Kidney International, Vol. 46 (1994), pp. 1192–1198

Epidemiology of primary glomerular diseases in a French region. Variations according to period and age

PIERRE SIMON, MARIE-PAULE RAMÉE, VALÉRIE AUTULY, ERIC LARUELLE, CHRISTOPHE CHARASSE, GÉRARD CAM, and KIM SENG ANG

Laboratoire d'Anatomie Pathologique, Centre Hospitalier et Universitaire Rennes, and Service de Néphrologie, Hôpital La Beauchée, Saint-Brieuc, France

Epidemiology of primary glomerular diseases in a French region. Variations according to period and age. Between January 1, 1976 and December 31, 1990, histological diagnosis of primary glomerular diseases (PGD) was made in 480 patients born and living at the time of diagnosis in a region of France, comprising 410,664 inhabitants, of whom 390,574 were aged from 10 to 80 years. The prevalence of PGD during a 70 year exposure to risk (10 to 80 years of age) was evaluated to 5.7 in 1000 (7.6 in 1000 males and 3.8 in 1000 females). The most common PGD was IgA nephropathy with a prevalence of 1.9 in 1000 (3.3 in 1000 males, 1 in 1000 females). The annual incidence of the disease was evaluated separately for three consecutive five-year periods: period A (1976–80), period B (1981–85), and period C (1986–90). Within each of these three periods the number of patients with PGD was 179, 170 and 131, respectively, and annual incidence was 9.3, 8.8 and 6.7 in 100,000. The incidence of IgA nephropathy remained the same throughout the three periods: 2.6, 3.1 and 2.5 in 100,000. The incidence of membranoproliferative glomerulonephritis decreased from 1981 onward (0.9, 0.5 and 0.15 in 100,000), while that of membranous nephropathy increased slightly (1.2, 1.6 and 1.7 in 100,000). Acute streptococcal glomerulonephritis virtually disappeared during periods B and C. Lipoid nephrosis was less frequent in period C and idiopathic proliferative glomerulonephritis with crescents slightly increased (0.3, 0.4 and 0.6 in 100,000). There was no significant difference between the three periods regarding the incidence of other PGD. The incidence of IgA nephropathy was three- to fourfold higher in the adult aged from 20 to 59 years than in the elderly. In contrast, membranous nephropathy was threefold more frequent in the elderly than in the adult. Therefore, only some histopathological forms have a different incidence according to age, but the major information furnished by this study is that the risk of occurrence of a PGD is similar in the population living in the area, whatever the age group (10 to 19 years, 6.4 in 100,000 inhabitants; 20 to 39, 7.1 in 100,000; 40 to 59, 8.4 in 100,000; 60 to 79, 8.4 in 100,000). We also confirm that the most common PGD going to end-stage renal disease is IgA nephropathy, particularly under 60 years of age (0.8 in 100,000). In contrast, membranous nephropathy is a less frequent cause of ESRD (0.2 in 100,000).

The prevalence of primary glomerular diseases (PGD) in the general population is poorly known because optimal conditions for performing epidemiological surveys are difficult to find. A great number of PGD are "silent" at onset of the disease and are diagnosed on urinary tests during routine medical examination. In a previous study [1] we showed that in 60 percent of adults with idiopathic IgA nephropathy (IgAN), the disease was discovered by chance in employment or military-related routine urinary tests. Worldwide, IgAN is the most common PGD [2–8] and in our region the first cause of end-stage renal disease (ESRD) [9]. Variations in the incidence of PGD between periods of time suggest an influence of environmental factors on the occurrence of glomerular disease. In the 1980s a decrease in the annual incidence of membranoproliferative glomerulonephritis (MPGN) was suggested in retrospective studies [3, 10, 11]. Our prospective study confirmed these data [4, 12] and indicated that streptococcal diseases such as acute poststreptococcal glomerulonephritis (AGN) and acute rheumatic fever were decreasing in parallel with MPGN [13].

Our prospective study on the epidemiology of PGD was started in 1976. Following our previous preliminary reports at 10 [14] and at 12 years [4], we can now present results at 15 years. This study shows the incidence of PGD according to period, age and gender. It suggests some hypotheses on the role of genetic and environmental factors in the onset of PGD.

Methods

The study was carried out from January 1, 1976, to December 31, 1990, during which time renal biopsy was performed in 942 patients, of whom 480 (51%) had PGD. There were twofold more males (316) than females (164). All patients were born and living in the study area at the time of diagnosis. The area is located in western France in the north of Brittany (Cotes d'Armor Department) and comprised 410,644 inhabitants, of whom 390,574 were aged from 10 to 80 years. The mean evaluation of inhabitant number was calculated according to the results of the three last censuses (INSEE 1975, 1982, 1990) [15]. The distribution of the population in each age group was as follows: under 10 years of age, 20,070 inhabitants (this group has been excluded from the study); 10 to 19 years, 58,668 inhabitants (males 29,634, females 29,034); 20 to 39 years, 122,969 inhabitants (males 63,471, females 59,478); 40 to 59 years, 108,707 inhabitants (males 54,183, females 54,524); 60 to 79 years, 100,230 inhabitants (males 43,727, females 56,503). This region of France has a homogeneous and stable population in terms of migratory behavior (99.3% Caucasians). Only one hospital with a nephrology department served this population (La Beauchée Hospital, Saint-Brieuc). The Cotes d'Armor region fulfills the criteria of a standard metropolitan statistical area (SMSA) [16]: (1) a large population nucleus with a city of at least 50,000 residents (Saint-Brieuc is a city of 102,966); (2) a total population of at least 100,000 in the area studied (the studied region has 410,644 inhabitants); (3)

Received for publication September 22, 1993
and in revised form March 22, 1994
Accepted for publication May 10, 1994

Table 1. Incidence of ESRD and annual rate of renal biopsy according to the major subdivisions of the area

	Major subdivisions (n/10^5)			
	St Brieuc	Guingamp	Lannion	Dinan
ESRD	5.2	4.6	4.8	4.6
Renal biopsy	20.4	18.8	19.1	17.8

adjacent communities well integrated with the population of the major center (Saint-Brieuc is the administrative center for the rural and fishing population of the area).

