PAPERS AND ORIGINALS

Incidence of Uraemia and Requirements for Maintenance Haemodialysis

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Summary

The biochemistry laboratory records of a 400-bed general hospital serving a population of about 120,000 showed that during the three-year period 1966-8 inclusive 487 patients had at some stage during their admission a blood urea of 100 mg/100 ml or more. Ninety per cent. were aged 50 or over, 79% were 60 or over, and 52% were 70 or over.

The case notes of all patients with renal failure admitted during 1966 and 1967 were examined together with those of patients under 60 admitted during 1968. Three observers agreed about the most likely cause of the renal failure in 90% of patients whose case notes were available, or 74% of the total. The raised blood urea was thought to be due to "prerenal" factors in 60% of the patients, to acute tubular necrosis in 8%, to obstructive uropathy in 12%, and to "intrinsic" renal disease in 20%. Renal failure precipitated by such factors as cardiac failure, chest infections, cerebrovascular accidents, and shock was particularly common in old people.

The hospital survey and replies to a questionnaire sent to all general practitioners in the area suggest that in the three-year period 14 patients may have been suitable for treatment by maintenance haemodialysis or renal transplantation. This represents a rate of about 39 per million per year under the age of 60 and 28 per million per year under 50.

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Introduction

The number of patients suffering from chronic renal failure who might benefit from treatment by maintenance haemodialysis or renal transplantation is uncertain. A figure often quoted for the United Kingdom is 40 per million per year, or between 2,000 and 3,000 patients per year (de Wardener, 1966; *British Medical Journal*, 1967). This estimate is based largely on information obtained from death certificates and is therefore apt to be inaccurate. There are, however, several other methods by which the estimate might be made—namely, (1) by detailed surveys on very large populations, (2) by making uraemia a notifiable disorder, (3) by asking general practitioners in a defined area to report all uraemic patients in their practices, (4) by study of hospital records, and (5) by analysis of biochemical data from hospital laboratories.

In practice, because of the relatively low prevalence of uraemia, a population survey would require biochemical measurements on at least 100,000 people. This is not practicable. Notification is unlikely to be an accurate source of data, and it presents administrative problems. The other three approaches are also likely to have considerable errors. We decided, therefore, to use all three in a study in one defined area. Unfortunately, the study of hospital records had to be abandoned because of inadequate classification.

In this paper we analyse the information provided by general practitioners and the biochemical data obtained from a hospital laboratory—that is, methods 3 and 5—and draw some conclusions about the incidence of uraemia and the need for treatment by maintenance haemodialysis and renal transplantation.

Plan of Study

The area selected for this pilot study is defined as the catchment area of a district general hospital in Glamorganshire, South Wales. It is a mixed urban and rural area with a population of about 120,000. The hospital has 408 beds, and is the only general hospital serving the area.

General Practitioners' Survey.—In January 1968 and again in January 1969 a letter was written to all family doctors in

the area asking for a list of all patients in their practice suffering from uraemia. In this context "uraemia" was defined as a blood urea of 100 mg/100 ml or more.

Hospital Laboratory Survey.—From the laboratory records a list was made of all patients with blood urea values of 100 mg/100 ml or more detected during 1966, 1967, and 1968. The case notes were studied and the relevant clinical information was abstracted on to cards. Three independent observers then analysed the cards and decided what the predominant cause of the uraemia was likely to be in each instance.

Results

HOSPITAL SURVEY

The hospital biochemistry laboratory records showed that at some stage during their admission 147 patients had a blood urea of 100 mg/100 ml or greater in 1966, 122 in 1967, and 218 in 1968. The highest blood urea recorded in each patient admitted during 1966 and 1967 is shown in Table I. Analysis of the age and sex distribution of patients with renal failure shows a remarkable preponderance of elderly patients (Table II). Ninety per cent. of all patients with blood urea of 100 mg/100 ml or more were aged 50 or over, 79% were 60 or over, 52% were 70 or over, and 22% were 80 or over; only 3·3% were under 40. There was nothing very unusual about the age and sex distribution of all admissions to the hospital during one randomly-selected month (Table III). The age and sex distribution (1961 Census) of the 120,000 people in the area served by the hospital is shown in Fig. 1.

