

Invited Comment

Nephrology, dialysis and transplantation in Brazil

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The European Renal Association welcomes this opportunity and feels that European nephrologists should be informed about the state of nephrology in South America, with which particularly our Latin colleagues maintain close cultural relationships. The following report on Nephrology in Brazil is a welcome addition to a series of reports designed to provide to European nephrologists a global view of nephrology. It is hoped that this is not misconstrued as a violation of nephrological Monroe doctrine.

Introduction

Nephrology in Brazil originated in the 1950s, when the first renal biopsies and dialytic procedures were implemented, being officially recognized as a distinct discipline of clinical medicine in 1960. In that same year, the Brazilian Society of Nephrology (SBN) was created. The SBN has now 1758 registered members including paediatric nephrologists (Table 1). There are 1310 medical doctors/per million population (p.m.p.), corresponding to 1 physician/710 inhabitants, and 10.5 nephrologists/p.m.p. (corresponding to 1 nephrologist/95 400 inhabitants), concentrated mainly in the more affluent South and South-east regions.

Despite the striking socioeconomic differences in Brazil, virtually the entire Brazilian territory is pro-

vided with renal replacement therapy (RRT) centres, comprising 534 dialysis and 111 renal transplant centres. Although there are several similarities with more developed countries, the clinical and academic activities in Nephrology exhibit some unique characteristics in this tropical, developing country.

Basic demographic data

With a territorial area of 8.5 million km², Brazil is the largest country in Latin America and the fifth largest country in the world. Politically and administratively Brazil is divided into five regions: North, North-east, Mid-west, South-east (where São Paulo, the largest South American city, and Rio de Janeiro are located) and South. Northern Brazil is widely occupied by the Amazon rain forest whereas the central region is mainly rural. Therefore, most of the 160 million Brazilians concentrate in the large urban, industrialized areas of the Eastern coast, especially in the South and South-east. The current demographic growth is about 1.3% per year.

Brazil has a mixed ethnic population. The largest fraction (60%) is made up of Caucasians, descended from the Portuguese colonizers as well as from European immigrants arriving in the country in the late 19th and early 20th centuries. Blacks and mulattos descended from African slaves constitute the second major ethnic group, while people from Asian and Semitic descent form small but influential minorities. Native Indians represent less than 1% of the total population.

Clinical Nephrology

Several biopsy studies showed that the epidemiological profile of primary glomerular diseases in Brazil is

Table 1. Nephrology and renal replacement therapy in Brazil

Brazilian Society of Nephrology members	1758	
Number of medical schools	84	
Nephrology residency programme	55	
Nephrology post-graduation programme	5	
Haemodialysis centres	534	
Number of patients on HD (1996)	25489	85%
Number of patients on CAPD (1996)	3805	12.7%
Number of patients on IPD (1996)	690	2.3%
Total number of patients on dialysis	29984	152/p.m.p.
Brazilian Association for Organ Transplantation members	462	
Kidney transplantation centres	111	
Number of kidney transplants (1996)	1713	11.31/p.m.p.
living donor	872	51%
cadaveric donor	841	49%

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similar to that observed in North America and Europe. A recent survey performed at the University of São Paulo showed that focal and segmental glomerulosclerosis (FSGS) accounted for 43% of all primary glomerulopathies, while membranous glomerulonephritis (GN) represented 20% and membranoproliferative GN 14% [1]. Likewise, the percentage of patients with IgA nephropathy ranges between 6.5 and 10.2%, similar to values reported in North America, but somewhat lower than the European and Asian figures [2]. In contrast, the incidence of poststreptococcal glomerulonephritis, a disease more closely related to poor social conditions, remains elevated, as opposed to the declining incidence observed in developed countries.

One of the most important progressive nephropathies associated with tropical diseases in Brazil is schistosomal glomerulopathy. Schistosomiasis is a parasitic disease transmitted through the intact skin by swimming in contaminated ponds. The disease is endemic in the poorest rural areas of the North-eastern region, afflicting hundreds of thousands of people. Patients at risk are mainly those suffering from the advanced hepatosplenic and hepatointestinal forms of the disease [3], 4.5% of which may develop schistosomal nephropathy [4]. Clinical manifestations of this nephropathy include proteinuria (in the nephrotic range in 60% of cases), haematuria, low C3 levels, and hyperglobulinaemia. The most common histological forms of the disease are membranoproliferative GN (Figure 1A), mesangial proliferative GN, and FSGS [5]. Immunofluorescence-microscopy reveals deposits of IgM, IgG, and C3 in the mesangial area. Glomerular deposition of specific *Schistosoma mansoni* antigens (Figure 1B) and respective antibodies have also been described [6].

Acute renal failure in Brazil

The acute renal failure (ARF) pattern in Brazil also reflects the country's continental size and striking socioeconomic contrasts. Acute renal dysfunction induced by tropical diseases coexist side by side with the usual ARF causes found in North America or Europe. Depending on the geographic area or the characteristics of the hospital, ARF secondary to malaria, leptospirosis, tetanus, and animal venom may constitute important causes of ARF, whereas in many tertiary hospitals in large cities or in Southern and South-eastern Brazil they represent only a small percentage of ARF cases.