To delineate the area of medical influence of our nephrology department, a method evaluating the performance of renal biopsy and the incidence of ESRD in each canton of the area was used. This method was already used in previous reports [1, 4]. When these values were zero in the cantons farthest from the hospital during a five year period, we considered that these cantons were outside the area served by our nephrology department. Verification was possible by collaboration with neighboring nephrology and pathology departments. During the period under study, the annual rate of renal biopsy was from 16 to 20 new patients for 100,000 inhabitants and incidence of ESRD was from 4.6 to 5.2 new cases for 100,000 inhabitants in the major subdivisions of the Côtes d'Armor (Table 1).

The diagnostic test for this epidemiological survey was renal biopsy. Unclassified diagnosis due to inadequate sampling (less than 7 glomeruli for light microscopy or absence of glomerulus for immunohistochemisty study) concerned 1.9% of all renal biopsies. A diagnosis of PGD was considered if there was at the time of biopsy: (1) no report of any known associated systemic disease (systemic lupus erythematosus, polyarteritis nodosa, Wegener's granulomatosis, Goodpasture syndrome, Henoch-Schönlein disease, lymphoma, carcinoma, Alport syndrome); (2) negative serology for hepatitis B and anti-nuclear factor. During the study period serology for anti-neutrophil cytoplasmic antibody was not collected; (3) no report of familial hematuria. Renal biopsy specimens were processed and stained for light microscopy and immunohistochemisty using polyclonal antisera against human IgG, IgM, IgA, C3, C1q, kappa, and lambda light chains. Electron microscopy was not systematically performed.

To evaluate the evolution of the incidence of PGD according to period and age, we distinguished three consecutive five-year periods (period A 1976–80; period B 1981–85; and period C 1986–90) and four age groups (10 to 19 years; 20 to 39 years, 40 to 59 years, and 60 to 79 years). Mean age (SD) at the time of renal biopsy increased slightly over the three periods [A, 47 (14); B, 50 (14); C, 52 (14) years], as did the sex ratio (males/females: 1.3, 1.5 and 1.6, respectively). Clinical indications for renal biopsy (Table 2) were recent onset uremia (acute uremia if onset was less than 2 months and chronic uremia if onset was more than 2 months), nephrotic syndrome, persisting proteinuria and hematuria, persisting idiopathic proteinuria or chronic hematuria. Annual rate of renal biopsy was not significantly different during the three periods: 18.7, 20.1 and 16.2 patients for 100,000 inhabitants for periods A, B and C, respectively. More than 80% of renal biopsies were performed by the same physician (PS) and all renal biopsy specimens were examined by the same pathologist (MPR).

We cannot prove that all patients having an indication of renal biopsy and living in the area were sent to our nephrology department. However, the leakage was probably low, since only 11 out of the 942 biopsied patients studied had undergone renal biopsy in another nephrology department in Brittany during the 15 year period. Clinical information about the evolution of PGD in these 11 patients was taken into account for the calculation of incidence of ESRD. Conditions for a prospective epidemiological study were maximized by close collaboration with practitioners, urologists and employment physicians in the area. In 1984 [1] we reported that more than 65% of patients with IgAN had been sent to a urologist before an outpatient visit in our nephrology department, no doubt since hematuria leads the practitioner to address the patient to a urologist for cystoscopy. The five urologists working in the area were closely associated to this study (**Acknowledgments**). As most cases of PGD are "silent" at onset, the role of routine screening by school, employment and army physicians is essential [1], and we were able to collaborate with the major medical screening institutions in the area.

Annual incidences of PGD and of each histological form in each age group of the general population at the time of renal biopsy and at the time of ESRD were studied. The annual incidence was calculated as follows:

$$\text{Annual incidence} = \frac{\text{Total number of new patients for the period under study}}{\text{Population in age group/duration of the period (years)}}$$

Prevalence was evaluated only when annual incidence was stable according to periods. It was calculated as follows:

$$\text{Prevalence} = \text{Annual incidence} \times \text{time of exposure to risk (years)}$$

Results of incidence are given as number per 100,000 inhabitants and those of prevalence as number per 1,000 inhabitants.

Among 348 patients who started dialysis during the period under study, 99 (28.4%) had PGD and 81 of 99 had had a renal biopsy at the time of diagnosis of the renal disease. However, only the 75 patients who underwent renal biopsy after January 1, 1976 were to be considered in determining the incidence of PGD at the time of ESRD. More than 85% of these patients who started renal replacement therapy with the diagnosis of PGD after January 1, 1981 had had a histological diagnosis of renal disease during the first period (A). Therefore, the annual incidence of ESRD due to PGD has been evaluated for the last decade (periods B and C) of the study. The risk of the evolution to ESRD due to PGD was calculated as follows:

$$\text{Percentage of patients at risk of ESRD (\%)} = \frac{\text{Incidence at the time of renal biopsy (n/10}^5\text{) (period A)}}{\text{Incidence at the time of ESRD (n/10}^5\text{) (periods B and C)}}$$

By means of chi-squared analysis we compared the different clinical presentations and the annual incidences of PGD and of each histological form according to period and age.

