
12	F/59	1·56	PK	900 (HD)	6·8	4·6	425	NT	ST-T/ST-T	Digitoxin 0·1 mg×1 Frusemide 500 mg×3

BSA, body surface area; CGN, chronic glomerulonephritis; CPN, chronic pyelonephritis; HD, haemodialysis; HT, hypertension; LAFB, left anterior fascicular block; LVH, left ventricular hypertrophy; N, normal; NT, normotension; PK, polycystic kidneys; RD, renal dysplasia; ST-T, non-specific ST-T changes

patients the catheter slipped out of the left ventricle during exercise. In these two patients the pulmonary capillary venous pressure or the pulmonary artery diastolic pressure was used as a measure of the left ventricular end diastolic pressure during exercise. The catheters were connected to electromechanical transducers (Siemens-Elema, EMT 34). The pressures were recorded on an ultraviolet recorder (ABEM, Ultralette 5651). Left ventricular pressure was also recorded on magnetic tape (Tandberg, Recorder Series 100) and subsequently processed in a computer (IBM 1800), which calculated haemodynamic indices such as aortic and left ventricular mean systolic pressures by planimetric integration during ejection. The mid-thorax was taken as the zero reference level of pressure.

MEASUREMENTS OF CARDIAC PERFORMANCE

Measurements were made with the patient supine (*a*) at rest, (*b*) with legs placed on the pedals 15 cm above the table, and during exercise, (*c*) with a six minute period of steady state work at a low workload followed by (*d*) a period of stepwise increases in workload (10 W per minute) until symptom limited maximum tolerance was reached. Cardiac output was determined by the thermodilution technique; 5 ml isotonic saline solution at 15°C was injected and output determined every 30 seconds during exercise. For technical reasons thermodilution was not used in one patient (case 6) and in another (case 9) during exercise. Cardiac output was also measured by the Fick method at rest and during steady state work to validate the thermodilution measurements. Comparisons between the thermodilution and Fick determinations showed good agreement ($r=0·88$, $p<0·01$).

The total number of thermodilution determinations of cardiac output averaged 20 per patient. Together with the continuous recordings of left ventricular pressure, these measurements were used to calculate the stroke work index (SWI) and left ventricular power index (LVPI) according to the formulas: $SWI=(LVMSP-LVEDP)\times SV\times c/BSA$ (J/beat/m^2 BSA), and $LVPI=SWI\times HR\times 1/60/m^2BSA$, where BSA is body surface area (m^2), HR is heart rate (beats/min), LVMSP is left ventricular mean systolic pressure (mm Hg), LVEDP is left ventricular end diastolic pressure (mm Hg), SV is stroke volume (ml), and c is constant ($1·33\times10^{-4}$). The systemic vascular resistance (SVR) was calculated according to the formula: $SVR=(80(AOm-RAm))/\dot{Q}$ dyn s cm^{-5}, where AOm and RAm are aortic (measured at rest before entering the left ventricle) and right atrial mean pressures (mm Hg) and $\dot{Q}$ is cardiac output (l/min). Pulmonary vascular resistance was calculated at rest according to the formula: $PVR=(80(PAm-PVCm))/Q$ where PAm and PVCm are pulmonary artery and pulmonary venous capillary mean pressure (mm Hg). This formula was used for all patients except for that in case 3, in whom left ventricular end diastolic pressure was used as a meas-

Table 2 *Maximum workload and heart rates in sitting and supine positions*

Case No	Heart rate sitting (beats/min)		Maximum workload (W)	Heart rate supine (beats/min)		Maximum workload (W)
	At rest	At maximum workload		At rest	At maximum workload	
1	70	146	70	66	114	50
2	64	135	190	77	146	100
3	59	132	160	95	120	100
4	65	152	140	70	115	100
5	70	144	90	77	140	60
6	70	115	90	76	—	—
7	70	116	200	62	105	100
8	68	156	90	70	130	70
9	66	160	100	59	—	—
10	90	108	40	92	100	15
11	75	104	60	76	95	60
12	80	128	50	81	112	20

ure of PVCm. During exercise left ventricular end diastolic pressure or pulmonary artery diastolic pressure was used as a measure of PVCm.

Blood volume was determined with the alveolar carbon monoxide method[19] and serum creatinine concentration was measured as recommended by Taussky.[20]

Results are given as mean with standard deviation (SD) or with range. In statistical analysis of the data Student's *t* test for non-paired observations and linear regression analysis were used.