About 67% of the patients with blood urea of 100 mg/100 ml or more were under the care of physicians and 27% under the care of general surgeons. The number of patients admitted under various specialties during 1966 and 1967 is shown in Table IV. Medicine, geriatrics, and general surgery account for about 39% of the total number of admissions but for 94% of the "uraemic" patients.

To determine whether the high incidence of uraemia was due to "routine" measurement of blood urea in very ill patients, all deaths occurring during January-March 1967 inclusive were studied. Patients with a recorded blood urea of 100 mg/100 ml or more constituted only a small proportion of all deaths (Fig. 2).

TABLE I—*Blood Urea Values in* 269 *Patients with Renal Failure Admitted During* 1966 *and* 1967

Blood Urea (mg/100 ml)	No. of Patients	
	1966	1967
100–200	75	76
201–300	38	29
301–400	21	6
401–500	7	9
>500	6	2
	147	122

TABLE II—*Age and Sex Distribution of* 487 *Patients with Blood Urea of* 100 *mg/*100 *ml or more Admitted During the Three-year Period* 1966-8

Age (Years)	No. of Patients			% of Total
	Male	Female	Total	
0– 9	3	1	4	3·3
10–19	2	0	2	
20–29	2	3	5	
30–39	2	3	5	
40–49	19	12	31	6·4
50–59	27	26	53	10·9
60–69	87	46	133	27·2
70–79	80	67	147	30·2
80–	54	53	107	22·0

TABLE III—*Age and Sex Distribution of* 1,068 *Patients Admitted During January* 1967

Age (Years)	No. of Patients			% of Total
	Male	Female	Total	
0– 9	69	61	130	12·1
10–19	50	43	93	8·7
20–29	46	210	256	24·0
30–39	35	96	131	12·3
40–49	40	76	116	10·9
50–59	60	61	121	11·3
60–69	61	46	107	10·0
70–79	38	30	68	6·4
80–	18	28	46	4·3

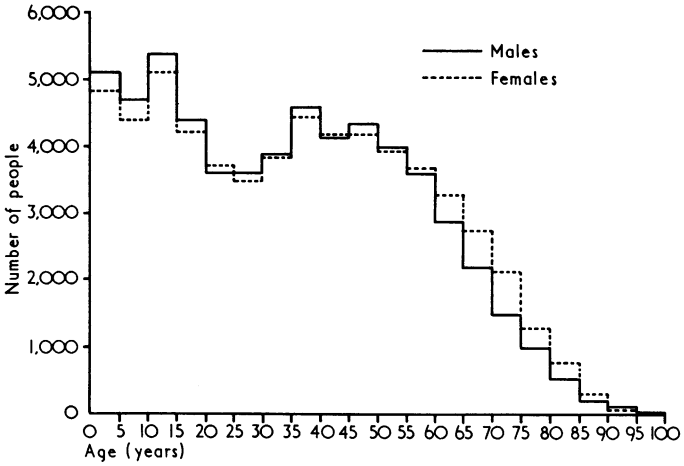

FIG. 1—Age and sex distribution of the 120,000 people living in the area (1961 Census).

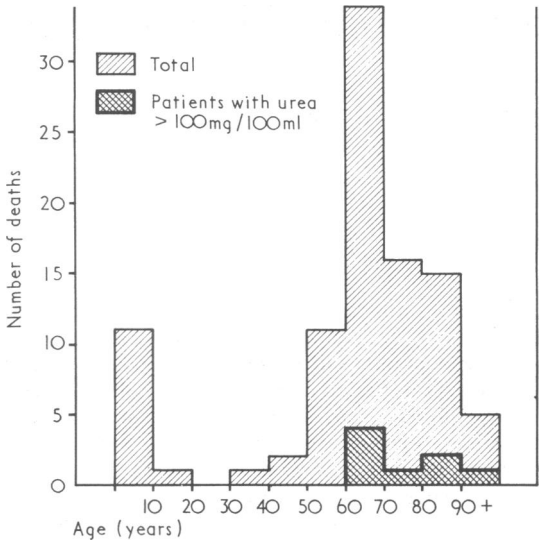

FIG. 2—Total number of deaths in patients admitted during January-March 1967 and the number with blood urea of 100 mg/100 ml or more.

