

Comparison of patients in low pH and high pH groups

	Low pH group (n=34)	High pH group (n=27)	p Value
No (%) of patients	34 (57)	27 (43)	
Mean (SEM) baseline pH	2.9 (1.1)	6.7 (0.9)	
Mean (SEM) age	41.1 (19.5)	55.4 (20.2)	NS*
Male to female ratio	1.6	3.5	NS**
Mean (SEM) duration of ventilation (h)	146 (141)	177 (156)	NS*
No (%) of patients who underwent surgery	15 (44)	15 (55)	NS**
Mean (SEM) duration of surgery	2.3 (1.9)	3.2 (1.5)	NS*
No (%) of patients who suffered hypoxia	15 (44)	10 (37)	NS**
No (%) of patients who suffered hypotension	13 (38)	21 (78)	<0.01**
No (%) of patients who received inotropes	8 (23)	16 (59)	<0.02**
No (%) of patients who died	12 (35)	8 (30)	NS**

*Student's *t* test. ** χ^2 test.

Discussion

All patients in this study were critically ill and would be considered to be at high risk of stress ulceration and subsequent gastrointestinal bleeding. We observed that almost half of our patients failed to maintain a normal acid gastric juice of <5 in the fasting state and that this seemed to be related to episodes of severe hypotension immediately before the six hour control phase.

While gastric pH may be one of the most important factors in the aetiology of stress ulceration, maintenance of optimal intramural

pH is probably related to normal oxygen delivery to the gastric mucosa.⁴ In addition tissue hypoxia has been shown to contribute to the production of acute gastric mucosal injury in animals,⁵ and it has been suggested that decreased gastric mucosal blood flow may be important in the pathogenesis of stress ulceration.⁶

Our study suggests that severe hypotension in critically ill patients has a profound effect on gastric exocrine function. The risk of erosive gastritis in this subgroup of patients with high pH gastric juice is currently unknown, but prophylaxis with antacids or H_2 antagonists perhaps seems less logical than with drugs that improve gastric mucosal blood flow.

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Prevalence of microalbuminuria, arterial hypertension, retinopathy and neuropathy in patients with insulin dependent diabetes

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Abstract

Diabetic nephropathy is the main cause of the increased morbidity and mortality in patients with insulin dependent diabetes. The prevalence of microalbuminuria was determined in adults with insulin dependent diabetes of five or more years' duration that had started before the age of 41. All eligible patients (n=982) attending a diabetes clinic were asked to collect a 24 hour urine sample for analysis of albumin excretion by radioimmunoassay; 957 patients complied. Normoalbuminuria was defined as urinary albumin excretion of ≤ 30 mg/24 h (n=562), microalbuminuria as 31-299 mg/24 h (n=215), and macroalbuminuria as ≥ 300 mg/24 h (n=180). The prevalence of

microalbuminuria and macroalbuminuria was significantly higher in patients whose diabetes had developed before rather than after the age of 20. The prevalence of arterial hypertension increased with increased albuminuria, being 19%, 30%, and 65% in patients with normoalbuminuria, microalbuminuria, and macroalbuminuria respectively. The prevalence of proliferative retinopathy and blindness rose with increasing albuminuria, being 12% and 1.4%, respectively, in patients with normoalbuminuria, 28% and 5.6% in those with microalbuminuria and 58% and 10.6% in those with macroalbuminuria. An abnormal vibratory perception threshold was more common in patients with microalbuminuria (31%) and macroalbuminuria (50%) than in those with normoalbuminuria (21%).

This study found a high prevalence (22%) of microalbuminuria, which is predictive of the later development of diabetic nephropathy. Microalbuminuria is also characterised by an increased prevalence of arterial hypertension, proliferative retinopathy, blindness, and peripheral neuropathy. Thus, urinary excretion of albumin should be monitored routinely in patients with insulin dependent diabetes.