Results

Table 1 shows the individual values for haemoglobin concentration, blood volume, and relative heart volume. The maximum workload and heart rate at rest and at maximum workload sitting and supine is given for each patient in Table 2. Dyspnoea or leg fatigue or both were the most common reasons for stopping the test. No patient complained of chest pain during exercise. The electrocardiographic pattern at rest did not alter during exercise. Table 3 shows the individual haemodynamic data.

Eight patients, including the three undergoing maintenance haemodialysis, had a normal arteriovenous oxygen difference, one patient (case 3) had a high value both at rest and during exercise (arteriovenous oxygen difference 54 and 118 ml/l respectively), whereas three patients (cases 2, 5, and 9) had a low value with a high cardiac output in relation to oxygen uptake. The arteriovenous oxygen difference correlated with the haemoglobin concentration ($r=0{\cdot}68$, $p<0{\cdot}05$). Thus those patients with the lowest haemoglobin concentrations had a smaller arteriovenous oxygen difference than the others. Resting cardiac output was higher in the three patients undergoing maintenance haemodialysis (cases 10, 11, and 12) than in the three patients with the lowest serum creatinine concentrations (cases 1, 2, and 3) (7·6 *v* 5·5 l/min^{-1}), but the difference was not significant. The resting cardiac output did not correlate with the haemoglobin concentration.

Left ventricular end diastolic pressure was raised both at rest (range 8–36 mm Hg) and during exercise (range 20–42 mm Hg) in most patients. The value at rest inversely correlated with the haemoglobin concentration ($r=-0{\cdot}65$, $p<0{\cdot}05$)—that is, the highest values were recorded in those with the lowest haemoglobin concentrations.

There was no correlation between serum creatinine concentrations and left ventricular end diastolic pressure at rest. Systemic vascular resistance and pulmonary vascular resistance were within normal limits (Table 3).

Left ventricular function curves were constructed for three groups, stratified according to serum creatinine concentrations (group 1, the three patients with concentrations <500 μmol/l; group 2, the six patients with concentrations 500–1000 μmol/l, and group 3, the three patients undergoing maintenance haemodialysis), by plotting means for stroke work index and left ventricular pressure index against the corresponding means for left ventricular end diastolic pressure at rest, with legs elevated, during steady state exercise, and at maximum workload (Figure *a*). The relation between stroke work index and left ventricular end diastolic pressure was normal for patients in group 1, but for those in groups 2 and 3 left ventricular end diastolic pressure was significantly raised with exercise. Left ventricular end diastolic pressure at rest did not differ significantly between the three groups. Stroke work index remained constant or even fell in groups 2 and 3 during exercise. The relation between left ventricular pressure index and left ventricular end diastolic pressure in group 2 and more notably for those in group 3 indicated the poor heart rate response to work. Grouping the patients according to blood pressure at rest (normotensive or hypertensive) showed no significant intergroup difference with respect to stroke work index or left ventricular end diastolic pressure (Figure *b*).

Table 3 *Haemodynamic measurements at rest and during steady state workloads*

Case No	Workload (W)	Cardiac output (Fick method) (l/min)	SV (ml)	HR (beats/min)	AVD (ml/l)	Oxygen uptake (ml/min)	SVR (dyn s cm^{-5})	PVR (dyn s cm^{-5})	SWI (J/beat per m^2 BSA)	LVPI (W/m^2 BSA)	Mean RA pressure (mm Hg)
1	Rest	4·5	68	66	43	193	1742	124	0·55	0·63	6
	20	6·2	63	99	79	489		103	0·63	1·04	4
2	Rest	8·0	104	77	30	240	1300	133	1·48	1·90	6
	80	16·4	139	118	78	1276		63	1·75	3·65	8
3	Rest	4·1	43	95	54	223	2107	136	0·47	0·75	4
	70	9·3	82	113	118	1104		77	0·94	1·73	
4	Rest	5·2	74	70	45	235	2353	92	0·96	1·01	8
	60	11·1	102	109	94	1042		94	0·97	1·48	15
5	Rest	7·2	94	77	29	206	1311	44	1·50	1·50	10
	30	12·7	98	130	56	704		50	1·38	2·74	16
6	Rest	5·0	66	76	45	228	1872	112	—	—	3
	30	9·8	83	118	64	626		82	—	—	
7	Rest	6·1	98	62	46	280	944	92	0·47	0·49	7
	40	9·9	111	89	91	896		121	0·52	0·77	
8	Rest	4·0	57	70	46	185	2300	80	0·82	0·84	11
	30	8·4	73	115	63	535		114	0·84	1·43	16
9	Rest	5·7	97	59	30	172	1574	42	1·29	1·33	6
	30	11·9	105	113	51	608		54	—	—	8
10	Rest	6·8	74	92	38	256	1459	153	0·65	0·85	6
	10	(10·81)	(104)*	103					0·87	1·40	16
11	Rest	9·7	128	76	35	333	1072	91	1·47	1·89	10
	15	10·7	123	87	49	521		82	1·32	1·95	20
12	Rest	6·3	78	81	31	197	1194	114	0·80	1·18	5
	15	8·6	72	120	57	492		121	0·78	1·30	16