Patients Admitted during 1966 and 1967

The hospital records department were unable to trace the case notes of 24 (16%) of the patients admitted during 1966 and 23 (19%) of the 1967 patients. For the two-year period, therefore, 222 case notes were available for examination out of a possible 269 (83%). All three observers agreed about the likely cause of the "uraemia" in 69% of these 222 cases; two agreed and one differed in 25%; and all three differed in 6%. After this initial analysis 18 patients were rejected because at least two observers had failed to reach a diagnosis on the information available. The remaining 204 were reconsidered. In nearly all cases disagreement was due to difficulty either

TABLE IV—*Total Number of Admissions During* 1966 *and* 1967

Specialty	No. of Admissions	% of Total
General medicine	2,436	12·9
Geriatrics	885	4·6
Paediatrics	1,366	7·2
General surgery	4,014	21·2
Orthopaedics and trauma	2,403	12·6
Obstetrics	3,609	19·1
Gynaecology	2,212	11·7
Urology	932	4·9
Ophthalmology	539	2·9
Others	545	2·9
Total	18,941	100

TABLE V—*Predominant Cause of Uraemia in* 199 *Patients with Blood Urea of* 100 *mg*/100 *ml or more* (1966 *and* 1967)

Cause of Renal Failure	No. of Patients	% of Total
Primary renal disease	39	19·5
? Acute tubular necrosis	16	8·0
Obstructive uropathy	24	12·0
Prerenal uraemia	120	60·5
(*a*) Cardiac	40	20·0
(*b*) Cerebral	17	8·5
(*c*) Respiratory	16	8·0
(*d*) Malignancy	15	12·0
(*e*) Diabetes	8	4·0
(*f*) Miscellaneous	24	7·5

TABLE VI—*Diagnosis in* 39 *Patients with Blood Urea of* 100 *mg*/100 *ml or more Due to Primary Renal Disease*

Diagnosis	Male	Female	Total
Chronic glomerulonephritis	5	0	5
Chronic pyelonephritis (including acute exacerbations)	4	8	12
Acute pyelonephritis	1	2	3
Hypertension	5	2	7
Polycystic kidneys	1	0	1
Polyarteritis nodosa	1	0	1
? Gout nephropathy	0	1	1
Uncertain	6	3	9
Total	23	16	39

TABLE VII—*Age and Sex Distribution of* 120 *Patients with Prerenal Uraemia*

Cause of Prerenal Uraemia	Age in Years												Total
	<40		40—49		50—59		60—69		70—79		⩾80		
	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	
Cardiac	0	0	2	0	5	3	7	6	5	6	1	5	40
Respiratory	0	0	0	0	1	1	6	1	2	1	2	2	16
Cerebral	0	0	0	0	1	1	2	1	5	1	1	5	17
Malignancy	0	0	0	0	1	0	1	0	3	5	3	2	15
Diabetes	0	0	0	0	0	1	2	0	0	4	0	1	8
Misc.	1	1	1	1	0	1	3	5	3	3	2	3	24
Total	1	1	3	1	8	7	21	13	18	20	9	18	120

TABLE VIII—*Age and Sex of* 34 *Patients under* 60 *with Primary Renal Disease Admitted During* 1966, 1967, *and* 1968

Age	Males	Females	Total
0– 9	0	1	1
10–19	0	0	0
20–29	1	3	4
30–39	0	2	2
40–49	12	4	16
50–59	7	4	11
Total	20	14	34

TABLE IX—*Diagnosis in* 34 *Patients Under* 60 *with Blood Urea of* 100 *mg*/100 *ml or more Due to Primary Renal Disease Admitted During* 1966, 1967, *and* 1968