Introduction

About 40% of all patients with insulin dependent diabetes develop diabetic nephropathy, which is the main cause of the increased morbidity and mortality in these patients.^{1,2} Several longitudinal studies have shown that raised urinary albumin excretion (based on

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TABLE I—Clinical data and prevalence of normoalbuminuria, microalbuminuria, and macroalbuminuria in 957 patients with insulin dependent diabetes

	No of patients	Prevalence of total (%) (95% confidence interval)	Sex ratio (men:women)	Mean (SD) age years	Mean (SD) age at onset of diabetes (years)	Mean (SD) duration of diabetes (years)	Median albuminuria (mg/24 h) (range)	Mean (SD) serum creatinine ($\mu\text{mol/l}$)
Normoalbuminuria	562	59 (57 to 62)	1.03	41 (13)	21 (10)	20 (11)	9 (1-30)	70 (13)
Microalbuminuria	215	22 (19 to 25)	1.17	41 (15)	17 (10)	24 (12)	71 (31-296)	75 (19)
Macroalbuminuria	180	19 (17 to 22)	1.28	41 (14)	15 (10)	26 (11)	906 (15-8213)*	130 (120)
p Value			NS	NS	<0.01	<0.01		<0.01

*Some patients with diabetic nephropathy receiving antihypertensive treatment had albuminuria below 300 mg/24 h.

TABLE II—Prevalence of normoalbuminuria, microalbuminuria, and macroalbuminuria in relation to age at onset of diabetes (≤ 20 or > 20) in 957 patients with insulin dependent diabetes

	Prevalence (%) (95% confidence interval)		Mean (SD) age (years)		Mean (SD) duration of diabetes (years)	
	Age ≤ 20	Age > 20	Age ≤ 20	Age > 20	Age ≤ 20	Age > 20
	Normoalbuminuria (n=562)	50 (46 to 54)*	70 (65 to 74)*	35 (12)	46 (11)	23 (12)
Microalbuminuria (n=215)	27 (23 to 31)*	17 (14 to 22)*	35 (12)	51 (13)	25 (12)	23 (12)
Macroalbuminuria (n=180)	23 (20 to 27)*	13 (10 to 16)*	34 (10)	55 (11)	24 (12)	28 (10)
p Value	<0.0001,* NS†				NS‡	<0.0001§

*Normoalbuminuria v microalbuminuria: $\chi^2_{MH} = 16.5$, $df = 1$.

†Microalbuminuria v macroalbuminuria: $\chi^2_{MH} = 0.06$, $df = 1$.

‡Comparison between each of the three different groups: F ratio = 14, $df = 2$.

§Comparison between each of the three different groups: F ratio = 24.8, $df = 2$.

a single measurement) below the level of clinical albuminuria (Albustix), so called microalbuminuria, strongly predicts the development of diabetic nephropathy in patients with insulin dependent diabetes.³⁻⁶ This conclusion was reached despite differences among centres in the procedure for collecting urine (overnight,³ over 24 hours,^{4,5} or short term collections at rest⁶); the value of urinary albumin excretion designated microalbuminuria ($> 30 \mu\text{g}/\text{min}$,³ $> 28 \mu\text{g}/\text{min}$,^{4,5} or $> 15 \mu\text{g}/\text{min}$ ⁶); and the duration of follow up (14 years,³ six years,^{4,5} and 10 years.⁶)

Mathiesen *et al* advocated that patients with insulin dependent diabetes and urinary albumin excretion exceeding $70 \mu\text{g}/\text{min}$ should be classed as having incipient diabetic nephropathy; this value predicted the development of diabetic nephropathy in all their patients during six years of observation.⁵ Until recently the definition of microalbuminuria has varied slightly from centre to centre, but at a recent conference on early diabetic nephropathy consensus was obtained, microalbuminuria being defined as urinary albumin excretion greater than $20 \mu\text{g}/\text{min}$ ($30 \text{ mg}/24 \text{ h}$) and less than or equal to $200 \mu\text{g}/\text{min}$ ($300 \text{ mg}/24 \text{ h}$), irrespective of how the urine is collected.⁷ Furthermore, incipient diabetic nephropathy is considered to be present if microalbuminuria (persistent) is found in two out of three urine samples collected consecutively, preferably within six months. Recently, we found a high prevalence (37%) of persistent microalbuminuria in young people aged 15-18 with insulin dependent diabetes.⁸

The aim of our cross sectional study was to determine the prevalence of microalbuminuria (as defined above) in adults with insulin dependent diabetes of more than five years' duration attending a diabetes clinic in Copenhagen, and to evaluate the relation between urinary albumin excretion and arterial blood pressure, retinopathy, blindness, and peripheral neuropathy. This study began in 1985 as a part of a prospective study on the development of diabetic nephropathy.

