Lasker Clinical Medical Research Award

The development of renal hemodialysis

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The artificial kidney and its effect on the development of other artificial organs

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The birth of the artificial kidney

I was the youngest unpaid assistant in internal medicine at the University of Groningen in The Netherlands in 1939. I was responsible for four patients, one of whom was a 22-year-old man who slowly and miserably died from chronic uremia. I determined that if I could have removed 20 g of urea per day from his blood, this man might have survived[1–3].

To solve the problem of how to effect such a treatment, I took a piece of artificial sausage skin (cellophane tubing) 40 cm in length and, instead of filling it like a sausage, put in 25 ml of blood to which I had added 400 mg/100 ml of urea. I shook this in a bath with saline and found, to my surprise, that within 5 minutes, almost all of the urea had been removed by dialysis. Multiplying the length by 20 gave me the length of the tubing I would need for an effective artificial kidney.

Then came the Second World War, and I went to the city of Kampen. I tried five different devices before finally settling on wrapping cellophane tubing around a large drum that rotated with its lower third immersed in an enamel tank filled with dialyzing fluid. Gravity transported the blood through the cellophane, and it moved in and out through the hollow axle of the drum. This was the first clinically effective artificial kidney, the Rotating-drum artificial kidney (Fig. 1).

In 1943, we treated our first patient with this artificial kidney in Kampen. She was a 28-year-old housemaid in chronic renal failure. We started dialysis very slowly with 50 ml at a time; when we dialyzed 12 and later 20 liters of blood, we obtained a definite decrease in blood urea content. Moreover, she became more alert, and even wanted to read a newspaper. After the twelfth dialysis, we could not find a port of access, and she died.

Of the first 15 patients treated in the next 2 years, only 1 survived. This patient was a 52-year-old man who became anuric. The artificial kidney reduced his blood urea from 222 to 104 mg/100 ml, and the next day, one ureter was unblocked by retrograde catheterization and he immediately underwent diuresis. I have never thought or said that the artificial kidney saved this man's life. Indeed, he might not have needed the artificial kidney had we done the cystoscopy first. However, on 11 September 1945, the seventeenth patient, 67-year-old Maria Schafstaat, was our first patient whose life was saved by dialysis. She had hepatorenal syndrome and was comatose. She was in prison with other Dutch Nazi collaborators. After she had undergone 8 hours of dialysis, I bent over her and asked, "Can you hear me?" She opened her eyes and said, "I am going to divorce my husband!"

I discussed my results with the highest authority on renal failure. I had chosen to use Darrow's interstitial fluid solution for the composition of my dialyzing fluid. "But Mr. Kolff," asked my colleague, "Why don't you leave out the potassium? Our body is full of potassium." I left out the potassium in the next dialysis, and in a few hours, the patient was paralyzed. The only thing he could move voluntarily was his thumb, although fortunately he continued to breathe. We did not realize at that time that potassium is not freely moveable through the cell membrane into the interstitial fluid.

A total of eight artificial kidneys were made, of which four were stored in different parts of the town to reduce the risk of total elimination by bombing. Soon after the war, I gave away three of the four kidneys I had. One went to the British Post-Graduate School in London at Hammersmith Hospital; one to Mount Sinai Hospital in New York; and one to the Royal Victoria Hospital in Montreal. The last one disappeared into Poland behind the Iron Curtain, and nothing has been heard of it since.

The Twin-coil artificial kidney and washing-machine dialysis

In 1955, I went to Philadelphia to see the coil-type artificial kidney made by Inoyou and Engelberg. It consisted of a coil of cellophane tubing wound together with window screening around