Tropical disease-induced ARF

Plasmodium falciparum malaria occurs mainly in the Amazon area. The Manaus Tropical Medicine Institute has a huge experience with this disease with 3074 cases admitted in a 10-year period. ARF (serum creatinine over 3 mg/dl) occurred in approximately 4% of these patients, mainly in subjects with severe forms of mal-

aria, with an average mortality of 19.8% [7]. This mortality has decreased to around 4% in the last 2 years (Bulbol W.S., personal communication). Renal pathology shows acute tubular necrosis and/or acute interstitial nephritis. ARF aetiology is probably multifactorial and related to intravascular haemolysis, hyperbilirubinaemia, hypotension, hypovolaemia, blood hyperviscosity, renal ischaemia due to microvascular injury and glomerular fibrin deposition, and massive parasitaemia [7].

Leptospirosis is a zoonosis acquired mainly through direct or indirect contact with urine of infected animals. Outbreaks of this disease have occurred during the rainfall season from exposure of people to contaminated floodwaters. In São Paulo, the incidence was 3.88 cases/100 000 inhabitants in 1995 [8]. Approximately 10% of the infected patients can develop a severe form of leptospirosis characterized by jaundice, acute renal failure, and haemorrhagic manifestations, known as Weil's disease. The mechanisms of renal dysfunction have been related to dehydration, jaundice rhabdomyolysis, and leptospira-induced direct renal tissue injury [8]. Renal histology always discloses acute interstitial nephritis (even in patients without ARF), which may or may not be associated with acute tubular necrosis [8]. Leptospirosis-induced ARF has a particular presentation. Although it is frequently severe and hypercatabolic, oliguria and hyperkalaemia are uncommon and actually many patients have hypokalaemia [9]. These peculiar characteristics have been explained by proximal tubular dysfunction in presence of distal tubular integrity, inner medullary collecting duct resistance to vasopressin, high blood levels of aldosterone and cortisol, and leptospira toxin-induced Na-K-ATPase inhibition [8,10].

Tetanus is a self-limiting disease, whose clinical picture is almost exclusively due to adrenergic dysfunction caused by *Clostridium tetani* neurotoxin. Even after decades of compulsory immunization it still remains a health problem in developing countries. In the State of São Paulo, the incidence in 1990 was 0.4 per 100 000 inhabitants. ARF is a serious complication of tetanus. It has a high prevalence (40–50%), is related to important mortality, is usually non-oliguric, and occurs in the first 2 weeks of disease [11]. Renal histology is normal or shows acute tubular necrosis. Recent studies suggest that autonomic nervous system overactivity is probably the most important factor causing renal dysfunction in these patients [11].

There are four genera of poisonous snakes in Brazil (Bothrops, Crotalus, Lachesis and Micrurus) responsible for an annual report of around 20 000 venomous snake-bites [12]. ARF is probably the most serious and lethal complication of Bothrops and Crotalus accidents. Renal failure develops early and is usually oliguric and severe, frequently requiring dialysis. Snakes of the genus Bothrops are responsible for 80–90% of the reported venomous snake-bites. The venom has a strong local proteolytic effect, promotes the release of vasoactive substances, activates the coagulation cascade, and causes haemolysis and vascu-