Diagnosis	Male	Female	Total
Chronic glomerulonephritis	5	3	8
Chronic pyelonephritis (including acute exacerbations)	4	4	8
Acute pyelonephritis	0	2	2
Hypertension	7	2	9
Polycystic kidneys	1	1	2
? Polyarteritis nodosa	1	1	2
? Diabetic nephropathy	1	0	1
Uncertain	1	1	2
Total	20	14	34

in deciding whether uraemia was "renal" or "prerenal" or in assigning patients to the various subgroups of prerenal uraemia referred to below. After discussion five more were excluded, leaving 199 patients regarding whom all three observers agreed about the most likely diagnosis. Agreement was thus reached in 74% of the total number of patients and in 90% of those whose case notes were available. The number of patients in the various categories is shown in Table V.

Primary Renal Disease

In 39 patients (20%) the raised blood urea was thought to be due to "intrinsic" or "primary" renal disease. The presumptive diagnoses are shown in Table VI. Twenty-two of the 39 patients died, either in hospital or shortly after discharge. Death was due to "uraemia" in 11; others died of cardiac failure, cerebrovascular accident, myocardial infarction, and pneumonia.

Sixteen of the 39 patients were under 60 years of age and might therefore have been potential candidates for maintenance haemodialysis. This group, together with similar patients admitted during 1968, is discussed in more detail below.

Acute Tubular Necrosis

In spite of our difficulty in distinguishing between acute tubular necrosis and prerenal uraemia, dehydration, hypotension, and uraemia were sufficiently severe and prolonged in 16 patients to justify a presumptive diagnosis of acute tubular necrosis. This diagnosis could be made with confidence in six patients; three of these were transferred to the regional renal unit. In the remaining 10 patients some doubt exists; eight of these 10 died in hospital. All 16 patients were aged 60 or over and eight were 70 or over; 12 of the 16 were men.

Postrenal or Obstructive Uropathy

Twenty-four patients (12%) fell into this category; 21 were male. Only four patients were under 60 years of age, 16 were 70 or over, and six were 80 or over. Nine of the 24 were discharged well, 14 died while in hospital, and one patient with flaccid paraplegia due to spinal secondary deposits was transferred to another hospital, where he died later.

Prerenal Uraemia

The raised blood urea was thought to be due to prerenal factors in 120 of the 199 patients (60%). They have been subdivided into six main groups according to the predominant cause of the uraemia, but it was often difficult to allocate patients to these subgroups, and in many instances more than one factor was involved. The age and sex distribution of patients in these various subgroups is shown in Table VII.

Cardiac.—This subgroup contained one-third of all patients with prerenal uraemia. In 26 patients the raised blood urea was probably due to congestive cardiac failure, and in the remaining 14 it was related to cardiogenic shock secondary to myocardial infarction. Thirty-one of the 40 patients died, but renal failure was probably not an important factor except perhaps in three. One of these had a blood urea of 330 mg/100 ml, and in the other two the serum potassium was 6·4 and 7·5 mEq/l. respectively.

Cerebral.—In 17 (14%) of the 120 patients with prerenal uraemia the raised blood urea was probably due to inadequate fluid intake in those who were confused, drowsy, or unconscious as a result of some cerebral or cerebrovascular lesion. Twelve of the 17 were aged 70 or over (Table IV).

Only four patients recovered sufficiently to leave hospital, but uraemia contributed to death in probably only two of the 13 who died; these two patients were aged 84 and 99 years.

Respiratory.—Sixteen (14%) of the patients with prerenal uraemia had severe respiratory disease. This group includes elderly patients with bronchopneumonia and patients with respiratory failure due to acute or chronic bronchitis, asthma, or pneumoconiosis. Five were discharged with good renal function after treatment of the acute episode; 10 died from cardiorespiratory failure and another from a severe melaena. The highest blood urea recorded in the patients who died was 210 mg/100 ml.