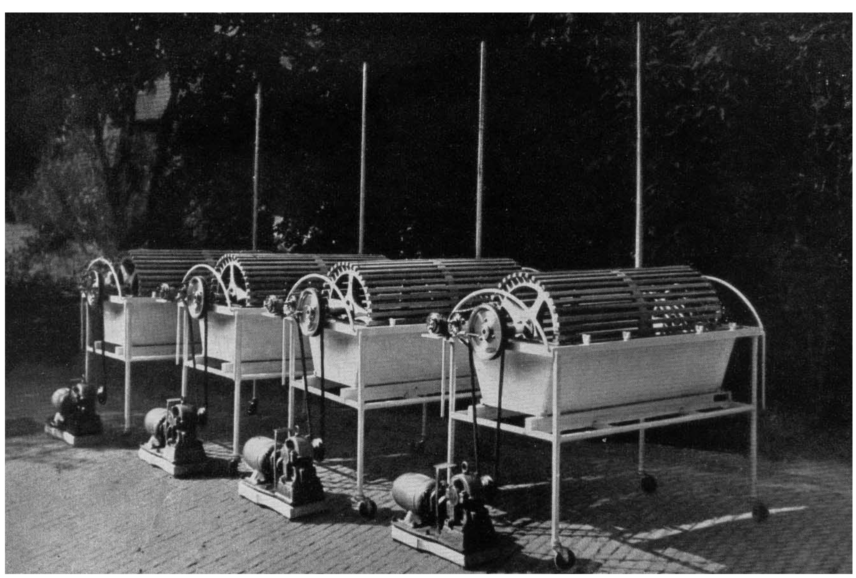

Fig. 1 Rotating-drum artificial kidneys. Four are shown ready to be shipped abroad. In 1946, one was sent to London; one to New York; one to Montreal; and the last one to Poland.

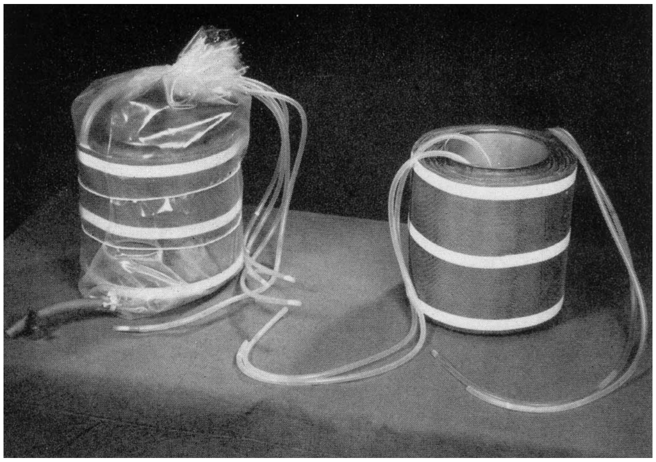

Fig. 2 Artificial organ development. Left, a disposable membrane oxygenator, made by replacing the cellophane tubing of the Twin-coil artificial kidney with polyethylene tubing. Oxygen can be blown into the bag surrounding the oxygenator. Right, a disposable Twin-coil artificial kidney with tubing wrapped around a fruit juice can.

a core, and was placed in a pressure cooker. I learned that they were no longer using it and had, in fact, abandoned it. I adapted this technique for the so-called Twin-coil artificial kidney (Fig. 2). I made it by winding cellophane tubing around a fruit juice can with window screening and the necessary spacers. Blood is pumped through the cellophane tubing and the dialyzing fluid is perfused cross-wise through the screening. The whole unit is placed in a gallon-sized can. I gave the twin-coil artificial kidney to Baxter laboratories, and they sold it worldwide.

In the 1960s at the Cleveland Clinic Foundation, we developed the 'Washing-machine artificial kidney'. It consisted of four units of coil 'kidneys' (different from the twin-coil dialyzer) connected in parallel and put in an ordinary household washing machine. We compared the dialysis of washing machines with the dialysis of custom-built percolators and found that the washing machine was hard to beat. Washing machines were successfully used for home dialysis.

'Dialysis in Wonderland'

In 1970, we came up with a device to rehabilitate patients dependent for life on hemodialysis: the Wearable artificial kidney. The wearable unit consists of a combined blood and dialysate pump (1.2 kg), rechargeable batteries, tubing, dialyzer and a charcoal regeneration module with a total weight of 3.5 kg (ref. 4). Wearable artificial kidney dialysis has undergone extensive clinical trials with results comparable to those of standard hemodialysis[5].

Using the Wearable artificial kidney, we could send patients on what we called 'Dialysis in Wonderland' trips. In 1 year, we made 28 such trips. Patients would raft down the Colorado River and dialyze themselves on shore, or they would drift down the Salmon River in Idaho and live on a houseboat on Lake Powell or go to the Bahamas or Hawaii, dialyzing in the mornings and perhaps water-skiing in the afternoons. These 'Dialysis in Wonderland' trips were excellent programs to rehabilitate renal patients and show them that despite their kidney problems, they could still enjoy life.

Ease of operation and portability were the main assets of our Wearable artificial kidney compared with other artificial kidneys. Our wearable artificial kidney used charcoal to adsorb some of the retention products. This was very effective for most retention products, but urea must be removed in such large amounts that large amounts of charcoal were also required. One artificial kidney used zirconium to adsorb urea. All of these should be considered as daily dialysis becomes a real possibility. Attempts to re-institute daily dialysis and continuous dialysis, perhaps using the Wearable artificial kidney, should be encouraged.