Patients and methods

PATIENTS

All patients with insulin dependent diabetes aged 18 or more whose disease had started before the age of 41 and was of five or more years' duration who were attending the outpatient clinic at Hvidøre Hospital in 1985 were asked to participate in the study ($n = 1024$). Forty two patients with diabetic nephropathy were excluded because of selective referral to the

hospital in October 1983; they participated in various prospective studies conducted by one of us (HHP) at another diabetes clinic in Copenhagen. Twenty four hour home urine collections (at least one) were obtained from 957 of the remaining 982 patients (97%). Table I shows the clinical data for these patients.

All patients had been dependent on insulin from the time of diagnosis and received at least two daily injections. All gave their informed consent, and the experimental design was approved by the local ethical committee.

METHODS

The urine volume was recorded and aliquots stored at -20°C until the albumin concentration was determined by radioimmunoassay with a single antibody.⁹ This assay had a sensitivity of 0.5 mg/l and an interassay coefficient of variation of 9%. The coefficient of variation for the 24 hour urinary albumin excretion rate in samples collected at home was 43% in patients with insulin dependent diabetes in our hospital. Sterility of urine was checked by culture (Uricult, Orion, Helsinki, Finland), and urine was collected after treatment if bacterial growth had been found. The normal range for urinary albumin excretion in our laboratory was $3-30 \text{ mg}/24 \text{ h}$, median $7 \text{ mg}/24 \text{ h}$ (32 women, 23 men; mean age 32, range 21-45).

Arterial blood pressure was measured once on the right arm with a standard clinical sphygmomanometer cuff $25 \times 12 \text{ cm}$, while the patient was sitting after 10 minutes' rest. The measurements were performed "blind" by two trained nurses, who had no knowledge of the urinary albumin excretion rate. Diastolic blood pressure was recorded at the disappearance of the Korotkoff sounds (phase V). Arterial hypertension was diagnosed according to the World Health Organisation's criteria ($> 160/95 \text{ mm Hg}$) or if antihypertensive treatment was being prescribed.

Ophthalmoscopy through dilated pupils was carried out by the same observer (EL). Visual acuity was assessed through a pin hole in all patients. Blindness was defined as a corrected visual acuity ≤ 0.1 in the best eye. Vibratory perception threshold was measured in the big toe with a biothesiometer (Biomedical Instruments Co, Newbury, Ohio, United States), a threshold of more than 20 V indicating neuropathy in subjects below the age of 50.¹⁰ Serum creatinine concentration was measured according to the method of Haeckel.¹¹ Haemoglobin A_{1c} concentration was measured by an isoelectric focusing method (normal range 4.1 to 6.1%).¹² Owing to technical errors haemoglobin A_{1c} values were obtained for only 480 of the 957 patients.

STATISTICAL ANALYSES

The complications studied are irreversible, or almost irreversible, and therefore their prevalence increased with time, except when modified by the high mortality in the patients with macroalbuminuria. To exclude this effect

of duration of disease in comparisons of complications we performed divided Mantel-Haenszel analyses,¹³ using intervals of duration of diabetes of 5-9, 10-14, 15-19, 20-24, 25-29, 30-39, and 40-59 years. A p value of <0.05 was considered to be significant. To indicate when we applied Mantel-Haenszel analyses, a subscript MH is added to χ^2 values.

In comparisons of continuous variables (arterial blood pressure, age, age at onset of diabetes, and duration of diabetes) analyses of variance was performed in the same subgroups as mentioned above.

The relation between the logarithm of urinary albumin excretion and age at onset of diabetes, duration of diabetes, systolic blood pressure, and diastolic blood pressure was analysed in patients not receiving antihypertensive treatment by stepwise multiple regression analysis. The variables were entered into the model if the F ratio exceeded 4. A p value for the partial correlation of 0.05 was considered to be significant.

In comparisons of serum creatinine concentrations, which were not normally distributed, the Kruskal-Wallis test of variance was used.

TABLE III—Prevalence of diabetic retinopathy and blindness in relation to urinary albumin excretion in 957 patients with insulin dependent diabetes. Values in parentheses are 95% confidence intervals

	Prevalence of retinopathy (%)			Prevalence of blindness (%)
	Proliferative	Simple	None	
Normoalbuminuria (n=562)	12 (10 to 14)*	56 (53 to 59)*	32 (29 to 35)*	1.4 (0.8 to 2.4)*
Microalbuminuria (n=215)	28 (25 to 31)*	58 (55 to 61)*	14 (12 to 16)*	5.6 (4.3 to 7.2)*
Macroalbuminuria (n=180)	58 (55 to 61)*	41 (38 to 44)*	1 (0 to 2)*	10.6 (8.8 to 12.7)*
p Value	<0.0001, * <0.0001†			<0.01, † NS‡

*Normoalbuminuria v microalbuminuria: $\chi^2_{MH}=26$, df=2.
 †Microalbuminuria v macroalbuminuria: $\chi^2_{MH}=38.1$, df=2.
 ‡Normoalbuminuria v microalbuminuria $\chi^2_{MH}=6.7$, df=1.
 §Microalbuminuria v macroalbuminuria: $\chi^2_{MH}=2.7$, df=1.