Results

General data on the incidence of PGD

The annual incidence of PGD in the area was 8.2 per 100,000 inhabitants. It was significantly decreased in period C compared to period A (Table 3). The incidence of ESRD due to PGD was

Table 2. Indications of renal biopsy: Evolution of annual rate according to period

	Period A (1976–80)			Period B (1981–85)			Period C (1986–90)			1976–90		
	N	(%)	I	*N*	(%)	I	*N*	(%)	I	*N*	(%)	I
ARF	52	(16.5)	3.2	83	(24.2)	5.0	52	(18.6)	3.2	187	(19.8)	3.8
CRF	50	(15.5)	3.0	69	(20.2)	4.2	48	(17.2)	2.9	167	(17.7)	3.4
NS	70	(21.8)	3.6	71	(20.7)	3.7	78	(28.0)	4.0	219	(23.2)	3.8
P + H	91	(28.5)	5.5	80	(23.3)	4.8	58	(20.7)	3.5	229	(24.3)	4.6
P	33	(10.5)	2.0	25	(7.3)	1.5	23	(8.3)	1.4	81	(8.6)	1.6
H	24	(7.)	1.4	15	(4.3)	0.9	20	(7.2)	1.2	59	(6.2)	1.2
Total	320	(100)	18.7	343	(100)	20.1	279	(100)	16.2	942	(100)	18.4

Abbreviations are: ARF, acute renal failure; CRF, chronic renal failure; NS, nephrotic syndrome; P, chronic proteinuria; H, chronic hematuria; I, annual rate ($n/10^5$).

Table 3. Primary glomerular disease diagnosed by renal biopsy for a 15 year period comprising 3 consecutive five year periods

	Period A (1976–80)			Period B (1981–85)			Period C (1986–90)			Total (1976–90)		
Type of glomerular disease	*N*	(%)	I	*N*	(%)	I	*N*	(%)	I	*N*	(%)	I
Nephrosis	24	(13.4)	1.2	17	(10.0)	0.9	14	(10.7)	0.7	55	(11.4)	0.95
FSG	22	(12.3)	1.2	21	(12.3)	1.1	8	(6.1)	0.4	51	(10.6)	0.80
MN	22	(12.3)	1.2	30	(17.6)	1.6	33	(25.2)	1.7	85	(17.7)	1.40
IgAN	52	(29.2)	2.6	61	(35.8)	3.1	48	(36.6)	2.5	161	(33.4)	2.70
MPGN	19	(10.6)	0.9	10	(5.9)	0.5	3	(2.3)	0.15	32	(6.6)	0.55
Poststrept AGN	22	(12.3)	1.2	8	(4.7)	0.4	3	(2.3)	0.15	33	(6.8)	0.55
Mes prolif GN	9	(5.0)	0.5	10	(5.8)	0.5	9	(6.8)	0.5	28	(5.8)	0.45
Crescentic prolif GN	6	(3.3)	0.3	8	(4.7)	0.4	11	(8.5)	0.6	25	(5.2)	0.60
Foc seg prolif GN	3	(1.6)	0.2	5	(2.9)	0.3	2	(1.5)	0.1	10	(2.0)	0.20
Primary glomerular disease	179	(100)	9.3	170	(100)	8.8	131	(100)	6.7[a]	480	(100)	8.2

[a] $X^2 = 6.9$ $p < .02$ with period A

Abbreviations are: nephrosis, idiopathic nephrotic syndrome with minimal change or focal segmental glomerular sclerosis; FSG, focal segmental glomerular sclerosis (without nephrotic syndrome); MN, membranous nephropathy; IgAN, IgA nephropathy (Bergers' disease); MPGN, membranoproliferative glomerulonephritis type I; Poststrept AGN, poststreptococcal acute glomerulonephritis; Mes prolif GN, mesangial proliferative glomerulonephritis; Crescentic prolif GN, idiopathic crescentic proliferative glomerulonephritis; Foc seg prolif GN, focal segmental proliferative glomerulonephritis (excluding idiopathic IgA nephropathy and Henoch Schönlein disease).

Table 4. Histological forms of primary glomerular disease according to period: Incidence at the time of ESRD

	Period A (1976–80)			Period B (1981–85)			Period C (1986–90)			1981–90		
Histological forms of PGD	*N*	(%)	I	*N*	(%)	I	*N*	(%)	I	*N*	(%)	I
Nephrosis	—	—	—	1	(2.3)	0.05	1	(3.2)	0.05	2	(2.6)	0.05
FSG	2	(8.3)	0.1	10	(22.7)	0.6	3	(9.7)	0.15	13	(17.4)	0.35
MN	2	(8.3)	0.1	2	(4.6)	0.1	5	(16.1)	0.3	7	(9.3)	0.18
IgAN	5	(20.9)	0.3	17	(38.6)	0.9	11	(35.5)	0.6	28	(37.3)	0.80
MPGN	2	(8.3)	0.1	1	(2.3)	0.05	3	(9.7)	0.15	4	(5.3)	0.10
Crescentic prolif GN	2	(8.3)	0.1	6	(13.6)	0.35	3	(9.7)	0.15	9	(12.0)	0.23
Other	1	(4.2)	0.05	3	(6.8)	0.15	1	(3.2)	0.05	4	(5.3)	0.10
Unclassified	10	(41.7)	0.6	4	(9.1)	0.2	4	(12.9)	0.20	8	(10.8)	0.20
Primary glomerular disease	24	(100)	1.35	44	(100)	2.4	31	(100)	1.65	75	(100)	2.01

evaluated to 2 per 100,000 inhabitants (Table 4). Thus, 21.5% of patients with PGD were at risk to reach ESRD after at least ten years of evolution of PGD (Table 5). Idiopathic IgA N was the most frequent PGD going to ESRD (0.8 per 100,000 inhabitants) in our area. The incidence of PGD in each age group was similar (Table 6). A predominance of males was found in each age group (incidence in general, male and female populations): 10 to 19 years, 6.4, 8.3 and 4.4 per 100,000; 20 to 39 years, 7.1, 9.1 and 4.8 per 100,000; 40 to 59 years, 8.4, 11.0 and 5.5 per 100,000; and 60 to 79 years, 8.4, 11.0 and 5.8 per 100,000 inhabitants. The similar incidence of PGD in all age groups made it possible to evaluate the prevalence of PGD in the general population living in the area to 5.7 per 1,000 inhabitants and according to gender to 7.6 per 1,000 males and 3.8 per 1,000 females. The risk of going to ESRD due to PGD peaked in the 40 to 59 year age group (2.8 per 100,000) and decreased after 60 years (2.0 per 100,000). Risk of evolution to ESRD was fourfold higher in males than in females (3.23 vs. 0.86 per 100,000; Table 7). It was the highest in males with IgAN and those with crescentic proliferative glomerulonephritis (CGN; Table 5).