Malignancy.—Fifteen patients with prerenal uraemia (12%) had malignant disease; 10 died in hospital. The site of the primary tumour was the lung in three, upper alimentary tract in five, lower alimentary tract in four, breast in one, carcinoid tumour of small intestine in one, and not known in the other. Renal failure was due to fluid and electrolyte depletion, either as a result of diarrhoea and vomiting or after major surgery.

Diabetes.—Dehydration due to uncontrolled diabetes was responsible for prerenal uraemia in eight patients. Six were known diabetics; all but one were 60 or over. Six of these patients died, but in only two was renal failure an important factor.

Miscellaneous.—In the remaining 24 patients the prerenal uraemia was due to various disorders, such as diarrhoea, vomiting, intestinal obstruction, postoperative dehydration, bleeding peptic ulcers, paralytic ileus, or mesenteric artery thrombosis. In 17 of the 24 the blood urea fell after rehydration.

Patients Investigated During 1968

Forty-eight of the 218 patients found to have a blood urea of 100 mg/100 ml or more during 1968 were under 60 years of age, and further analysis was confined to this group. There was no evidence that six had been admitted to hospital, and a presumptive diagnosis could be made in only 35 of the 48 patients. The renal failure was thought to be due to primary renal disease in 19, and these are considered in more detail below.

Patients Under 60 with Primary Renal Disease (1966-9)

This group consists of 34 patients—16 admitted during 1966 and 1967 and 19 during 1968, one patient having been admitted during both periods. The age and sex distribution of these 34 patients is shown in Table VIII and the presumptive diagnoses in Table IX. Sixteen died in hospital and in 11 of them uraemia was an important factor; the others died of subarachnoid haemorrhage, cerebral haemorrhage, dissecting aneurysm, hypertensive cardiac failure, and myocardial infarction.

Study of the case notes suggests that 10 of the 11 patients who died of uraemia were potential candidates for treatment by regular haemodialysis. In addition to those who died of renal failure two patients were accepted for maintenance haemodialysis during 1968. During 1969 three more were treated by maintenance haemodialysis or transplantation.

GENERAL-PRACTITIONER SURVEY

January 1968.—All 54 general practitioners completed the questionnaire. A total of nine patients were reported. Five of these were potential candidates for maintenance haemodialysis. One was already receiving treatment and the other four were detected by the hospital survey. Three of the nine patients were over 60, and a fourth, aged 57, was considered unsuitable for dialysis because of severe coronary artery disease.

January 1969.—Again all the general practitioners completed the questionnaire. On this occasion 13 patients were reported, but three of these had already been included in the January 1968 survey. Five were aged 60 or over. Of the remainder, three died of uraemia without referral to the regional centre, one was considered unsuitable for dialysis, and one was accepted during 1969.

MAINTENANCE DIALYSIS REQUIREMENTS

The number of patients who might have been suitable for treatment by maintenance haemodialysis detected by the hospital survey was 15, compared with only seven by the general-practitioner survey. Two of the patients detected by the general-practitioner survey, however, were missed by the hospital survey. One of these was receiving treatment by maintenance haemodialysis at the time. The total number detected by both surveys, therefore, was 17. Three of these, however, were not in need of treatment until after January 1969, so the number of patients actually receiving treatment, or who died through lack of treatment, during the three-year period 1966-8 inclusive was 14. Four of these patients were 50 years of age or over.

With a population at risk of 120,000 this represents a rate of about 39 per million per year under the age of 60 and 28 per million per year under 50.

Discussion

INCIDENCE OF URAEMIA

Analysis of the Registrar General's Report (England and Wales) shows that during 1967 diseases likely to terminate in uraemia caused 7,379 deaths. This represents 1·4% of all deaths, or 137 deaths per million of the population per year. About three-quarters of the patients were aged 50 or over, 60% were 60 or over, 37% were 70 or over, and 13% were 80 or over (Table X).

