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Review Article

# Integrated Renal Care from Proteinuria to Transplantation in the Department of Nephrology of Toho University

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**ABSTRACT:** Since the advent of hemodialysis, peritoneal dialysis and renal transplantation, these three renal replacement therapies have become common practice in the management of end-stage renal disease. Our department was established in 1980 and has brought together nephrologists, urologists and even pediatric nephrologists who are focused on the treatment of chronic kidney disease using these renal replacement therapies. This review outlines the history of renal replacement therapy and describes the future directions in this area based on the activity in our department, which ranges from management of proteinuria to transplantation for patients at any age.

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**KEYWORDS:** Willem Johan Kolff, chronic kidney disease, low protein diet, dialysis, transplantation

## The history of dialysis and the Department of Nephrology

Hemodialysis in the clinical setting was developed by Dr. Willem Johan Kolff in Cleveland Clinic, Cleveland, Ohio, in 1950 (Fig. 1). He was a pioneer in hemodialysis and invented the dialysis machine. His first dialysis machine contained a cellulosic membrane made from sausage skin obtained from a meat shop in Cleveland. His first wish was to treat a young woman in his native country of Holland who suffered from uremia. It was saddening for Dr. Kolff to inform the woman's mother about her daughter's impending death. That was the driving force for him to make a new dialysis machine in order to remove 20 g of urea nitrogen.

The outpatient dialysis clinic was started in Seattle by Dr. Belding H Scribner in 1962. Dr. Scribner, along with a

committee of citizens, selected patients who should be treated with dialysis. This is a famous story because death resulting from withholding dialysis was decided by ordinary citizens, and this committee decided whether a patient would live or die. "Life" magazine reported this story (Fig. 2). In fact, a lack of government support meant that the cost of dialysis in those days was very high, so only rich patients could survive. The Seattle dialysis patients survived longer compared with those in Cleveland because Dr. Kolff never selected his patients. The poor survival rate of Cleveland encouraged those physicians to consider transplant as the treatment of choice. Therefore, dialysis and transplantation progressed simultaneously in Cleveland with the same intention to save the patient's life.

The dialysis technique spread worldwide and it also reached Japan. With government support, it became





Fig. 2 Cover of "Life" on November 9, 1962. The magazine reported on the Seattle patient selection committee, which decided who lives and who dies.



Fig. 3 Prof. Kiyofumi Hirata, the first chairman of nephrology at Toho University Omori Hospital, dedicated his life's work to chronic kidney disease patients by developing a low protein diet. (Photo taken by colleague in Department of Nephrology)

which ABO incompatible renal transplantation in Japan was performed, where the patient received a kidney from a donor with a different blood type. Before the procedure, plasma apheresis and splenectomy were performed. This patient also had an IgA deficiency due to plasma cell class switch abnormalities that were probably caused by SLE.

She experienced frequent anal abscesses as a result of IgA deficiency. Interestingly, her IgA level returned to normal after successful renal transplantation. After 26 years, her graft function remains good (serum creatinin: SCr 0.9mg/dl) and lupus nephritis has not recurred, setting a world record for graft survival in ABO incompatible renal transplantation (Fig. 4). ABO incompatible kidney transplantation is now common worldwide—a procedure that originated from Japan,<sup>5)</sup> here in Toho University.

Recurrence of glomerulonephritis after transplantation is another interest for physicians in the field of nephrology.<sup>6-8)</sup> Including SLE, as described in the case above, IgA nephropathy, focal segmental glomerulosclerosis and hemolytic uremic syndrome frequently reoccur even after transplantation. The natural progression of these conditions and regression while under immunosuppressant treatment led us to develop a treatment strategy for native glomerulonephritis.