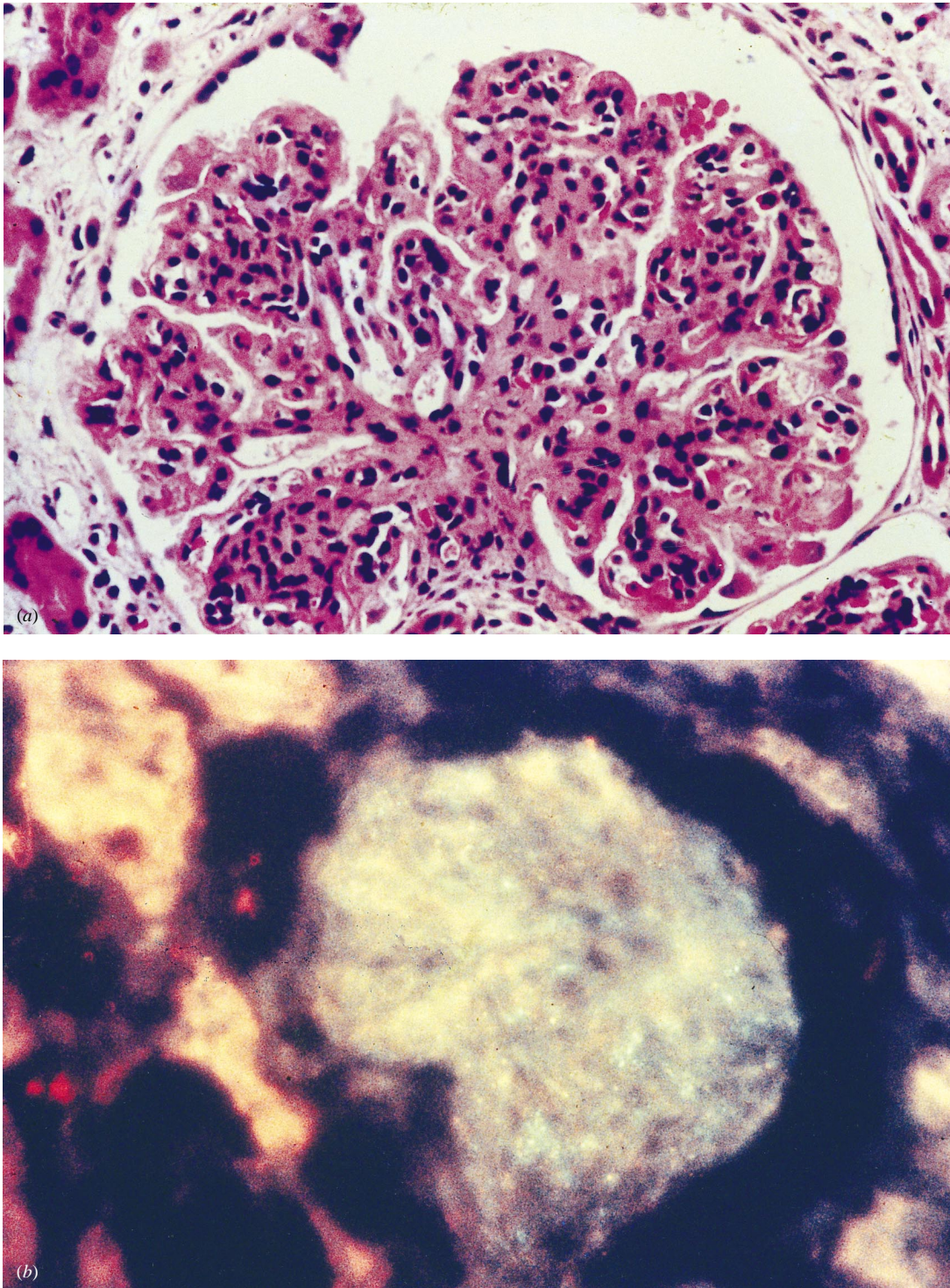


Fig. 1. (a) Membranoproliferative GN in a patient with hepatosplenic schistosomiasis (HE 400 \times). (b) *Schistosoma mansoni* antigen demonstrated in a human glomerulus (mesangioproliferative GN) detected by immunofluorescence [6]. (Courtesy of Prof. Thales de Brito, São Paulo, Brazil.)

lar injury [12]. ARF occurs in 2–10% of the cases [13]. Renal histology showed acute tubular necrosis and in some instances, acute cortical necrosis. The most important factors in the aetiopathogenesis of renal injury seems to be ischaemia caused by massive

glomeruli fibrin deposition and intravascular haemolysis, although a direct venom nephrotoxicity cannot be excluded [14]. *Crotalus* snakes are responsible for 7–8.5% of the total of venomous snakebites with a high mortality (72%) in the non-treated cases [12].

The venom is neurotoxic, has a strong systemic myotoxic action, and can activate the coagulation system [12,15]. ARF prevalence after *Crotalus* bite ranges from 9 to 31% [16]. Pathology showed acute tubular necrosis or acute interstitial nephritis [17]. Clinical and recent experimental studies suggest that renal failure is probably related to myolysis, direct nephrotoxicity of the venom, and the extracellular volume status [18].

Poisonous arthropods such as bees, caterpillars and spiders can also cause ARF. Patients receiving hundreds of simultaneous bee stings may develop a complex clinical picture with intravascular haemolysis, rhabdomyolysis, hepatic injury, low platelet count, coagulopathy, bleeding, cardiovascular and pulmonary changes, and early development of ARF [19]. The proliferation of africanized bees increased the number of accidents in recent years. In the few cases where renal histology was available it showed acute tubular necrosis [19]. The aetiopathogenesis of renal injury might be related to hypotension, myoglobinuria, haemoglobinuria and direct nephrotoxicity of the venom [19]. Accidents with caterpillars of the genus *Lonomia* produce haemorrhagic disorders of varied severity. Studies on caterpillar venom have identified a strong fibrinolytic action and enzymatic activities similar to tissue plasminogen activator, kallikrein, factor Xa, and urokinase. The haemorrhagic diathesis induced by this venom is therefore complex, with both fibrinolytic and disseminated intravascular coagulation-like (DIC) activity. Recently, ARF was reported in patients who had contact with *Lonomia obliqua* in Southern Brazil [20]. *Lonomia* venom caused severe and prolonged ARF, with renal histology suggesting ischaemic injury [21]. The mechanisms of renal dysfunction are unclear and might be related to DIC-induced glomeruli fibrin deposition or to direct venom nephrotoxicity. Spiders of the genus *Loxosceles* may induce late local necrosis at bite site, intravascular haemolysis, coagulation system changes, and renal injury. Patients with mild cutaneous lesion may present severe haemolysis and ARF, which is the main cause of mortality after these accidents.

Tertiary hospital ARF

In order to exemplify the ARF pattern in large hospitals in Brazil, the data of the Clinical Hospital of the University of São Paulo, a 2000-bed tertiary university complex, will be presented. During the year of 1993 the ARF unit assisted 393 cases of a total of 49 953 hospitalized patients, which gave an ARF incidence of 0.79%. In 55% of the cases the patients were in intensive care units, in 24% in the emergency ward, and only 21% of the patients were in routine surgical or clinical units. There was a clear prevalence of medical (62%) over surgical ARF (37.7%) and almost no obstetric ARF (0.3%). The most frequent aetiologies for ARF in these 393 patients were respectively sepsis, hypovolaemia, low cardiac output due to severe heart failure, drug nephrotoxicity, surgical trauma, and hypotension.