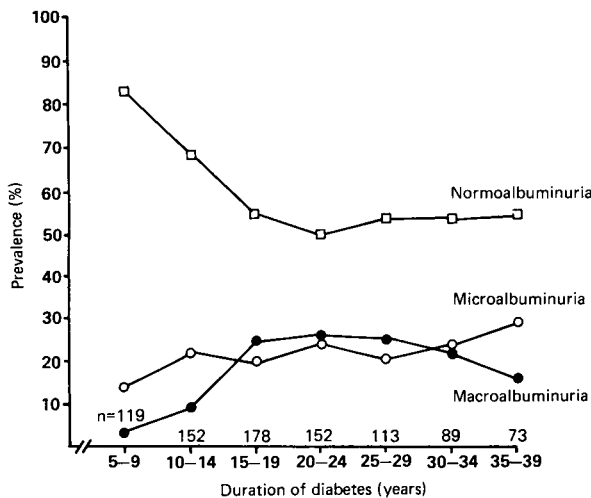


FIG 1—Prevalence of albuminuria in relation to duration of insulin dependent diabetes.

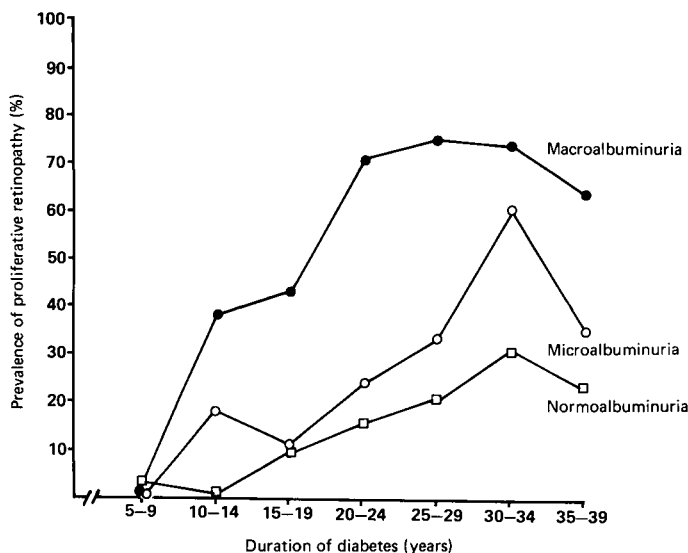


FIG 2—Prevalence of proliferative retinopathy in relation to duration of insulin dependent diabetes and type of albuminuria.

Results

Our cross sectional study showed a prevalence of microalbuminuria and macroalbuminuria of 22% and 19%, respectively (table I). Patients with raised urinary albumin excretion were characterised by an earlier onset and longer duration of diabetes and tended to be men ($0.05 < p < 0.10$; $\chi^2=7.62$; df=2) when compared with patients with normoalbuminuria. Stepwise multiple regression analysis showed a significant correlation between the logarithm of urinary albumin excretion and both age at onset and duration of diabetes ($p < 0.0005$, $r^2=0.07$). Altogether 80 of the 215 patients with microalbuminuria had a urinary albumin excretion rate of 100-300 mg/24 h. The prevalence of microalbuminuria and macroalbuminuria was much higher in patients whose diabetes had started before rather than after the age of 20 ($p < 0.0001$, table II). The duration of diabetes was nearly identical.

Figure 1 shows the relation between duration of diabetes and albuminuria. The prevalence of normoalbuminuria declined to 55% after 14 years of diabetes and remained constant thereafter. The prevalence of microalbuminuria increased to reach a plateau of 20-25% from 15 to 34 years' duration of diabetes. The prevalence of macroalbuminuria was much lower than that of microalbuminuria during the first 14 years of diabetes but slightly higher afterwards until it started to decline after a duration of diabetes of 35 years.