Donor health is also an important issue in living donor renal transplantation. Living donors are the primary source of kidneys in Japan, and further study is needed in this area in order to develop a strategy to protect their life and kidney.<sup>9)</sup>

### Nutritional therapy for non-dialysis CKD patients

As described above, renal nutritional therapy remains the main field of study in this department. Profs. Hirata and Mizuiri have spent a considerable amount of time do-



Fig. 4 The woman next to Prof. Aikawa had systemic lupus erythematosus (SLE) requiring hemodialysis and received a kidney transplant from her mother in 1989. She has the record of longest graft survival in ABO blood incompatible renal transplantation in Japan. (We have obtained a written permission from the patient of this photo taken by colleague in Department of Nephrology)

ing research in this area. Dr. Yasushi Ohashi, an associate professor, is a young investigator who is staying in the Cleveland Clinic for a period of time to study the body composition of CKD patients. As the CKD stage increases with time, their total body water content decreases, especially intracellular fluid. Such fluid imbalance (the shrinkage of the intracellular fluid compartment may be due to muscle wasting) might be related to malnutrition and poor patient outcome. Dr. Ohashi has reported this in many articles.<sup>10, 11)</sup> In cooperation with the Department of Nutrition, we will continue to work on a low protein diet to delay the progression of CKD patients and to maintain their nutritional status.

### Summary

Under the direction of Prof. Aikawa, the number of transplants has increased to 800 cases in our department. In Japan, the order of choice of renal replacement therapy has changed: first is hemodialysis, with transplantation in the second position, and third is peritoneal dialysis. Hemodialysis patients with cardiovascular disease are now the target of a national study. Drs. Hiroki Hase and Nobuhiko

Joki in the Department of Nephrology in Ohashi Medical Center have extensively reported their work in this field.<sup>12)</sup>

Renal issues ranging from proteinuria to transplantation as well as complications involving patients at any age are our concern, and we will carry on study, practice and education to tackle these challenges.

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**Ken Sakai, Professor      Curriculum vitae**

March	1986	Graduated from Toho University and National Examination for Medical Practitioners
June	1986	Resident, Toho University Omori Medical Center
June	1987	Resident, Kawasaki Municipal Ida Hospital
July	1989	Assistant, Department of Nephrology, School of Medicine, Faculty of Medicine, Toho University
July	1990	Physician, Kawasaki Municipal Ida Hospital
Dec.	1991	Board Certified Member of the Japanese Society of Internal Medicine
July	1992	Assistant, Department of Nephrology, School of Medicine, Faculty of Medicine, Toho University
Dec.	1993	Clinical Research fellow, Department of Nephrology and Hypertension, Cleveland Clinic (Cleveland, Ohio, USA)
Jan.	1996	Assistant, Department of Nephrology, School of Medicine, Faculty of Medicine, Toho University
June	1999	Board Certified Senior Member of the Japanese Society for Dialysis Therapy
Nov.	1999	Doctor of Philosophy (PhD), Toho University
April	2002	Board Certified Senior Member of the Japanese Society of Nephrology
April	2004	Lecturer, Department of Nephrology, School of Medicine, Faculty of Medicine, Toho University
May	2007	Director of Department of Internal Medicine and Dialysis Treatment Center, Saiseikai Yokohamashi Nanbu Hospital
Nov.	2008	Associate Professor, Department of Nephrology, School of Medicine, Faculty of Medicine, Toho University
Nov.	2011-present	Professor, Department of Nephrology, Toho University Omori Medical Center

**Major Research Interests**

Nephrology in Comprehensive medical care for chronic nephritis, peritoneal dialysis, hemodialysis and kidney transplant

**Professional and Society Memberships (including Community Activities)**

Board member of Society for Kidney Transplant Pathology  
 Councilor and board member of committee for promotion of renal transplantation of Japanese Society of Nephrology  
 Board member of the Japan Society for Transplantation  
 Councilor of the Japanese Society of Dialysis Therapy (Committee for medical specialist system, chairperson of curriculum committee; member of working group for Guideline for Renal Anemia in Chronic Kidney Disease)