Our survey shows that the prevalence of significant renal failure (blood urea 100 mg/100 ml or more) is about 10 times greater than the national death rate from renal diseases. With a population at risk of 120,000 the mean prevalence during 1966-8 inclusive was about 1,350 per million per year. On average, about three new patients with renal failure were

TABLE X—*Deaths Due to Diseases Likely to Terminate in Chronic Renal Failure in England and Wales,* 1967 (*Data from Registrar General's Report*)

Diseases	Age in Years																		Total
	0–	1–	5–	10–	15–	20–	25–	30–	35–	40–	45–	50–	55–	60–	65–	70–	75–	80–	85–	
Nephritis and nephrosis	12	8	17	16	51	51	43	52	66	108	148	170	230	273	302	317	306	274	233	2,677
Pyelitis, pyelocystitis, and pyelonephritis	17	9	5	3	14	15	23	20	34	40	83	107	184	250	328	427	516	482	510	3,067
Calculi of kidney and ureter	0	1	0	0	0	0	0	1	2	4	10	7	17	29	28	34	29	21	13	196
Essential malignant hypertension	0	0	0	1	2	8	14	9	26	49	76	101	101	67	47	29	10	8	1	549
Hypertension with arteriolar nephrosclerosis	0	0	0	0	0	1	0	1	0	2	3	7	11	18	24	61	84	85	135	432
Congenital malformation of genitourinary system	165	12	10	3	1	9	3	11	12	26	28	33	43	19	29	22	17	10	5	458
Total	194	30	32	23	68	84	83	94	140	229	348	425	586	656	758	890	962	880	897	7,379
Cumulative percentage	2·6	3·0	3·4	3·7	4·6	5·7	6·8	8·1	10·0	13·1	17·8	23·6	31·5	40·4	50·7	62·8	75·8	87·7	100	100

detected per week in a general hospital with 400 beds. Since all patients with renal failure were almost certainly not detected, this is a minimum estimate. The preponderance of elderly patients was even more striking than in the national mortality statistics; 92% were aged 50 or over.

Renal function decreases progressively after about 30 years of age (Lewis and Alving, 1938; Davies and Shock, 1950). Even in old age, however, this impairment of renal function is usually not apparent under ordinary circumstances, because the blood urea does not rise significantly until more than half the functioning renal tissue has been destroyed. But the elderly patient is particularly vulnerable to conditions of stress, and prerenal uraemia is very readily induced by such factors as cardiac failure, shock, dehydration, and chest infection. This high incidence and mortality of prerenal uraemia in old age has been emphasized previously (Agate, 1963; Heider and Brest, 1963), and attention has been drawn to the frequency of unusual clinical presentation of urinary infection in the elderly (Black and Moore, 1969). Whether the gradual reduction in renal function with age is due to an increasing incidence of renal disease in the elderly (Lapides and Zierdt, 1967) or to "senile nephrosclerosis" (Oliver, 1952) is debatable.

Despite the high incidence, renal failure was probably directly responsible for death in only about 10-15% of our patients. The death rate from uraemia in this population is thus similar to the national mortality rate. In most patients renal failure merely reflected the severity of the underlying disease, and it is unlikely that correction of the uraemia would have had much effect on the ultimate outcome in patients with cardiac failure, cerebral lesions, severe respiratory failure, or malignant disease. Nevertheless, the figures given above may be taken in some way as representing not only the work load but also the need for a physician with a special interest in renal disease in every district general hospital.

MAINTENANCE HAEMODIALYSIS REQUIREMENTS

Most estimates of the number of patients with renal failure who require treatment by maintenance haemodialysis or renal transplantation are based on mortality statistics. de Wardener (1966) analysed the data in the Registrar General's Report, England and Wales (1962), and found that, whereas nearly 7,000 deaths were probably attributable to renal failure, if treatment were to be limited to patients aged between 16 and 55 the number involved would be 2,230. A similar analysis of deaths in 1967 due to renal diseases likely to terminate in renal failure is shown in Table X. Of the 7,379 patients 68·5% were aged 55 or over; 2,057 deaths occurred in the age group 15-59. If the upper age limit is reduced from 59 to 54 years the number falls sharply to 1,471, and if treatment were to be further restricted to the age group 15-49 years inclusive only 1,046 patients would be involved. Some of these patients, for a variety of reasons, would undoubtedly have been unsuitable for treatment by maintenance haemodialysis. Furthermore, death was probably due to cardiovascular complications, rather than to uraemia, in many of these patients. Unfortunately, the Registrar General's Report does not classify deaths from renal failure separately.