*Determined by thermodilution. †Recorded 10 min after exercise. SV, stroke volume; HR, heart rate; AVD, arteriovenous oxygen difference; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance, SWI, stroke work index; LVPI, left ventricular power index; RA, right atrial; PCV, pulmonary capillary venous pressure; M, mean; S, systolic; D, diastolic; ED, end diastolic.

Discussion

The comparisons in this study were made between patients in various stages of renal failure including three who were undergoing maintenance haemodialysis. The series of patients thus represented a heterogeneous group, which was also reflected by their individual differences in cardiac performance. The common feature was that all patients had abnormal renal function and when stratified according to serum creatinine concentrations had increasing left ventricular dysfunction on exercise in relation to decreasing renal function.

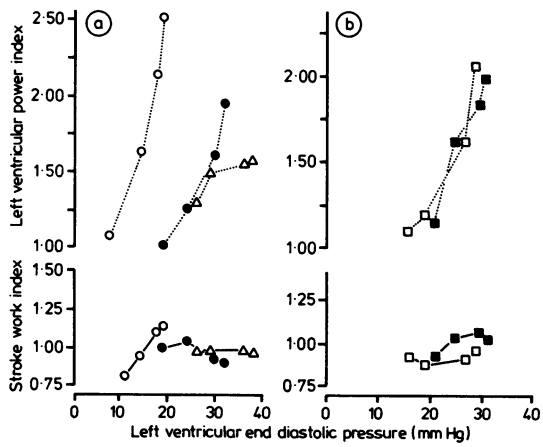

Figure *Relation of left ventricular power index and stroke work index to left ventricular end diastolic pressure (a) in three patients with serum creatinine concentrations <500 μmol/l (group 1) (○), six patients with concentrations of 500–1000 μmol/l (group 2) (●), and three patients undergoing maintenance haemodialysis (△); and (b) in five normotensive (□) and seven hypertensive (■) patients.*

The three patients with serum creatinine concentrations <500 μmol/l (group 1) had essentially normal left ventricular function, and the electrocardiographic patterns at rest and in response to exercise were normal. Thus myocardial disease was not apparently present in the earliest stages of renal failure. The six patients with serum creatinine concentrations in the range 500–1000 μmol/l (group 2) and the three patients undergoing haemodialysis (group 3), on the other hand, clearly had abnormal left ventricular function with increased left ventricular end diastolic pressure and an inability to achieve the increase in stroke work index during exercise that would normally occur (Figure *a*).[21] These results may thus indicate an increased stiffness of the ventricular wall and diminished systolic contractile function in most patients with a serum creatinine concentration >500 μmol/l. Similar results with abnormal contractile indices associated with increased left ventricular end diastolic pressure have previously been observed in patients undergoing long term haemodialysis.[15 16]