A large number of patients had an association of two or more precipitating factors. There was a high prevalence of non-oliguric ARF (46%) probably due to the elevated number of nephrotoxic drug-induced ARF and to early and intense resuscitation manoeuvres in oliguric patients. Almost half of the ARF patients (46%) required dialysis with different modalities being employed (peritoneal dialysis, classical haemodialysis, slow continuous haemodialysis, isolated ultrafiltration and haemofiltration, or haemodiafiltration).

Mortality of the ARF group was 50% against an overall hospital mortality of 6.9% in the same interval. It is important to note that the characteristics reported for this population are basically similar to those found in other large series in Brazil, North America, or Europe.

Renal replacement therapy (RRT) in Brazil

The first dialysis in Brazil was performed in March 1949 in São Paulo. Although there was some development in this field in the 1950s and 1960s, it was only in 1974 that an official RRT programme was implemented for patients with end-stage renal disease (ESRD), while the CAPD programme started in 1980.

According to data provided by the Ministry of Health, there were 29 984 patients on dialysis in Brazil in 1996. Of these, a total of 25 489 were on haemodialysis (85%), 3805 on CAPD (12.7%), and 690 on intermittent peritoneal dialysis (2.3%). Thus, the prevalence of ESRD patients on dialysis in 1996 was 179 p.m.p. (152 p.m.p. on HD, 23 p.m.p. on CAPD and 4 p.m.p. on IPD), mostly concentrated in the Southeastern and Southern areas of the country (Figure 2). From December 1994 to November 1995 there were around 50 000 hospitalizations related to ESRD.

Unfortunately, no complete nationwide registry for ESRD is currently available in Brazil. The data that follows was obtained from regional registries, available only in some Brazilian states. In a major epidemiological study, Sesso *et al.* [22] analysed 2905 patients on dialysis in São Paulo. The three major causes of ESRD in Brazil were chronic glomerulonephritis (27.5%), hypertensive nephrosclerosis (16.8%), and diabetic nephropathy (8%). Additional causes of ESRD were interstitial nephritis (4%), polycystic kidney disease (3%), lupus nephritis (1.3%), and other causes (3.4%). In 36% of all cases no precise aetiology could be determined. The annual mortality rate among patients under chronic dialysis in the city of São Paulo was 17.2%.

The current prevalence of hepatitis B virus infection among patients on chronic dialysis ranges from 0 to 15%. The prevalence of hepatitis C virus (HCV) infection is higher, ranging from 16 to 82% in hemodialysis units [23,24]. However, the seroconversion incidence in the Dialysis Unit of the University of São Paulo during an 18-month follow-up period was reduced from 8% per year to zero by isolating HCV-positive patients in the last shift [Noronha *et al.* unpublished]. The genotypes detected in this dialysis

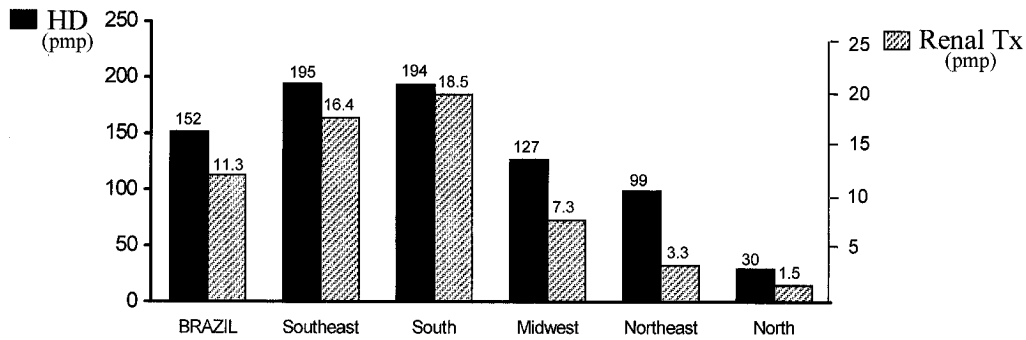


Fig. 2. Prevalence of haemodialysis (HD) and renal transplants (Tx) in 1996 in Brazil and in Brazilian regions.

unit were 1a, 1b, 2b and 3a [Noronha *et al.* unpublished].

Brazil possesses a total of 534 dialysis units, mostly concentrated in medium to large cities, as illustrated in Figure 3. The majority of haemodialysis machines used until the late 80s were manufactured in Brazil, a result of the prevailing protectionist policies. With the major political and economic changes initiated in this decade, the importation taxes for most goods were drastically reduced, facilitating the acquisition of imported dialysis equipment. The current availability of modern and reliable dialysis machines made it possible to increase the efficiency of the procedures and to individualize treatments. The use of cuprophane dialysers has decreased in contrast with an enhanced utilization of polysulphone or cellulose acetate dialysers.