Since 1961 the Danish National Health Service Report has included a subdivision denoting deaths from renal disease in which uraemia is considered to be the immediate cause of death. The mortality from renal disease (excluding patients with cancer and generalized systemic disease) remained relatively constant in Denmark around 260 deaths per million per year between 1958 and 1964; uraemia was the immediate cause of death in about 80% of these patients (Thaysen, 1966). The number of patients with end-stage chronic renal failure needing treatment by maintenance haemodialysis was estimated to be about 43 per million per year in the age group 15-54 years but only 19 per million per year in the age group 15-44 years (Thaysen, 1966).

A survey in south-eastern Ontario, based on a questionnaire sent to all physicians in the area, suggested an incidence of persons under 50 with blood urea of 100 mg/100 ml or more of between 22 and 33 per million per year (Morrin, 1966). The estimate reached on the basis of the present survey is very similar to that based on national mortality statistics. During a three-year period the rate was 39 per million per year for the age group 15-59 years and 28 per million per year for those aged 15-49 years. Since a proportion of these patients would almost certainly have proved to be unsuitable for treatment by maintenance haemodialysis this is probably an overestimate. On the other hand, some patients with chronic uraemia were probably not diagnosed, and the medical records were not available in nearly 20% of the ones detected.

Contrary to experience in Australia (Sheil *et al.*, 1969), the number of patients suitable for treatment by maintenance haemodialysis actually referred to our regional haemodialysis centre has been less than would be expected if the incidence were 40-50 per million per year. During the first two years 68 patients from the adjacent counties of Glamorganshire and Monmouthshire (population 1,470,000) were treated; this represents a rate of only 23 per million per year. No valid estimate can be made of the number of suitable patients not referred, but as local physicians were aware of the facilities available it is unlikely to have been very large. If the results of the survey and the number of patients referred to the regional centre are taken into account it seems reasonable to conclude that the number of patients who would be regarded as suitable for treatment by maintenance haemodialysis, by present criteria, is somewhere between 25 and 30 per million per year.

The evidence whether or not the mortality of maintenance haemodialysis and renal transplantation increases with age is conflicting (Cameron *et al.*, 1970; Cohen *et al.*, 1970). Lowering the upper age limit of acceptance, even by only 5 years, certainly has a pronounced effect on the number of patients involved, but it may be argued that in a country with a socialized health service it is not justifiable to let a certain arbitrary age be an obstacle to treatment. The implications of failing to apply any restrictions, however, are well illustrated by the data obtained by Alwall (1966), who examined the records of all patients who died in hospital during the five-year period 1960-4 in an area of Sweden with a population of 400,000. After careful sifting there were 137 patients who would in all probability have been judged suitable for maintenance haemodialysis. To deal with all renal services, in a country with a total population of eight million, Alwall estimated that eight medical renal clinics would be required, each with 50 beds and 15 dialysis beds, together with a further 80 beds divided into units of seven or eight beds at medical clinics in county hospitals. These calculations, admittedly, do not take into account the important contributions of home dialysis and renal transplantation, but, even so, it is unlikely that facilities on this scale can be provided in the United Kingdom, where the population is about nine times greater. This being so, it may be justifiable, at least for the time being, to restrict treatment by maintenance haemodialysis and renal transplantation to patients under 50 years of age.

We wish to thank the consultants for permission to examine case notes, the general practitioners for completing the questionnaires, and the staff of the medical records and biochemistry departments for their invaluable help.