Pressures (mm Hg)													*Systolic pressure × heart rate*
Right ventricular†			*Pulmonary artery*			*Mean PCV*	*Left ventricular*			*Aorta*			
S	*D*	*ED*	*S*	*D*	*M*		*S*	*D*	*ED*	*S*	*D*	*M*	
			24	10	16	9	136	6	10	136	82	104	8976
			38	19	28		165	6	20				16335
22	5	14	21	9	15	8	176	8	14	176	104	136	13552
			49	23	33		220	8	20				25960
23	3	5	23	5	15		138	7	8	138	90	112	13110
			38	17	26					140	84	110	15820
55	5	15	28	18	22	16	218	6	24	218	120	161	15260
			57	32	48		196	12	41				21364
36	4	10	30	14	19	15	182	8	22	182	94	128	14014
			47	28	38		226	8	37				29380
31	2	8	26	10	16	9	180	0	16	180	84	120	13680
			37	13	22	25				214	100	148	25252
			23	13	17	10	105	4	13	105	61	79	6510
			37	17	30		148	9	30				13172
32	5	13	25	15	19	15	176	10	20	176	94	126	12320
			53	28	40		200	0	24				22770
32	0	4	20	9	14	11	152	6	14	152	92	116	8968
			40	17	28		184	0	24				20792
45	2	8	50	24	38	25	168	24	36	168	100	130	15456
			76	36	52		204	20	42				
46	6	14	44	23	33	24	186	16	28	180	108	140	13680
			59	31	46		188	15	35				16356
27	2	7	27	12	18	9	146	8	15	146	70	99	11826
			71	34	49		180	16	36				21600

Abnormal cardiac performance in end stage renal failure may result from a variety of mechamisms, such as hypertension, hypervolaemia, pericarditis with or without pericardial effusion, anaemia, and electrolyte and metabolic disturbances. Hypertension is commonly associated with renal failure, and volume overload has been suggested as the predominant cause of renal hypertension.[22-25] In possible contradiction to this hypothesis, however, is the fact that uraemic patients are usually hypertensive at an early stage of renal failure, when as a rule the blood volume is normal or even low.[26 27] Hypertension also plays an important role in the pathogensis of heart failure in uraemic patients.[16] But the normotensive and the hypertensive patients in the present study showed similar abnormal left ventricular function at different stages of renal failure (Figure *b*). This comparison suggested that uraemic heart failure develops irrespective of hypertension.

Accelerated atherosclerosis occurs in patients undergoing long term haemodialysis, and also a high mortality from arteriosclerotic complications in chronic renal failure has been reported.[28] In subsequent studies, however, the incidence of cardiovascular deaths from atherosclerosis was lower than previously stated and, in fact, not more common than in the total population.[29-31]

In the present series of patients the absence of chest pain and of electrocardiographic characteristics of ischaemic heart disease during exercise indicated that advanced coronary atherosclerosis had not developed. The severe anaemia in some of the patients could have been expected to unmask any significant coronary artery disease.

High output congestive heart failure resulting from the arteriovenous fistula in patients undergoing maintenance dialysis has been reported by several authors.[32-34] Resting cardiac output up to 10 l/min, which falls substantially during temporary occlusion of the shunt, was found in such patients. The relatively high resting cardiac output in three of the present patients undergoing maintenance haemodialysis did not, however, differ significantly from that in the non-dialysed patients. The high values probably also reflect the chronic anaemia present in most of these patients. In this study the haemoglobin concentration was found to be correlated with the left ventricular end diastolic pressure and the arteriovenous oxygen difference. Nevertheless, the effect of isolated severe chronic anaemia on cardiac function has been reported to be minimal,[35] with no influence on left ventricular end diastolic pressure.[36] Furthermore, the cardiac output at rest is usually not increased until the haemoglobin concentration is $<7{\cdot}0$ g/d.[36] The abnormal left ventricular function in the present patients in group 2 could not, however, be explained by severe anaemia, an arteriovenous shunt, or haemodialysis. We, therefore, consider that anaemia and the presence of arteriovenous shunts—for example—should be regarded as factors potentiating or unmasking the underlying myocardial disease rather than as causal agents in their own right.

A specific uraemic cardiomyopathy has been postulated,[14 16 17 37] but documentation of the condition has been hampered by all the abovementioned factors that may underlie abnormal cardiac performance. The findings in the present series of patients are not inconsistent with the concept of a specific uraemic heart disease, since in most patients with abnormal cardiac performance the aetiology of the cardiac dysfunction was otherwise obscure. As early as 1944 Raab suggested that a specific myocardial toxin may be present in uraemia and constitute the primary cause of uraemic heart disease.[38] Many substances can accumulate in the body in uraemia, and some of them may act as toxins. Among the chemicals that could lead to cardiac damage and dysfunction, no specific myocardial toxin has yet been identified. Excess parathyroid hormone, however, has been suggested from clinical[39 40] and experimental[41] observations to have a significant effect on the myocardium, causing ectopic calcifications. Parathyroidectomy has been reported to improve cardiac function in patients with end stage renal failure.[40] Other agents that may play an important role in the pathogenesis of uraemic heart failure are certain trace elements. These elements were found in appreciably increased concentrations in the myocardium of uraemic patients.[42]

An accumulation of toxins would be consistent with the progressive deterioration in cardiac performance in the present series of patients. The removal of such toxins after renal transplantation would accordingly be expected to result in improved cardiac performance and this has recently been reported.[43]

In conclusion, the observations in our study indicate that uraemic heart failure is a result of several different pathogenic factors and arises at a relatively early stage of renal failure.