Since 1974, the National Health Ministry has ensured that all ESRD patients have access to Government-sponsored RRT. Less than 5% of the cases are covered by private health plans or by other kinds of health insurance. The Brazilian Government pays approximately 98 US\$ per haemodialysis session including the medical fees, and 35 US\$ per patient per month for CAPD treatment. However, CAPD costs the Government 1200 US\$ per patient per month. Therefore, the Government expenses with the chronic dialysis in 1996 were approximately US\$ 341 millions (US\$ 279 million for haemodialysis, 57 million for CAPD and 5.4 million for intermittent peritoneal dialysis) corresponding to US\$ 11 380 per patient per year. In addition, the Ministry of Health provides several medicaments used in the treatment of these patients, such as recombinant erythropoietin, calcitriol, antihypertensive drugs, and hepatitis B vaccination.

In 1996, new legislation on RRT was promulgated by the Brazilian Government, setting rigorous and detailed rules for the implementation of new dialysis centres as well as for the operation of already functioning units. Several technical prerequisites were defined, such as minimal space and design standards, operational procedures and qualification of the professional staff. In addition, detailed protocols were established, making mandatory the use of proportion dialysis machines and water treatment based on reverse

osmosis membranes, and regulating dialyser reuse practices.

Renal osteodystrophy in Brazil

Renal osteodystrophy in Brazil has distinctive features resulting mainly from two factors. First, patient compliance with calcitriol therapy was until recently very low due to financial limitations of acquiring the drug. Second, the high aluminium content in water (ranging from 5 to 180 µg/l), together with the inability of many centres to perform aluminium assays and to implement appropriate measures, led to a high incidence of aluminium-related bone disease. The specific policies adopted by the health authorities and an increased awareness of these problems on the part of nephrologists have considerably improved this picture in latter years.

In a recent national multicentre study, 782 crest iliac bone biopsies, performed in dialysis patients from 1985 to 1996, were analysed. Bone biopsies were indicated in patients with bone pain, muscle symptoms, or fractures. The biopsies were classified according to morphometric criteria: osteitis fibrosa (OF), mixed bone disease (MBD), adynamic bone disease (ABD), and osteomalacia (OM). The results are summarized in Table 2. OF was observed in 245 patients (31%), MBD in 171 (22%), ABD in 170 (22%), and OM in 196 cases (25%). There was no difference in serum calcium, phosphate and alkaline phosphatase concentrations among the groups. However, iPTH levels were increased in OF and in MBD compared to ABD and OM. Aluminium overload, diagnosed when the aluminium surface extent exceeded 20% of the total trabecular surface, was present in 44% of OF cases, 56% of MBD, 75% of ABD, and 69% of OM. Notably, hypercalcaemia (defined as a serum calcium concentration in excess of 10.5 mg/dl), was observed in only 9.3% of cases. In addition, serum phosphate below 6.0 mg/dl was detected in 43% of cases. This peculiar pattern may relate to different degrees of malnutrition in the dialysis population, associated with deficient calcitriol therapy.