Table 5. Percentage of patients at risk of ESRD during period 1981–90

Histological forms of PGD	Percentage of patients %		
	Males	Females	All
Nephrosis	7	—	4.2
FSG	62	37	29.2
MN	22	8	15
IgAN	54	12	30.7
MPGN	20	—	11.2
Poststrepto GN	—	—	—
Crescentic prolif GN	85	20	76
Other and unclassified	16	8	14.3
Primary glomerular disease	35	18	21.5

Evolution of annual incidence of various histological forms of PGD according to period and age

We studied six histological forms of PGD in particular: IgAN, membranous nephropathy (MN), MPGN, poststreptococcal AGN, nephrosis with minimal change or focal segmental glomerular sclerosis (nephrosis), and CGN (excluding crescentic IgAN).

(1.) Idiopathic IgA nephropathy. IgAN was the most common PGD, with a frequency of 33.4% in biopsied patients. Its annual incidence in the general population over 10 years of age was 2.7 per 100,000 and remained unchanged during the 15 year period (Table 3). Prevalence of IgAN in the general population was 1.9 per 1,000 inhabitants, 3.3 per 1,000 males and 1 per 1,000 females. Mean age (SD) at the time of diagnosis by renal biopsy was 38 (15) years. Peak of incidence of diagnosis was between 20 and 40 years of age. Threefold more males than females had IgAN whatever the period and the age group (Table 6). However, the sex ratio (males to females) was the highest between 10 and 19 years of age. IgAN was detected in 60 percent of the patients by routine urinary tests at school, work and military medical visits. Two out of three patients with IgAN had undergone cystoscopy. Incidence of ESRD due to IgAN was the highest in the 40 to 59 year age group (Table 7). It was at least sevenfold higher in males than in females (1.5 vs. 0.2 per 100,000). Thus, 30.7% of patients with IgAN were at risk to reach ESRD after at least ten years of evolution of the disease. The risk was higher in males (1 out of 2) than in females (1 out of 8). No case of ESRD due to IgAN in patients less than 25 years of age was observed in the area during the period under study.

(2.) Membranous nephropathy. Idiopathic MN was the second most frequent PGD with a frequency in biopsied patients of 17.7% (Table 3). Its annual incidence increased from period A (1.2 per 100,000) to periods B and C (1.6 and 1.7 per 100,000 inhabitants) ($P < 0.05$ between periods A and C). Peak of incidence of diagnosis according to age group occurred between 60 and 80 years (Table 6). Prevalence of males was low and sex ratio males to females was 1.2. In at least 80% of patients, diagnosis of MN was made at onset of a nephrotic syndrome. MN was an infrequent cause of ESRD (0.18 per 100,000) but its incidence was threefold higher in males than in females (0.3 vs. 0.1 per 100,000). The risk of such an evolution involved 1 out of 5 males and only 1 out of 12 females. Thus, 15% of patients with MN were at risk to reach ESRD after at least ten years of evolution of the disease (Table 5).

(3.) Membranoproliferative GN and poststreptococcal AGN. MPGN was diagnosed in 6.6% of biopsied patients with PGD. The annual incidence decreased from the beginning of the study. During the first period, it was 0.9 per 100,000 inhabitants and sharply dropped during the two following periods (0.5 and 0.15 per 100,000 for periods B and C, respectively; $P < 0.02$ between periods A and C). Simultaneously, we observed a progressive decrease in the incidence of poststreptococcal AGN: 1.2, 0.4 and 0.15 per 100,000 for periods A, B and C, respectively. An update of a survey on the frequency of outpatient visits to cardiologists for complications of acute rheumatic fever showed a concomitant decrease in such visits: 1.3, 0.3 and 0.1 per 100,000 for periods A, B and C, respectively ($P < 0.01$ between periods A and C). The annual incidence according to gender was similar in patients with MPGN and those with poststreptococcal AGN (0.9 and 0.3 per 100,000 for males and females, respectively), with a threefold higher incidence in males than in females. Both glomerular diseases had two peaks of incidence of diagnosis according to age groups (10 to 19 and 40 to 79 years, respectively). Prevalence of males was found in all periods and age groups. About 11.2% of patients with MPGN were at risk to reach ESRD after at least ten years of evolution of the disease, and the frequency of ESRD due to MPGN was 5.3% of patients with PGD. No case of ESRD that could be due to poststreptococcal AGN of which the diagnosis was made in period A was observed during the last decade of the study.

(4.) Crescentic proliferative glomerulonephritis. CGN was diagnosed in 5.2% of biopsied patients with PGD. The annual incidence was 0.6 per 100,000 inhabitants. It was slightly increased in period C (0.6 per 100,000) compared to period A (0.3 per 100,000) and was diagnosed more often over 60 years of age (1.7 per 100,000) than under 60 years (0.4 per 100,000, $P < 0.02$). The incidence was twofold higher in the 60 to 79 year age group than in the 40 to 59 year age group (0.8 per 100,000) and eightfold higher than in the 20 to 39 year age group (0.15 per 100,000, $P < 0.01$). The sex ratio was from 1.8 to 2. In 8 out of 10 patients, diagnosis of CGN was suggested because renal failure with glomerular signs (hypertension, proteinuria and hematuria) was rapidly progressive. ESRD due to CGN was eight times higher in males than in females (0.4 vs. 0.05 per 100,000), and male prevalence was the highest between 60 and 80 years of age (0.9 per 100,000 males vs. 0.1 per 100,000 females, $P < 0.02$). Thus, 76% of patients with CGN were at risk to reach ESRD after at least ten years of evolution of the disease and the risk existed in about two out of three males and in one out of five females with CGN.