References

1 Wing AJ, Brunner FP, Brynger H, *et al.* Combined report on regular dialysis and transplantation in Europe, VIII, 1977. *Proc Eur Dial Transplant Assoc* 1978; **15**: 4–76.

2 Lazarus JM, Lowrie EG, Hampers CL, Merrill JP. Cardiovascular disease in uremic patients on hemodialysis. *Kidney Int* 1975; **7** (suppl 2): 167–75.

3 Scharf S, Wexler J, Longnecker RE, Blalufox MD. Cardiovascular disease in patients on chronic hemodialytic therapy. *Prog Cardiovasc Dis* 1980; **22**: 343–56.

4 Lewis BS, Milne FJ, Goldberg B. Left ventricular function in chronic renal failure. *Br Heart J* 1976; **38**: 1229–39.

5 Cohen MV, Diaz P, Scheuer J. Echocardiographic assessment of left ventricular function in patients with chronic uremia. *Clin Nephrol* 1979; **12**: 156–62.

6 D'Cruz IA, Bhatt GR, Cohen HC, Glick G. Echocardiographic detection of cardiac involvement in patients with chronic renal failure. *Arch Intern Med* 1979; **138**: 720–4.

7 Riley SM Jr, Blackstone EH, Sterling WA, Diethelm AG. Echocardiographic assessment of cardiac performance in patients with arteriovenous fistulas. *Surgery Gynecol Obstet* 1978; **146**: 203–8.

8 Miach PJ, Dawborn JK, Louis WJ, McDonald IG. Left ventricular function in uremia: echocardiographic assessment in patients on maintenance dialysis. *Clin Nephrol* 1981; **15**: 259–63.

9 Abbasi AS, Slaughter JC, Allen MW. Asymmetric septal hypertrophy in patients on long-term hemodialysis. *Chest* 1978; **74**: 548–51.

10 Ikäheimo M, Huttunen K, Takkunen J. Cardiac effects of chronic renal failure and hemodialysis treatment — hypertensive versus normotensive patients. *Br Heart J* 1981; **45**: 710–6.

11 Bornstein A, Zambrano SS, Morrison RS, Spodick DH. Cardiac effects of hemodialysis: noninvasive monitoring by systolic time intervals. *Am J Med Sci* 1975; **269**: 189–92.

12 Dongradi G, Dubois D, Bécart J, Coy JL, Fendleu JP. Function myocardique de l'hémodialysé chronique. Evaluation par la mesure des intervalles de temps systoliques. *Nouv Presse Med* 1977; **6**: 2039–42.

13 Ireland MA, Mehta BR, Shiu MF. Acute effects of haemodialysis on left heart dimensions and left ventricular function: an echocardiographic study. *Nephron* 1981; **29**: 73–9.

14 Hung J, Harris PJ, Uren RF, Tiller DJ, Kelly DT. Uremic cardiomyopathy — effect of hemodialysis on left ventricular function in end-stage renal failure. *N Engl J Med* 1980; **302**: 547–51.

15 Drüeke T, Le Pailleur C, Meilhac B, *et al.* Congestive cardiomyopathy in uraemic patients on long-term haemodialysis. *Br Med J* 1977; **1**: 350–3.

16 Capelli JP, Kasparian H. Cardiac work demands and left ventricular function in end-stage renal disease. *Ann Intern Med* 1977; **86**: 261–7.

17 Drüeke T, Le Pailleur C, Sigal-Saglier M, Zingraff J, Crosnier J, Di Mattéo J. Left ventricular function in hemodialyzed patients with cardiomegaly. *Nephron* 1981; **28**: 80–7.

18 Aström H, Joknsson B. Design of exercise test with special reference to heart patients. *Br Hear J* 1976; **38**: 289–96.