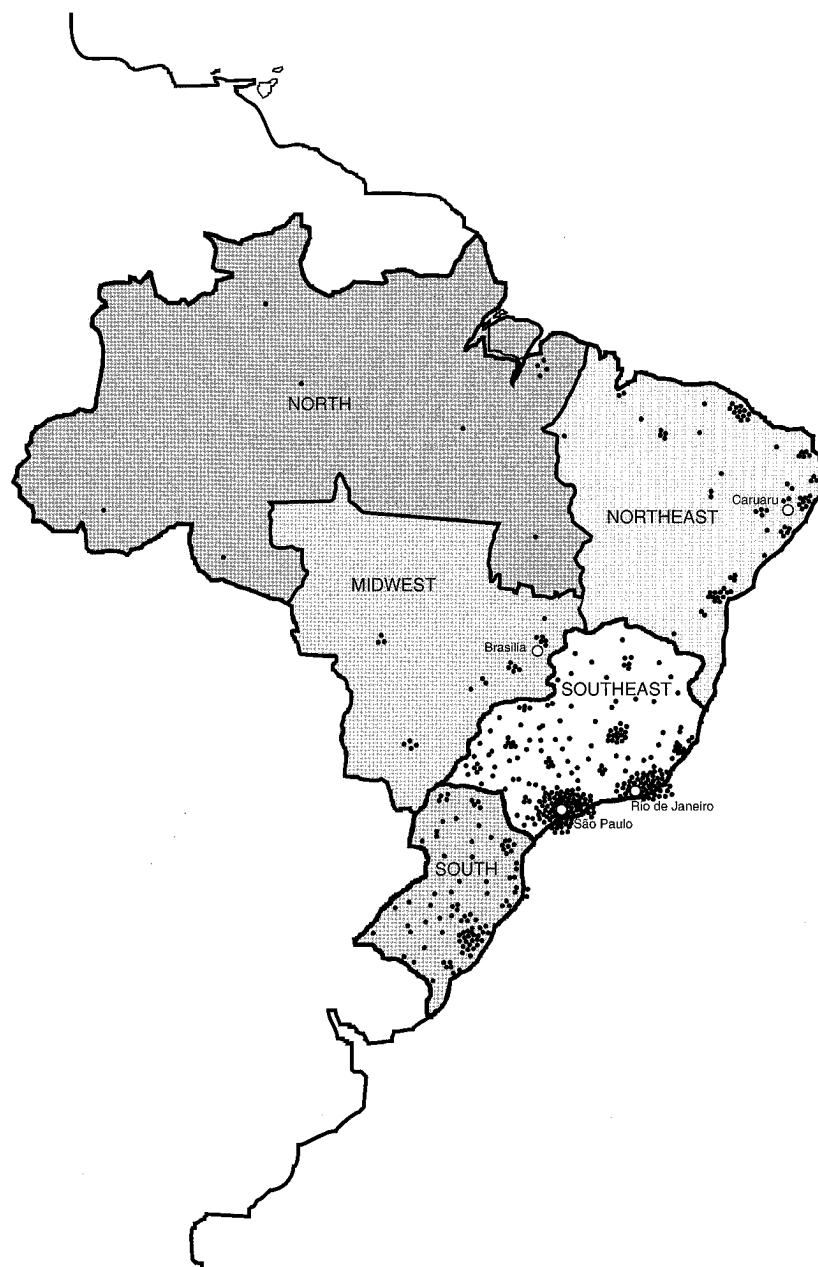


Fig. 3. Distribution of dialysis centres in Brazil.

Outbreak of toxic hepatopathy at a haemodialysis unit in Caruaru: microcystin water contamination

In February 1996, a bizarre accident at a 131-patient dialysis centre resulted in 60 deaths in Caruaru, a countryside city of 217 430 inhabitants located in North-eastern Brazil. The city has a dry weather with prolonged droughts, temperatures ranging from 20 to 38°C, and a deficient and irregular water supply, largely dependent on transportation by tank trucks.

Between 17 and 20 February 1996 (the hottest period of summer in the Southern Hemisphere), almost all patients dialysed in this Unit experienced visual disturbances, nausea, and vomiting. Curiously, the sever-

ity of the symptoms varied according to the dialysis shift. During the following 3 weeks, 12 patients died after seizures and/or acute haemorrhage. Fourteen patients subsequently died of liver failure or required hospitalization.

Deaths continued to occur over the following weeks, even though all dialytic procedures had been stopped at the original unit. By the end of May, 48 of 131 patients (37%) had died. Hospitalized patients showed hepatomegalia, cholestasis, and haemorrhagic diathesis. Liver failure and eventual death were not prevented by additional dialysis.

Local nephrologists and health authorities were initially at a complete loss as to the cause of these events,

Table 2. Clinical and laboratory data of 782 bone biopsies classified according to morphometric parameters (data presented as mean \pm SD)

	Osteitis fibrosa (OF)	Mixed bone disease (MBD)	Adynamic bone disease (ABD)	Osteomalacia (OM)
Number (%)	245 (31%)	171 (22%)	170 (22%)	196 (25%)
Age (years)	38 \pm 13	39 \pm 12	46 \pm 14	40 \pm 14
Months on dialysis	72 \pm 40	78 \pm 43	51 \pm 36	70 \pm 42
Ca (mg/dl)	9.3 \pm 0.8	9.1 \pm 1.0	9.5 \pm 1.0	9.0 \pm 1.0
P (mg/dl)	6.0 \pm 1.3	6.2 \pm 1.8	6.0 \pm 1.7	5.0 \pm 1.7
AP (\times normal)**	4.6 \pm 4.4	5.5 \pm 6.2	1.3 \pm 0.8	3.2 \pm 3.30
Serum iPTH (\times normal)**	14.65 \pm 9.89	13.79 \pm 9.62	2.65 \pm 3.6	5.62 \pm 5.95
N of biopsies with aluminium overload	108 (44%)*	96 (56%)*	128 (75%)*	136 (69%)*

*% positive cases related to the morphometric classification; **results presented as the ratio between the observed and respective reference values (due to the lack of uniformity in reference values among different laboratories).

except for the obvious relationship with haemodialysis. Leptospirosis, other bacterial and viral infections, and intoxication by heavy metal or pesticides, all of which might produce similar symptoms, were successively excluded. Investigations carried out by the local Secretary of Health, by the Federal University of Rio de Janeiro and by the Hospital Infection Branch of the Center of Disease Control (CDC), Atlanta, USA, eventually discovered that the water used for dialysis was contaminated by a toxin denominated microcystin-LR, produced by blue-green (cyanobacterial) algae. This possibility had been first raised by an ecobiologist from the Federal University of Rio de Janeiro, Sandra Azevedo, who by coincidence was studying these organisms as part of a research project unrelated to dialysis. Investigation then pointed to the presence of algae in the city water reservoir. The haemodialysis clinic had received inappropriately treated water by a tank truck. Aluminium had been added to the water, which was not subsequently filtered or chlorinated. At the Caruaru Dialysis Unit, the delivered water is passed through a sand filter, a charcoal filter, a deionizer, and a micropore filter before being used for haemodialysis. According to the maintenance workers, the charcoal filter was changed every 6 months and the micropore filter every 3 months, although no filters had been changed during the 3 months before the outbreak. Water samples from the lake, truck, charcoal filter, and dialysis filter were positive for microcystin. It was also detected in the blood and liver tissue of afflicted patients. There were no reports of non-uraemic individuals affected by this toxin. Whether local chlorination and more appropriate filtering of the contaminated water would have prevented the passage of the toxin to the dialysers has not been determined. The accident could not be directly attributed to misconduct on the part of the involved nephrologists. Even though, the unit has been closed by the Health Ministry.