(5.) Nephrosis. Frequency of nephrosis was 11.4 percent of biopsied patients with PGD. The annual incidence was 0.9 per 100,000 inhabitants. It regularly decreased during the 15 year period: 1.2, 0.9 and 0.7 per 100,000 for periods A, B and C, respectively. Nephrosis was diagnosed more often in females than in males (sex ratio males to females, 0.6). Peak of incidence of diagnosis occurred between 10 and 20 years of age (1.5 per 100,000) and was 0.6 to 1 per 100,000 in other age groups. Incidence of ESRD due to nephrosis was rare in our area (0.05 per 100,000), with only 5.5% of patients with nephrosis at risk to reach ESRD after at least ten years of evolution.

Discussion

This work reports on a 15 year prospective epidemiological study of PGD that started in January 1976 in the area of Saint-Brieuc. Our results confirm those published after 10 and 12 years of the study [1, 4, 9, 12, 13, 17] and bring new data. We

Table 6. Annual incidence at biopsy of some histological types of primary glomerular disease according to age and gender

Histological type of primary glomerular disease	Age groups *years*												Total no. of patients		
	10–19			20–39			40–59			60–79					
	M	F	all	M	F	all	M	F	all	M	F	all	M	F	all
IgAN	4.0	0.5	2.3	5.8	2.4	4.2	5.4	1.7	3.9	1.5	0.4	1.1	4.8	1.4	2.7
MN	1.1	0.7	0.9	0.9	0.7	0.8	1.3	1.2	1.2	3.2	2.4	2.8	1.9	1.6	1.4
Crescentic prolif GN	—	—	—	0.3	—	0.2	1.0	0.6	0.8	2.3	1.3	1.7	0.9	0.5	0.6
Nephrosis	0.9	2.1	1.5	0.8	1.2	1.0	0.7	0.6	0.6	0.5	1.0	0.8	0.7	1.1	0.95
MPGN	0.7	0.5	0.6	0.3	0.2	0.2	1.6	0.5	1.0	1.0	0.2	0.6	0.9	0.3	0.55
Poststrept AGN	1.3	0.5	0.9	0.6	0.2	0.4	0.3	0.4	0.3	1.5	0.2	0.7	0.9	0.3	0.55
Other and unclassified	0.3	0.1	0.2	0.4	0.1	0.3	0.7	0.5	0.6	1.0	0.3	0.7	0.8	0.3	1.45
Primary glomerular disease	8.3	4.4	6.4	9.1	4.8	7.1	11.0	5.5	8.4	11.0	5.8	8.4	10.9	5.5	8.2

Table 7. Annual incidence at ESRD of some histological types of primary glomerular disease according to age and gender (1981–90)

Histological type of primary glomerular disease	Age groups *years*												Total of patients		
	10–19			20–39			40–59			60–79					
	M	F	all	M	F	all	M	F	all	M	F	all	M	F	all
IgAN	—	—	—	0.9	0.15	0.6	2.9	0.2	1.6	0.9	0.3	0.4	1.5	0.2	0.80
MN	—	—	—	—	—	—	0.4	0.2	0.3	0.7	0.2	0.4	0.3	0.1	0.18
Crescentic prolif GN	—	—	—	0.3	—	0.2	0.1	—	0.1	1.1	0.2	0.6	0.4	0.05	0.23
Nephrosis	—	—	—	0.15	—	0.08	—	—	—	—	0.17	0.1	0.05	0.05	0.05
MPGN	—	0.3	0.17	0.15	—	0.08	0.4	—	0.2	0.2	—	0.1	0.18	0.06	0.10
Postrept AGN	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Other and unclassified	—	—	—	—	—	—	0.9	0.4	0.6	0.6	0.5	0.4	0.8	0.3	0.65
Primary glomerular disease	—	0.3	0.17	1.5	0.15	1.0	4.7	0.8	2.8	3.5	1.37	2.0	3.23	0.86	2.01

confirm that IgAN is the most common PGD, not only among the patients biopsied for PGD [2] but also in the general population of the area. Additionally, in this area IgAN is the most frequent PGD in the adult, while MN is the most frequent PGD in the elderly [18].

We also confirm that the decline in MPGN, poststreptococcal AGN and acute rheumatic fever was closely associated in this area [13]. The decline in the incidence of streptococcal diseases in developed countries has been accompanied by a comparable decrease in the incidence of nonsuppurative complications of streptococcal infection such as acute rheumatic fever and acute glomerulonephritis [19, 20]. This evolution suggest the role of streptococcal infection in the onset of MPGN [13, 21]. The decline in these streptococcal diseases [6, 7, 9–11, 20–22] is commonly attributed to an improved standard of living, better public health and the generalized early treatment of pharyngeal infections. The role of antibiotics in preventing these diseases is questionable, since the decline began prior to the introduction of antibiotics [19]. However, it seems likely that antibiotics are responsible for some acceleration in the rate of decline [11, 13, 19]. Therefore the progressive disappearance of these two forms of PGD can explain the decrease in the incidence of PGD during the last period (C) of our study. The incidences of the various forms of PGD that we found are similar to those recently published in France [3, 6, 8] and in the Netherlands [5]. It is also interesting to point out the similarity in frequencies of histological forms of PGD in the 480 biopsied patients with those reported in the USA [23], the United Kingdom [24] and Taiwan [22].

The major information furnished by this epidemiological study is that the risk of occurrence of a PGD is similar in the population living in our region, whatever the age group. Only some histopathological forms have a different incidence according to age. Therefore, it is possible to evaluate the prevalence of PGD in the general population to 5.4 per 1,000 inhabitants, this value being the same as was speculated in 1988 [4] and higher than that evaluated in 1984 on the basis of the literature [25]. The prevalence of PGD in the male population (7.6 per 1,000) is twofold that in the female population (3.8 per 1,000). However, this predominance was not similar in different forms of PGD. The prevalence of IgAN in the general population is 1.9 per 1,000 inhabitants and according to gender is 3.3 per 1,000 males and 1 per 1,000 females. In contrast, prevalence of MN in the general population is 1.2 per 1,000 inhabitants and is as frequent in males (1.4 per 1,000) as in females (1.3 per 1,000). Today two out of three patients with PGN have either IgAN or MN. The prevalence of nephrosis in the general population is evaluated to 0.6 per 1,000 inhabitants. This glomerular disease is more frequent in the female (0.8 per 1,000) than in the male population (0.5 per 1,000). Therefore the frequency of nephrosis in the adult would be threefold [26] to sevenfold [27] lower than in a child under 15 years of age. Males would be more prevalent in childhood nephrosis [26] and females more prevalent in adult nephrosis [28].