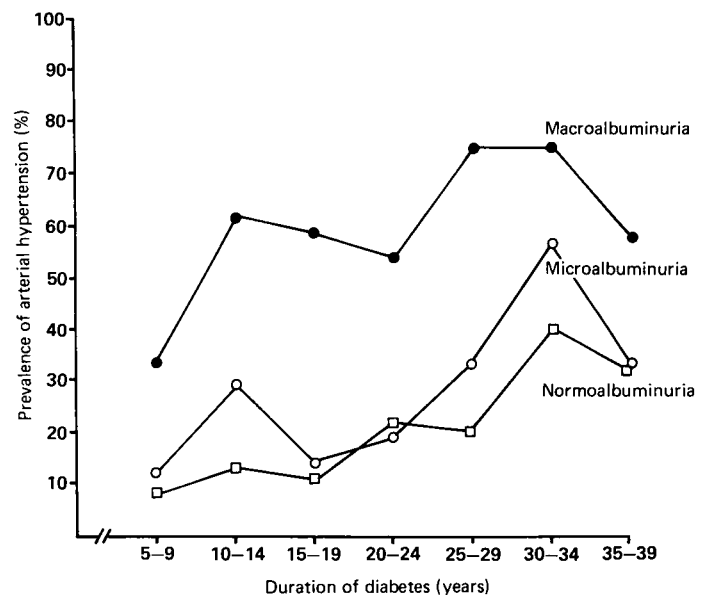


FIG 3—Prevalence of arterial hypertension in relation to duration of insulin dependent diabetes and type of albuminuria.

Bacteriuria of $\geq 10^5$ micro-organisms/ml was rare in men (0.4%) but more common in women; in those with normoalbuminuria bacteriuria was 3%, in those with microalbuminuria 12%, and in those with macroalbuminuria 6%.

The prevalences of proliferative retinopathy and blindness rose with increasing albuminuria ($p < 0.01$, table III). The prevalence of proliferative retinopathy increased with the duration of diabetes, but a more accelerated course was seen in patients with microalbuminuria and, particularly, those with macroalbuminuria (fig 2).

The prevalence of arterial hypertension and antihypertensive treatment, and arterial blood pressure in patients not receiving antihypertensive treatment, were compared (table IV). The prevalence of arterial hyper-

ence.⁷ Our cross sectional study showed an overall prevalence of microalbuminuria of 22%. This figure agrees with the prevalence of microalbuminuria (25%) found previously in a randomly selected group of adults who had had insulin dependent diabetes for more than five years.⁵ The prevalence was much higher in patients whose diabetes had developed before rather than after the age of 20 (27% *v* 17%, respectively), which agrees with the high prevalence of microalbuminuria (37%) found in insulin dependent diabetics aged 15-18.⁸ Microalbuminuria was not detected in diabetic children below the age of 15.⁸

TABLE IV—Prevalence of hypertension and antihypertensive treatment, and measurement of arterial blood pressure, in relation to urinary albumin excretion in 957 patients with insulin dependent diabetes

	Prevalence (%) (95% confidence interval)		Mean (SD) arterial blood pressure in untreated patients (mm Hg)
	Hypertension	Antihypertensive treatment	
Normoalbuminuria (n=562)	19 (17 to 22)*	8 (6 to 10)*	132/79 (17/9) (n=513)
Microalbuminuria (n=215)	30 (27 to 33)*	14 (12 to 16)*	135/82 (17/9) (n=186)
Macroalbuminuria (n=180)	65 (62 to 68)*	51 (48 to 54)*	141/85 (18/9) (n=87)
p Value	<0.05, * <0.0001†	NS, ‡ <0.0001§	<0.01, <0.001¶

*Normoalbuminuria *v* microalbuminuria: $\chi^2_{MH} = 5.2$, df=1.

†Microalbuminuria *v* macroalbuminuria: $\chi^2_{MH} = 48.5$, df=1.

‡Normoalbuminuria *v* macroalbuminuria: $\chi^2_{MH} = 2.3$, df=1.

§Microalbuminuria *v* macroalbuminuria: $\chi^2_{MH} = 62.6$, df=1.

¶Systolic blood pressure: F ratio=11.2, df=2.

¶Diastolic blood pressure: F ratio=17.5, df=2.