Cyanobacteria or blue-green algae are prokaryotic organisms, with cellular organization and biochemistry similar to bacteria. Toxins are released after the organism's death [25]. Microcystin is a hepatotoxin inducing

liver failure. Animal death, resulting from intrahepatic haemorrhage and hypovolaemic shock, occurs within hours to days after the initial exposure. The mechanism of action is related to cytoskeleton changes and inhibition of phosphatase enzymes in hepatocytes. Blue-green algal toxicity is a worldwide problem causing death among animals and human gastroenteritis. Human parenteral exposure had not been previously reported.

Renal transplantation

The first renal transplantation in Brazil was done in 1964 in Rio de Janeiro. In 1965 the first regular kidney transplantation programme at the University of São Paulo began. However, it was only in 1986 that the Brazilian Organ Transplantation Association (ABTO) was created. There are currently 160 transplant centres in Brazil, 111 of which perform kidney transplantation.

Almost all renal transplant centres in Brazil start their respective programmes using living donors. The vast majority of these transplants have been performed using living related donors, considering parents, siblings, offspring, and spouses as family members. Living unrelated donors have also been accepted in many centres. In 1993, however, legislation was passed requiring legal authorization for all renal transplantation that employs living unrelated donors. There were several reasons for the predominance of living donors until the late 1980s. Brazilian families are usually larger compared to European countries (hence with better chances of finding compatible donors). The better biological match and the strikingly low cold ischaemia time thus contribute to a better outcome in these cases. In addition, emergency operation may be avoided with the presence of the complete transplant team in a planned manner. Finally, the living transplant programme developed mainly as a result of a deficiency of cadaveric donors until the late 1980s. In the last 10 years, however, considerable efforts have been developed to improve the cadaver transplant pro-

gramme, resulting in a significant increase in the number of these procedures (Figure 4).

One of the major goals is to increase organ supply by improving organ procurement. Even in the more developed Southern and South-eastern regions there are only five cadaver donors p.m.p./year. A major move in support of the cadaver transplant programme came with the 1997 passing of the 'presumed consent' law. According to this law, all Brazilians are presumed organ donors unless explicitly stated otherwise in an official document such as an ID or driver's license. Even so, the transplant teams still consult with the families about donation, a firm denial being always accepted. Whether this law will indeed contribute to increase the number of organ donations in Brazil is still a matter of controversy. There is no doubt that this cannot be the sole measure to improve the availability of cadaver donors, although the heated discussion it stirred among the population is regarded as a positive effect. A potentially favourable corollary of this new legislation is the mandatory organization of a single waiting list for organ sharing.

The most recent available registry of organ transplantation reports a total of 1713 kidney transplants during the year of 1996, corresponding to 11.3 renal transplants p.m.p. (57 renal transplants per 1000 patients on dialysis treatment) (Figure 2). The highest rates were reported in the South-east and South regions (Figure 5), which exhibited similar cadaver/living donor ratios.

Brazilian government pays approximately 8700 US\$ per kidney transplantation, including medical fees. The Health Ministry also finances the standard triple therapy for immunosuppression (cyclosporin (CsA), azathioprine (AZA), and steroids). More recently, several transplant centres introduced mycophenolate mofetil (MMF) in the immunosuppressive protocol. An ongoing national multicentre study compares the efficacy of two immunosuppressive protocols

(CsA + AZA + steroids vs CsA + MMF + steroids) in kidney transplant recipients.

Besides the kidney transplantation programme, other organ transplantations are being performed routinely. There are 13 centres for liver transplants (168 liver transplants performed in 1996), 21 for heart transplants (82 cardiac transplants in 1996), five for cornea (544 corneal transplants in 1996), four for bone marrow (140 transplants in 1996), and four for lung transplantation (6 transplants in 1996). In 1996 kidney-pancreas transplantation was restarted and 12 simultaneous kidney-pancreas transplantation have been performed since then.

Academic, educational and research activities in Brazilian nephrology

Education activities in Brazilian nephrology comprise: (a) a Residency programme, initiated in the 1960s and carried out at present by 55 accredited hospitals throughout the country. The programme consists of 3-4-year training, with the first 2 years in internal medicine and the last 2 in nephrology, with a rotating system comprising clinical nephrology, dialysis, and transplantation. (b) An optional postgraduation programme, initiated in the 1970s and lasting 3-6 years. This programme confers MS and PhD degrees, particularly important for those who desire to pursue an academic career. Five such programmes are currently active in the Nephrology area, including one for non-medical professionals.