The 'death committee'

At one point, there were 'death committees' to decide who should receive the dialysis treatment and who should be left to die. I strongly argued against this deplorable system. By the mid-1960s, fewer than 800 Americans were sustained by hemodialysis, although there were more than 10,000 qualified patients. This problem worsened by the early 1970s, when the number of qualified but untreated patients exceeded 20,000 (refs. 6–8). How can one decide whether a patient is sufficiently stable to benefit from treatment? The more I have seen, the less I feel that one can predict how a particular patient will react to the stresses and strains of dialysis.

Cadaver kidney transplantation and dialysis

Transplantation of kidneys can be extended by the use of cadaver kidneys even if the human donor has been dead for some time, provided that the recipient is adequately dialyzed[9,10]. The acute tubular necrosis in such kidneys is often reversible, although it may take a long time to effect this. In 1962, the use of cadaver kidneys was almost abandoned. Nakamoto and I have revised it to include vigorous dialysis of the recipient. When we compared the results of unrelated cadaver kidney transplantation with the results of the transplantation of kidneys of prisoners done by Startsel in Denver, we found that we had less rejection with the former.

Dialysis today

At present, more than one million people all over the world are being treated with dialysis. Of course, hollow-fiber dialyzers or capillary dialyzers have replaced other types of artificial kidneys. There are also more permeable membranes than cellophane or regenerated cellulose. Although regenerated cellulose capillaries are less expensive than others, some people are oversensitive to it. At one time, great efforts were made to mimic the natural kidney by providing ultrafiltration first and reabsorption of the excess water next. I hope that in the near future, with more-permeable membranes, this will no longer be required.

Dialysis three times a week is a poor substitute for continuous dialysis in replicating the uninterrupted removal of waste products that our natural kidneys provide. Continuous dialysis all the time would be preferable and might be possible if wearable artificial kidneys were provided. As this is not possible, at present we should aim for daily dialysis; the most practical way seems to be to do it at the end of the day. Home dialysis affords better opportunities for daily dialysis, but unfortunately seems to be more expensive for patients than dialysis in centers. At one time, the government provided paid, trained helpers for home dialysis; this should be reinstituted.

Effect on the development of other artificial organs

Directly or indirectly, the artificial kidney has had a profound influence on the development of other life-saving devices.

Fig. 3 Willem J. Kolff demonstrating the Wearable artificial lung. The whole unit is assembled on a vest. It has two components: a mi-LVAD and an oxygenator. The mi-LVAD consists of a concentric double-lumen cannula (held apart for better demonstration). A short wide cannula in the left ventricle has holes through which blood is sucked out and sent through a four-channel oxygenator (white area, right side of vest). Oxygenated blood is delivered into the aorta through the long cannula, the tip of which sits in the aorta. The mi-LVAD can be inserted transapically.

During dialysis in 1943 in Kampen, we noticed that the blue blood in the rotating-drum artificial kidney became red; this gave birth to the 'membrane oxygenator'. In 1949, a rotating convoluted-tube oxygenator was developed and used on a cow in a slaughterhouse. This inspired the development of the heart–lung machine. Later, we made the first successful disposable membrane oxygenator by replacing the cellophane tubing of the twin-coil kidneys with polyethylene tubing (Fig. 2). By 1955 at the Cleveland Clinic Foundation, we began using this successfully on patients, thereby opening a new era in open-heart surgery. Today, membrane oxygenators are used in more than 50% of open-heart surgeries worldwide.

After the development of the artificial kidney, I was fortunate enough to pioneer various other artificial organs, from the artificial heart to the artificial arm. Recently, my associate Sony Jacob and I embarked on the development of a Wearable artificial lung (Fig. 3). We developed a minimally invasive left-ventricular-assist device (mi-LVAD) and a four-channel membrane oxygenator for this purpose. The mi-LVAD is inserted transapically and the oxygenator is mounted on a vest outside the body[11] (Kolff, W.J. & Jacob, S. Minimally invasive left ventricular assist device (mi-LVAD) [abstract]. *ASAIO J.* **48**, 166 (2002).) Some of the facts learned from past experiences, but largely forgotten, have become the cornerstone of the development of the wearable artificial lung (Kolff, W.J. & Jacob, S. Forgotten facts of 1983 and 1973 lead to wearable artificial lung [abstract]. *ASAIO J.* **48**, 167 (2002).) The success of the wearable artificial kidney was very encouraging, and I have great optimism about the future of the Wearable artificial lung.

Artificial organs should permit patients to lead full and rich lives. The future of artificial organs is limited only by one's imagination, and I believe that a new horizon is waiting to be explored.

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