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Renal replacement therapy in children and adolescents

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The authors of a study now published in *Swiss Medical Weekly* [1] have made a large effort to combine data from different sources over a long period in order to study:

1. The *incidence* of end stage renal disease (ESRD). Here the upper age limit was 15.0 years to allow comparison with the European Paediatric Registry (ESPN)
2. The *primary diagnosis* (until age 20 years), using contemporary diagnostic terms
3. The *modalities of renal replacement therapy (RRT)*, including data from adult registries and, if needed, from individual and community registries
4. *The long-term results* of treatment, including beyond the age of 20 years

Cui bono? It is legitimate to ask whether such a study merits all this effort, as end-stage kidney disease in children concerns only a small minority of all patients requiring RRT. However, we have to look back to 1970, when the present study [1] began: at that time, RRT was considered to be a reasonable treatment modality for only a small minority of all patients, in fact only for those older than 15 and younger than 50 years [2]. Today, half of all dialysis patients in Switzerland are older than 70 years [3]. In 1970, we had no clear idea how many paediatric patients and with which diseases we would expect to see. Due to the relatively small population of Switzerland, it was essential to obtain data from the whole country, which has not been easy, but is one of the strengths of this study. The incidence calculated was 5.4 per million children per year; the increase observed over the years is due to the fact that during the first decade, children <5 years of age with ESRD were not always registered if they had no RRT.

Initially, no data were available about the *spectrum* of ESRD in children, although it was already evident that the aetiology was very different from that in adults. It is a strength of this study that diagnoses of ESRD were adapted to the present-day definitions, which are based on our much better understanding of the mechanisms leading to renal failure, thanks particularly to enormous progress in genetics and insights into the pathophysiology of renal failure. The present study on patients up to the age of 20 years shows that about one third of ESRD cases are due to each of *monogenetic* hereditary disease, *CAKUT* – a term coined in 1999 by the group of Ichikawa [4] for congenital anomalies of the kidney and urinary tract – and *acquired* disease. The situation is thus very different from the one in adult patients, where diabetic nephropathy, hypertensive nephropathy and polycystic kidney disease are now among the leading causes. An advantage is that in almost every paediatric renal patient, a firm diagnosis can be made – this is also in contrast to the situation in adult patients with renal failure.

Paediatric and adult nephrology can both learn a lot from each other. In particular, the spectrum of mono-genetic diseases, mainly a paediatric domain, has expanded tremendously. A prominent example is medullary cystic disease / nephronophthisis, which affected 11.2% of all patients up to the age of 20 years. The steroid-resistant nephrotic syndrome, which was due to monogenetic disorders in 7.1% (and to acquired disease in 9%), is also important. However, there is a large heterogeneity both in the phenotype (even within families) and in the genotype of many diseases. Currently, more than twenty and thirty genes respectively have been found for nephronophthisis and for the steroid-resistant nephrotic syndrome [5, 6]. Such diagnoses are now also increasingly observed in adult patients, either in ESRD occurring at adult age or in former paediatric patients who have reached adulthood.

Unlike the situation in adults, renal transplantation in paediatric patients is always the ultimate goal, as dialysis is considered a temporary measure. However, there is a serious lack of kidneys from deceased donors. Fortunately, since 2007 Swiss law has given some priority to children and adolescents waiting for a graft from a deceased donor. Still, inserting a graft from a living, related donor – in the majority of cases from one of the parents – is a valuable alternative. However, this is not possible in all cases. Live donor transplantation was introduced in Zurich only in 1986, by which time rejection could be better controlled, particularly by the introduction of ciclosporin. The optimal solution, although often not possible, is to start RRT directly with renal transplantation, thus circumventing dialysis (so called pre-emptive transplantation). This was achieved in 29% of all paediatric and adolescent patients during the years 2001–2015.

RRT in children is very demanding, not only regarding the somatic aspects, including nutrition and growth, but also the psychosocial side. Much can be achieved with school-

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ing and dialysis camps (which have been carried out yearly since 1981) and other social activities. The five-year *survival rates* have steadily increased, to 94% for patients and to 89% for *grafts,* in the fourth decade of the present study.

One as yet unsolved problem is recurrence of the primary disease in the transplanted kidney, particularly in nephrotic syndrome with focal segmental sclerosis without a genetic cause [7], in C3 glomerulopathy [8] and in atypical haemolytic uremic syndrome [9]. However, considerable progress in understanding the mechanisms behind and in the prevention of recurrent disease has been made recently [7, 9].

A serious problem (not dealt with in the paper) was poor growth, mainly due to the administration of high doses of prednisone to treat and prevent rejection. This was a major issue before the cyclosporine era. By preventing renal osteodystrophy, improving nutrition, use of human growth hormone and minimising steroid dosage, steady progress can be achieved, the goal being nearly normal growth. We are optimistic that progress will continue. Still, many of us were overly optimistic, expecting that immunosuppression could be replaced by lifelong tolerance by the year 2000. Indeed, a Swiss pilot study (interventional clinical trial) to induce immunological tolerance after renal transplantation in adults is ongoing (www.swisstolerance.ch). Therefore, 20 years later, we are one step closer to that dream.

Disclosure statement

No conflict of interest relevant to this article was reported.

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