Longitudinal study brings new data on the evolution of some histological types of PGD according to period and age. We confirmed the progressive decrease in the incidence of MPGN and poststreptococcal AGN in our area during the 15 year period, but we observed that this decrease was fundamentally in the youngest age group while these two forms of PGD still existed in the elderly [18, 29]. The incidence of IgAN remained similar throughout the period under study while that of MN was slightly increasing. Such a progressive increase during the last decade has also been suggested in other recent studies [3, 6, 30], and could be

interpreted as the consequence of the increase in average lifetime and also the possible role of some environmental factors such as drugs [31] or solvents [32]. The incidence of IgAN is three- to fourfold higher in the adult aged from 20 to 59 years than in the elderly. In contrast, MN is threefold more frequent in the elderly than the adult [18, 29]. Immunogenetic susceptibility to developing MN is known [33, 34] and is confirmed in our Caucasoid population with a significant association between class II allele HLA-DR3 and the disease [35]. Similarly, genetic factors could be implicated in the prognosis of IgAN, as recently reviewed [36]. The stability of the annual incidence of IgAN during our 15 year prospective study suggests that immunogenetic factors could be more important than environmental factors in the onset of IgAN. Moreover, we have recently shown a significant association between a familial history of arterial hypertension and the presence of arterial hypertension at the time of renal biopsy in IgAN patients [37]. In our area, class II allele DR4 is in linkage disequilibrium with B12 [44] in IgAN patients with familial arterial hypertension and in those who progress to ESRD [35, 37]. Therefore, HLA alleles in IgAN could be markers of the severity of the disease [38]. In adult nephrosis we found a convincing association with DR7 [28, 35], suggesting, as in the child [26], an immunogenetic susceptibility to developing this glomerular disease.

The incidence of ESRD due to PGD decreased by about 30% during the last five year period and is mainly due to the significant decrease in the incidence of MPGN, which was an important cause of ESRD [10, 11, 21]. Today, in our area MPGN has become a rare cause of ESRD, accounting for only 5% of glomerular causes of ESRD during the last decade. Such a decrease of incidence of ESRD due to PGD was confirmed in Western Europe [39] and in the USA [40]. Our study confirms the good renal prognosis of poststreptococcal AGN.

In our area, the average incidence of ESRD due to PGD was 2 per 100,000 inhabitants during the last decade, and about 21.5% of patients with PGD may develop ESRD. However, our study shows variations according to age and gender. ESRD due to PGD is more frequent in the 40 to 59 year age group (2.8 per 100,000) than in other age groups (1 to 2.0 per 100,000). The prevalence of males is found in every age group, confirming the recent data of the EDTA [39]. The risk of developing ESRD due to PGD is six- to eightfold higher in males than in females in the 20 to 59 year age group and two- to threefold only over 60 years. Thus, male gender is a risk factor for worse renal prognosis of PGD, particularly under 60 years, as already suggested with other nephropathies [41].

We confirm that IgAN is the leading cause of ESRD due to PGD in our area, representing 40% of PGD reaching ESRD during the last decade, as was already evaluated in 1988 [9, 17]. Such information cannot yet be obtained from the registry of the EDTA since only 40% of new patients accepted for renal replacement therapy in 1985 had PGD confirmed by histological examination. Histological diagnosis at ESRD varied among countries, ranging from less than 10 to nearly 90% with 42% in France [42]. In our area during the last decade more than 85% of patients who started renal replacement therapy with the diagnosis of PGD had had a histological diagnosis of renal disease during the first study period. A recent study carried out in another French region confirms our results [8]. About 30% of patients with IgAN are at risk to reach ESRD after at least ten years of evolution of the disease, confirming the evaluations made in several studies [2, 38]. Thus we can consider that about 400 new patients with IgAN go into renal remplacement therapy every year in France. This number is higher than that of a first evaluation made in 1987 [43]. The risk of such a poor renal prognosis is the highest between 40 and 59 years of age, where IgAN represents more than 60% of glomerular causes of ESRD in males and 40% in females. Over 60 years of age, IgAN still represents 25% of glomerular causes of ESRD in males, its frequency being equivalent to that of MN (20%) and CGN (25%). The greater frequency of arterial hypertension in the male population [44, 45] and increased genetic risk of hypertension [24, 37] could contribute to the progression to ESRD of patients with PGD, particularly in those with IgAN [37]. An interesting recent experimental study has examined the possibility of a Y-linked effect on blood pressure operating through the kidney [46]. In our area, MN is not a frequent cause of ESRD and only 15% of patients may reach ESRD ten years after the diagnosis of the disease. These results conflict with those of Ponticelli et al [47], but are in agreement with other studies in France [48] and in Italy [49]. It is interesting to point out the increasing incidence of diagnosis of MN, which seems to be associated with an increasing incidence of ESRD due to MN (during the last 5 year period of the study). A prevalence of females characterizes nephrosis, and this could explain a more benign renal prognosis of this glomerular disease. CGN is another PGD which essentially occurs after 60 years of age and where two out of three patients reaches ESRD. However, the risk of worse renal prognosis is nine- to tenfold higher in males than in females.

In conclusion, our study is the first to give epidemiological information on the similar frequency of PGD in every age group of a general population. It demonstrates that the two major chronic PGD are now IgAN and MN and that the IgAN is the first glomerular cause of ESRD in adults aged under 60 years, accounting for the prevalence of males among patients with ESRD due to PGD.

Acknowledgments

The authors express their gratitude to Mrs. J. Le Mee, C. Robin and D. Broneer for help in preparation of this manuscript. They also thank urologists working in the area: Drs. Jean-Pierre Mignard (Clinique Jeanne d'Arc), Pierre Bavay and François Triffard (Clinique Sainte-Thérèse), Michel Carlier and Catherine Cloup (Hôpital La Beauchée, Saint-Brieuc) for their invaluable collaboration.