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Use of Oxprenolol in Cardiac Arrhythmias Associated with Acute Myocardial Ischaemia

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Summary

Oxprenolol, a new beta-receptor blocking drug with intrinsic sympathomimetic activity, was used to treat 63 episodes of cardiac arrhythmia occurring in 43 patients with acute myocardial infarction or myocardial ischaemia. The drug was most effective in abolishing ventricular ectopic beats and supraventricular tachycardia. The best method of administration was by continuous intravenous infusion and the most satisfactory bolus dose was 6 mg. The main side effect was hypotension, which occurred in 59% of episodes of arrhythmia that had responded previously to intravenous administration. Oxprenolol was often effective in lignocaine-resistant arrhythmia. The two main advantages of oxprenolol over propranolol are the reduced likelihood of adversely affecting myocardial function and the diminished tendency to produce bronchospasm.

Introduction

Since the introduction of beta-adrenergic blocking drugs in cardiac arrhythmias by Stock and Dale in 1963 these drugs have been used extensively to treat a variety of arrhythmias associated both with acute myocardial infarction and with chronic heart disease (Harrison *et al.*, 1965; Bath, 1966; Epstein and Braunwald, 1966; Frieden *et al.*, 1967; Irons *et al.*, 1967; Theilen and Wilson, 1968). There are, however, two main disadvantages associated with the use of these drugs: firstly, a deleterious effect on myocardial function (Chamberlain, 1966; Stephen, 1966); and, secondly, an adverse effect on the bronchial musculature leading to bronchospasm (McNeill, 1964; Sandler and Clayton, 1970). Oxprenolol is a new beta-adrenergic blocking agent which is equipotent with propranolol in its negative chronotropic action, but is claimed to produce significantly less depression of myocardial contractility (Grandjean and Rivier, 1968). Preliminary observations have suggested that the antiarrhythmic action of oxprenolol is as effective as that of propranolol (Waal, 1968), but the assessment was based on oral therapy mainly in outpatients with arrhythmias associated with chronic heart disease. In view of the potential value of oxprenolol in treating acute arrhythmias after myocardial infarction, it was decided to investigate the use of parenteral therapy with oxprenolol in this situation.

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Patients and Methods

Forty-three patients aged 39 to 74 years were studied after admission to the coronary care unit. Thirty-four had typical QS and/or sequential S-T changes in the electrocardiogram associated with raised serum enzymes (aspartate aminotransferase and lactate dehydrogenase), confirming acute myocardial infarction. This was anterior in 24, inferior in eight, and high lateral in two. Three patients had classical ischaemic pain, with left bundle-branch block on the electrocardiogram in one and raised serum enzymes without E.C.G. changes in the other two. Five patients had ischaemic cardiac pain but no E.C.G. or enzyme changes, and one patient was admitted for a pulmonary embolus. Some of the patients had more than one episode of arrhythmia, so that the total number of attacks of arrhythmia treated was 63.

All patients were monitored continuously on an oscilloscope, and tracings were obtainable on a direct-writing recorder linked with the oscilloscope. Electrocardiographic records were taken before and at frequent intervals (usually every 30 seconds) after administration of oxprenolol. Particular attention was also paid to the effects of the drug on the blood pressure, and other side effects were also carefully noted.

Patients with bronchial asthma, heart failure, atrioventricular block, and bradycardia were excluded from the trial.

The acute effects of oxprenolol on the arrhythmias were studied by single intravenous bolus injections of the drug in various doses and also by means of continuous intravenous infusion. The bolus injection was given initially in a dose of 2 mg, and if this was not effective within 10 minutes a further injection of 4 mg was given. If no effect was obtained after a further 10 minutes a final bolus of 6 mg was given provided that no significant hypotensive or other adverse side effects appeared. The continuous intravenous infusion was given by electrically driven syringe pump, using 30 mg of oxprenolol mixed with 30 ml of sterile water *B.P.*, and the infusion rate was adjusted to deliver oxprenolol in a dose of 0·25 mg/minute. The infusion was continued until suppression of the arrhythmia or until the total dose was delivered over a period of two hours. In addition to the intravenous study, the effect of oral oxprenolol in a dose of 20 to 40 mg six-hourly was assessed in a number of patients as a prophylactic measure.

The types of arrhythmia studied included supraventricular