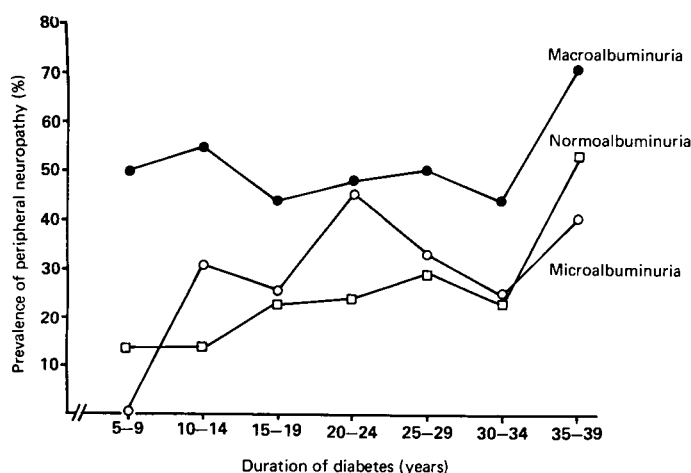


FIG 4—Prevalence of peripheral neuropathy in patients under 50 with insulin dependent diabetes in relation to duration of disease and type of albuminuria.

tension rose in all three groups with increasing duration of diabetes (fig 3). A significant correlation between age and untreated systolic blood pressure was shown in all three groups: normoalbuminuria, slope=0.63 mm Hg/year, $r=0.46$; microalbuminuria, slope=0.65 mm Hg/year, $r=0.55$; and macroalbuminuria, slope 0.68 mm Hg/year, $r=0.54$ ($p < 0.01$). Untreated diastolic pressure and age did not correlate in any of the three groups. Multiple regression analysis showed no correlation between the logarithm of urinary albumin excretion and arterial blood pressure in patients not receiving antihypertensive treatment ($n=786$). Haemoglobin A_{1c} concentration was about the same in all three groups: 9.0 (SD 2.0)% ($n=297$), 9.4 (2.2)% ($n=101$), and 9.8 (2.1)% ($n=82$) in patients with normoalbuminuria, microalbuminuria, and macroalbuminuria, respectively (NS).

The prevalence of peripheral neuropathy tended to be higher in patients with microalbuminuria (31% (range 28-35%)) compared with patients with normoalbuminuria (21% (range 18-24%)) ($p=0.09$, $\chi^2_{MH} = 2.9$, df=1), but only patients with macroalbuminuria (50% (range 46-54%)) showed a significant increase ($p < 0.02$, $\chi^2_{MH} = 6.2$, df=1; fig 4).

Discussion

The definition of microalbuminuria applied in our study is identical with that recommended recently at a consensus confer-

In patients with insulin dependent diabetes the day to day variation in urinary albumin excretion is high (the coefficient of variation ranging from 30% to 50%) and independent of the method of collecting urine.^{8,14,15} Furthermore, the coefficient of variation for the ratio of urinary albumin to creatinine excretion is equally high, suggesting that the variation is not due to inaccurate collection of urine.¹⁵ Thus urinary excretion of albumin probably does vary. Thus Mogensen *et al* decided that only patients with persistent microalbuminuria should be categorised as having incipient diabetic nephropathy,⁷ but, unfortunately, no data on the prevalence of persistent microalbuminuria was available.

As our study was not a survey based on the general population selection bias might have been a confounding variable. None of our patients, however, were referred to the hospital because of microalbuminuria because sensitive methods of determining urinary albumin concentration were not available to general practitioners or general hospitals in 1985. We cannot rule out the possibility of selective referral of patients with late complications of insulin dependent diabetes—for example, severe retinopathy or nephropathy, or both. The prevalence of macroalbuminuria in relation to the duration of diabetes agrees closely with the results obtained in study of 955 patients with insulin dependent diabetes based on the general population.¹⁶ In that survey proteinuria was diagnosed when testing of a random urine sample with Labstix (Ames) showed protein ≥ 300 mg/l. We have no evidence suggesting that the patients who dropped out were unrepresentative of the group as a whole except those suffering from diabetic nephropathy (excess mortality).