Reprint requests to Pierre Simon, M.D. Service de Néphrologie, Hôpital La Beauchée, rue Marcel Proust, 22000 Saint-Brieuc, France.

References

1. Simon P, Ang KS, Bavay P, Cloup C, Mignard JP, Ramee MP: Glomérulonéphrite à immunoglobulines A. Epidémiologie dans une population de 250,000 habitants. *Presse Méd* 13:257–260, 1984
2. D'Amigo G: The commonest glomerulonephritis in the world: IgA nephropathy. *Quart J Med* 64:709–727, 1987
3. Jungers P, Nochy D, Geffriaud C, Droz D, Noel LH, Berger J: Epidemiology of primary glomerulonephritis (GN) in a French urban area. *XIIth International Congress of Nephrology*, Jerusalem, June 13–18, 1993, abstract, p 77

4. SIMON P, RAMEE MP, ANG KS, CAM G: Epidémiologie des maladies glomérulaires dans une région française. Varations en fonction des époques et de l'âge des sujets. *Presse Méd* 41:2175–2182, 1988
5. TIEBOSCH A JMG, WOLTERS J, FREDERICK PF, VAN DER WIEL JWM, ZEFFENFELDT E, VAN BREDAVRIERMAN PJC: Epidemiology of idiopathic glomerular disease: A prospective study. *Kidney Int* 32:112–116, 1987
6. ABDULMASSIH Z, MAKDASSI R, BOE N, LALAU JD, LAMBREY G, COEVOET B, FIEVET P, BATAILLE P, RENAUD H, WESTEEL PF, FOURNIER A: Epidémiologie des glomérulonephrites primitives en Picardie. *Ann Med Interne* 141:129–133, 1990
7. Central Committee of the Toronto: Glomerulonephritis Registry. Regional program for the study of glomerulonephritis. *Can Med Assoc J* 124:1558–1564, 1981
8. FRIMAT L, AYMARD B, HESTIN D, MAYEUX D, RENOULT E, CAO HUU T, GAMBERONI J, KESSLER M: Epidemiological features of IgA mesangial nephropathy (Berger's disease) after 50 years of age. *Nephrol Dial Transplant* 7:687, 1992
9. SIMON P, ANG KS, CAM G, RAMEE MP: La glomérulonéphrite à dépôts d'immunoglobulines A est une des causes les plus fréquentes de l'insuffisance rénale terminale. *Press Méd* 17:121–122, 1988
10. BARBIANO DI BELBIOJOSO G, BONONI M, PAGLIANI B, LAVAGNI MG: Is membranoproliferative glomerulonephritis really decreasing? *Nephron* 40:380, 1985
11. JUNGERS P, FORGET D, DROZ D, NOEL LH, GRUNFELD JP: Rarefaction of membranoproliferative glomerulonephritis in France. *Proc EDTA-ERA* 22:730–735, 1985
12. SIMON P, RAMEE MP, ANG KS, CAM G: Epidemiological data in a population of 250,000 on minimal change nephrotic syndrome, IgA nephropathy, idiopathic membranous and membranoproliferative glomerulonephritis. *Proc EDTA-ERA* 21:28–29, 1984
13. SIMON P, RAMEE MP, ANG KS, CAM G: Evidence for a simultaneous reduction in the incidence of membranoproliferative glomerulonephritis and streptococcal diseases in a French rural area, edited by C. GIORDANO, in *Uremia,* Philadelphia, Field et Wood, 1988, pp 110–114
14. SIMON P, RAMEE MP, ANG KS, CAM G: Variations of primary glomerulonephritis. Incidence in a rural area of 400,000 inhabitants in the last decade. *Nephron* 45:171–172, 1987
15. Recensement général de la population de 1990. Logements—Population—Emploi—Evolution. 1975—1982—1990—Côtes d'Armor INSEE, 1991
16. MAUSNER JS, KRAMER S: Epidemiology. An Introductory Text. Philadelphia, W. B. Saunders Company, 1985
17. SIMON P, RAMEE MP, ANG KS, CAM G: Epidémiologie de l'insuffisance rénale chronique traitée par dialyse dans une région française. Evolution sur une période de 12 ans. *Presse Méd* 42:2225–2228, 1988
18. SIMON P, CHARASSE C, AUTULY V, ANG KS, CAM G, RAMEE MP: Epidemiology of primary glomerular disease in the elderly. in *Glomerulonephritis in the Elderly*, edited by SESSA A, MERONI M, BATTINI; Contrib Nephrol, Basel, Karger, 1993, vol 105, pp 161–166
19. MACCARTY M: The streptococcus and human disease. *Am J Med* 65:717–724, 1978
20. RODRIGUEZ-ITURBE B: (Nephrology Forum) Epidemic poststreptococcal glomerulonephritis. *Kidney Int* 25:129–134, 1984
21. DONADIO JV: Membranoproliferative glomerulonephritis, in *Diseases of the Kidney*, vol. II, edited by SCHRIER RW, GOTTSCHALK CW, Boston, Little, Brown and Company, 1993, pp 1815–1837
22. SHU-KUO-HSIUNG, LIAN JONG-DA, LU YVAN-SAN, CHEN CHI-HUNG, CHEN LAIPING: Primary glomerulonephritis in Taiwan: An analysis of 718 cases. *XIIth International Congress of Nephrology*, Jerusalem, June 13–18, 1993, abstract, p 82
23. ABRASS CK: Glomerulonephritis in the elderly. *Am J Nephrol* 5:409–418, 1985
24. JOHNSTON PA, DAVISON AM: Male to female ratios in idiopathic glomerulonephritis. *XIIth International Congress of Nephrology*, Jerusalem, June 13–18, 1993, abstract p 78
25. LAGRUE G, LAURENT J: Epidémiologie des maladies glomérulaires. *Presse Méd* 13:255–56, 1984