19 Sjöstrand T. A method for the determination of the total haemoglobin content of the body. *Acta Physiol Scand* 1948; **16**: 211–31.

20 Taussky AHH. *Standard methods of clinical chemistry.* vol 3. New York and London: Academic Press, 1961.

21 Ekelund LG, Holmgren A. Central hemodynamics during exercise. *Circ Res* 1967; **20** (suppl I): 33–43.

22 Dustan HP, Page IH. Some factors in renal and renoprival hypertension. *J Lab Clin Med* 1964; **64**: 948–59.

23 Vertes V, Cangiano JL, Berman LB, Gould A. Hypertension in end-stage renal disease. *N Engl J Med* 1969; **280**: 978–81.

24 De Planque BA, Mulder E, Mees EJD. The behaviour of blood and extracellular volume in hypertensive patients with renal insufficiency. *Acta Med Scand* 1969; **186**: 75–81.

25 Lazarus JM, Hampers CL, Merrill JP. Hypertension in chronic renal failure. Treatment with hemodialysis and nephrectomy. *Arch Intern Med* 1974; **133**: 1059–66.
26 Hull AR, Long DL, Prati RC, Pettinger WA, Parker TF. The control of hypertension in patients undergoing regular maintenance hemodialysis. *Kidney Int* 1975; 7 (suppl 2): 184–7.
27 McGrath BP, Ledingham JGG. Renin, blood volume and response to saralasin in patients on chronic haemodialysis: evidence against volume and renin — "dependent" hypertension. *Clin Sci Mol Med* 1978; **54**: 305–12.
28 Lindner A, Charra B, Sherrard DJ, Scribner BH. Accelerated atherosclerosis in prolonged maintenance hemodialysis. *N Engl J Med* 1974; **290**: 697–701.
29 Burke JF Jr, Francos GC, Moore LL, Yon Cho S, Lasker N. Accelerated atherosclerosis in chronic dialysis patients — another look. *Nephron* 1978; **21**: 181–5.
30 Nicholls AJ, Catto GRD, Edward N, Engeset J, Macleod M. Accelerated atherosclerosis in long-term dialysis and renal-transplant patients: fact or fiction? *Lancet* 1980; **i**: 276–8.
31 Clyne N, Lins LE, Pehrsson SK. Heart disease in uremia [Abstract]. *Blood Purification* 1983; **1**: 102.
32 Ahearn DJ, Maher JF. Heart failure as a complication of hemodialysis arteriovenous fistula. *Ann Intern Med* 1972; 77: 201–4.
33 Anderson CB, Groce MA. Banding of arteriovenous dialysis fistulas to correct high-output cardiac failure. *Surgery* 1975; **78**: 552–4.
34 Anderson CB, Codd JR, Graff RA, Groce MA, Hartner HR, Newton WT. Cardiac failure and upper extremity arteriovenous dialysis fistulas. *Arch Intern Med* 1976; **136**: 292–7.
35 Warrier ER, Balakrishnan KG, Sankaran K, Gupta GD. Systolic time intervals in chronic severe anaemia and effect of diuretic and digitalis. *Br Heart J* 1981; **46**: 80–3.
36 Varat MA, Adolph RJ, Fowler NO. Cardiovascular effects of anemia. *Am Heart J* 1972; **83**: 415–26.
37 Prosser D, Parsons V. The case for a specific uraemic myocardiopathy. *Nephron* 1975; **15**: 4–7.
38 Raab W. Cardiotoxic substances in the blood and heart muscle in uremia. *J Lab Clin Med* 1944; **29**: 715–34.
39 Massry SG, Goldstein DA. The search for uremic toxin(s) "x"−"x"=PTH. *Clin Nephrol* 1979; **11**: 181–9.
40 Drüeke T, Fauchet M, Fleury J, *et al.* Effect of parathyroidectomy on left ventricular function in hemodialysis patients. *Lancet* 1980; **i**: 112–4.
41 Ejerblad S. Uraemic myocardial disease. An experimental study with special reference to the effect of parathyroidectomy. *Acta Chir Scand* 1979; **145**: 345–53.
42 Pehrsson SK, Lins LE. The role of trace elements in uremic heart failure. *Nephron* 1983; **34**: 93–8.
43 Lai KN, Barnden L, Mathew TH. Effect of renal transplantation on left ventricular function in hemodialysis patients. *Clin Nephrol* 1982; **18**: 74–8.