Our patients with raised urinary albumin excretion were characterised by an earlier onset and longer duration of diabetes and tended to be men when compared with the patients with normoalbuminuria. These findings agree with results obtained in patients with insulin dependent diabetes with macroalbuminuria due to diabetic nephropathy.¹² A tendency for men to have various non-diabetic glomerulopathies has also been shown.¹⁷

Our data indicate that patients with microalbuminuria must be regarded as a high risk group not only because of the increased risk of progression to nephropathy but also because of the raised prevalence of proliferative retinopathy, blindness, arterial hypertension, and peripheral neuropathy (foot ulcers). These results confirm and extend previous observations in small selected groups of patients with insulin dependent diabetes and microalbuminuria.^{5,18,19} Furthermore, microalbuminuria is a predictor of

cardiovascular death at least in patients with non-insulin dependent diabetes.^{20,21} We emphasise, however, that the frequency of all these complications is much higher in patients with insulin dependent diabetes with macroalbuminuria.^{1,2,22,23}

Two studies have shown that the cumulative incidence of diabetic nephropathy is much higher in patients with insulin dependent diabetes when the onset of the disease is before rather than after the age of 20,^{2,23} and our data agree. The causes of this difference with age are not known, but the poor metabolic control often seen in small children and teenagers may have a role. The HLA system can be ruled out as a contributing factor,²⁴ but other genetic markers may play a part.²⁵

If microalbuminuria is a predictor or marker of progression to diabetic nephropathy, as suggested in several longitudinal studies,^{3,6} then its prevalence should be higher than that of macroalbuminuria early in the course of diabetes. Our study clearly shows that this is the case.

Our study showed a higher frequency of raised arterial blood pressure in patients with microalbuminuria and macroalbuminuria. Raised blood pressure accelerates the progression of nephropathy,^{26,28} and effective blood pressure reduction reduces it and reduces albuminuria.^{29,32} We have shown that microalbuminuria depends to a large extent on blood pressure, probably because of glomerular capillary hypertension.³³ Recently, Marre *et al* showed a reduction in persistent microalbuminuria in normotensive patients with insulin dependent diabetes during six months' treatment with an angiotensin converting enzyme inhibitor.³⁴

Several previous studies have found a slightly higher haemoglobin A_{1c} concentration in patients with microalbuminuria compared with those with normoalbuminuria.^{5,18,19} We saw the same trend in our study. More importantly, the progression of microalbuminuria is significantly reduced with continuous subcutaneous infusion of insulin compared with conventional insulin treatment.^{35,36} Thus long term, nearly normal blood glucose concentrations may delay or even prevent the progression from microalbuminuria to macroalbuminuria—that is, diabetic nephropathy.

In conclusion, urinary albumin excretion should be determined routinely in the management of patients with insulin dependent diabetes because microalbuminuria indicates a need for more frequent follow up of diabetic complications, arterial hypertension, and glycaemic control.

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ONE HUNDRED YEARS AGO

Dr. Norman Kerr delivered the second of his course of lectures on Inebriety on January 18th. He said that the predisposing and exciting causes of the disease in each case should be ascertained, and the treatment conducted on thoroughly scientific principles. Proceeding by an unscientific method, numerous alleged "cures" had been oracularly declared to be infallible; yet all these, such as alcoholic frog extract, raw meat and food steeped in alcohol, had been found to be ineffectual. There was no specific. The first indication of sound treatment was the withdrawal of the narcotic, so that the narcotising process might be terminated. This withdrawal should be immediate with alcohol, chloroform, chloral, and ether, but should be gradual with morphine and opium. The risk and suffering with the last named were as a rule too serious in sudden withholding. Bromides with hyoscyamus were useful in allaying the irritability of the nervous condition. When gastric irritability was present, the bromides could be administered in an effervescent form. Ice, milk, and soda or lime water were of service. The second indication of scientific treatment was the removal of the exciting cause, or its counteraction when it could not be got out of the way. The third indication was the reparation of the physical damage wrought by the disease, the remedying of the pre-inebriate morbid state, and the strengthening of inhibition. Good sound wholesome food was essential to the renovation of healthy tissue. No restricted diet suited all, and a judicious mixture of flesh, fruit, grains, and vegetables was generally the most desirable. Tonics, contra-indicated at an earlier stage of treatment, were useful here. Among the best was unintoxicating "port with bark." The correction of the pre-inebriate morbid state was of importance. Disordered function should be set right, and complicating disease attended to. The inhibitory power should be strengthened by exercise, by bracing hygienic measures, by mental, moral, and religious influences, and by nerve tonics, as strychnine. When seen early the inebriate could be treated while pursuing his usual calling, but resort was seldom had to medical advice till later. Then it was generally best to advise residence for at least twelve months in a genuine home for inebriates, preferably under the provisions of the Habitual Drunkards Act. When seen at an early stage this disease was as curable as most other diseases.

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