26. BROYER M, MEYRIER A, NIAUDET P, HABIB R: Minimal change and focal segmental glomerular sclerosis, in *Oxford Textbook of Clinical Nephrology*, edited by S CAMERON, AM DAVISON, JP GRÜNFELD, D KERR, E RITZ, Oxford, University Press, 1992, pp 418–433
27. HOYER JR: Idiopathic nephrotic syndrome with minimal glomerular changes, in *Nephrotic Syndrome, Contemporary Issues in Nephrology*, BM BRENNER, JH STEIN, vol. IX, New York, Churchill Livingstone, 1982, p 145–154
28. SIMON P, RAMEE MP, ANG KS, CAM G, CHARASSE C, BENZIANE A, KRIBBII H, BRIAND MY, BOGUAIS MT: Epidémiologie du syndrôme néphrotique idiopathique (LGM et HSF) de l'adulte. Etude prospective sur 15 ans dans une région française. *Nephrologie* 14:59, 1993
29. AUTULY V, SIMON P, CAM G, ANG KS, RAMEE MP: The nephrotic syndrome in the elderly: epidemiological data; in *New Therapeutic Strategies in Nephrology*, edited by ANDREUCCI VE, DEL CANTON A Boston, Kluwer Academic Publishers, 1991, pp 37–40
30. GORRIE M, NICHOLLS A: The impact of membranous nephropathy in a defined population: A nine-year audit. *XIIth International Congress of Nephrology*, Jerusalem, June 13–18, 1993, abstract p 76
31. FILLASTRE JP, DRUET P, MERY JP: Proteinuric nephropathies associated with drugs and substances of abuse in *The Nephrotic Syndrome*, edited by CAMERON JS, GLASSOCK RJ, New York, Marcel Dekker, 1988, pp 697–744
32. CRISTOFINI P, PAIRON JC, DE PALMAS J, BROCHARD P, LAGRUE G, BIGNON J: Etude cas-témoins sur la relation entre glomérulonephrite chronique et exposition aux solvants. *Arch Mal Prof* 48, 4:320–323, 1987
33. COGGINS CH: Membranous nephropathy, in *Diseases of the Kidney*, vol. II, edited by SCHRIER RW, GOTTSCHALK CW, Boston, Little, Brown and Company, 1993, pp 1785–1813
34. BURNS A, LI P, REES A: Immunogenetic of nephritis, in *Immunology of Renal Disease*, edited by PUSEY CD, Kluwer Academic publishers Dordrecht, Boston, London, Immunology and Medicine, 1991, vol. 16, pp 1–28
35. SIMON P, AUTULY V, FAUCHET R, SEMAMA G, ANG KS, CAM G, BENZIANE A, CHARASSE C, RAMEE MP: Associations entre maladies glomérulaires primitives et allèles HLA dans une population française d'origine caucasienne. *Néphrologie* 14:59, 1993
36. LEVY M, LESAVRE P: Genetic factors in IgA nephropathy, in *Advances in Nephrology*, edited by GRÜNFELD JP, BACH JF, KREISS H, MAXWELL MH St Louis, Mosby Year Book, 1992, vol 21, pp 23–51
37. AUTULY V, LARUELLE E, BENZIANE A, ANG KS, CAM G, RAMEE MP, SIMON P: Increased genetic risk of hypertension in immunoglobin A nephropathy but not in membranous nephropathy. *J Hypertens* 9 (Suppl 6):5220–5221, 1991
38. SCHENA PF: IgA nephropathies, in *Oxford Textbook of Clinical Nephrology*, edited by S. CAMERON, AM DAVISON, JP GRÜNFELD, D KERR, E RITZ, Oxford University Press, 1992, pp 339–369
39. WING AJ, BRUNNER FP: Twenty-three years of dialysis and transplantation in Europe: Experiences of the EDTA registry. *Am J Kidney Dis* 14:341–346, 1989
40. Excerpts from United States Renal Data System 1993 Annual Data Report. *Am J Kidney Dis* 22 (Suppl 2):30–37, 1993
41. GRETZ N, ZEIER M, GEBERTH S, STRAUCHM, RITZ E: Is gender a determinant for evolution of renal failure? A study in autosomal dominant polycystic Kidney disease *Am J Kidney Dis* 14:178–183, 1989
42. WING AJ: Causes of end stage renal failure. in *Oxford Textbook of Clinical Nephrology*, edited by CAMERON S, DAVISON AM, GRÜNFELD JP, KEN D, RITZ E, Oxford, Oxford Medical Publications, 1992, vol 2, pp 1227–1236
43. BERGER J, LEVY M: Epidemiology of idiopathic IgA nephropathy. *Semin Nephrol* 7:277–279, 1987
44. GORDON T: Blood pressure of adults by race and area, United States 1960–62. *Vital Health Stat* 11:1–20, 1964
45. BOE J, HUMERFELT S, WEDERVANG F: The blood pressure in a population. *Acta Med Scand* (Suppl)321:1–336, 1957
46. HARRAP SB, WANT BZ, MACLELLAN DG: Renal transplantation between male and female spontaneously hypertensive rats. *Hypertension* 19:431–434, 1992
47. PONTICELLI C, ZUCCHELLI P, PASSERINI P, CAGNOLI L, CESANA B, POZZI C, PASQUALI S, IMBACIATI E, GRASSI C, REDAELI B, SASDELLI M, LOCATELLI F: A randomized trial of methylprednisolone and chlorambucil in idiopathic membranous nephropathy. *N Engl J Med* 320:8–13, 1989
48. NOEL LH, ZANETTI M, DROZ D, BARBANEL C: Longterm prognosis of idiopathic membranous glomerulonephritis: Study of 116 untreated patients. *Am J Med* 66:82–90, 1979
49. SCHIEPPATI A, MOSCONI L, PERNA A, MECCA G, BERTANI T, GARATTINI S, REMUZZI G: Prognosis of untreated patients with idiopathic membranous nephropathy. *N Engl J Med* 329:85–89, 1993