Several hospitals affiliated to public Universities are qualified by the Ministry of Health to develop clinical research, especially in the States of São Paulo and Rio de Janeiro. In the Nephrology area, most of these studies address epidemiological aspects of renal disease, although the percentage of drug trials and pathophysiological studies is rising. As most medical activities,

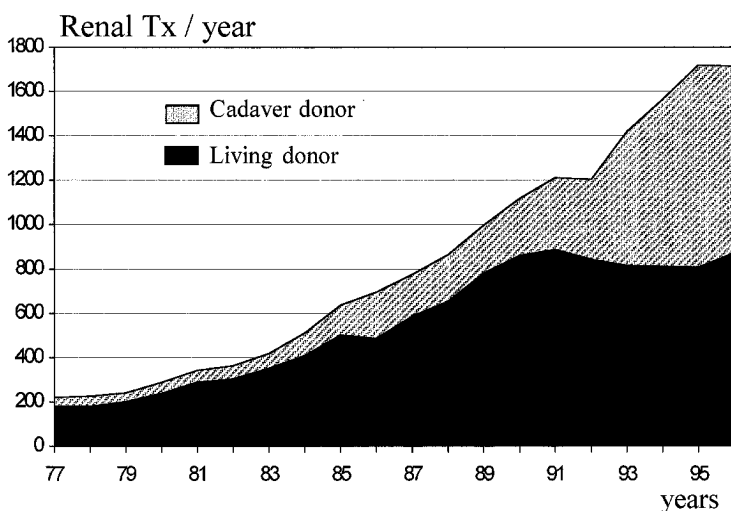


Fig. 4. Number of renal transplants performed in Brazil in the last 20 years.

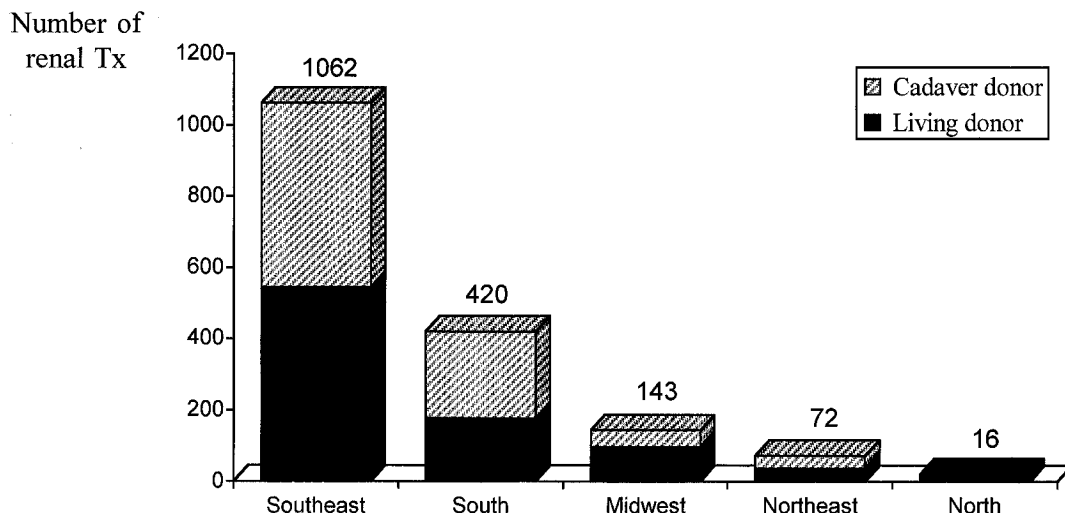


Fig. 5. Number of renal transplants performed in Brazil in 1996, by region.

basic research, initiated in the 1950s, concentrates in the South-east, although several new centres are now emerging in the South and North-eastern regions.

Unlike what happens in developed countries, research funding in Brazil is almost entirely dependent on Government money, from either public Universities (virtually no private university develops relevant research activities) or State and Federal funding agencies. Less than 10% of research money come from industry, while the contribution from private foundations and personal donations is virtually non-existent. Total research money corresponds to less than 1% of the GNP. Thirteen federal agencies operate in the country (<http://www.cnpq.br/guia8/indice.html>). Five of these are specially relevant to the Nephrology field: (1) CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico), which provides grants for both stipends (domestic and overseas) and direct research funding. It also carries an international cooperative programme. Its budget amounting to US\$ 800 million in 1996. (2) CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) supports the qualification of specialized research personnel such as researchers and technicians, through the concession of personal grants (domestic and overseas). CAPES also carries an international programme that funds both research and the exchange of students. Its budget reached US\$ 540 million in 1996. (3) FINEP-FNDCT (Financiadora de Estudos e Projetos), which in the last 25 years has supported research by funding both academic and non-academic institutions. Its 1996 budget amounted to US\$ 160 million. (4) PADCT (Programa de Apoio ao Desenvolvimento Científico e Tecnológico) supports large programmes of scientific and technological development. Between 1991 and 1995, the agency spent US\$ 600 million, provided by the Brazilian government and the BIRD. (5) CEME (Central de Medicamentos), specifically funds the development of drugs, having spent US\$ 13.5 million in 1996. Additionally, there are 13 State foundations

specifically created to support research. These Foundations receive a fixed percentage (between 1 and 2%) of the respective State budget. The largest of these agencies is the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), located in the state of São Paulo, whose 1996 budget reached US\$ 135 million.

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Note added in proof

Since submission of this paper a new decree by the Government further limited unrelated living donor transplantation by establishing that these procedures are allowed only if there are at least four HLA matches.