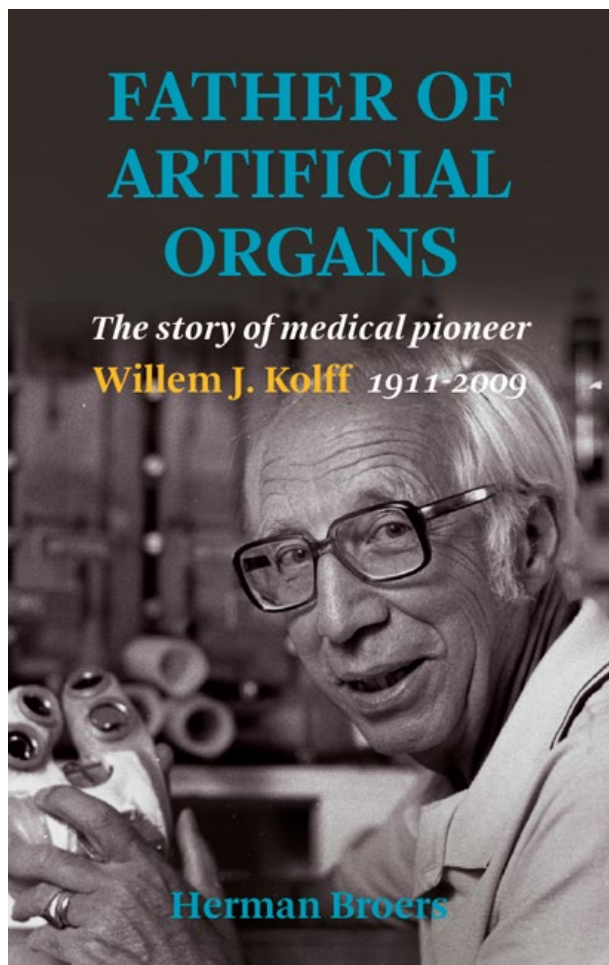




# Father of Artificial Organs - The story of medical pioneer Willem J. Kolff (1911-2009)



## 1 | THE BOOK IN A NUTSHELL

This biography of serial inventor and medical doctor Willem J. (“Pim”) Kolff is written by scientific/historical journalist Herman Broers. The book provides an objective and multi-perspective account of the life and work of Dr Kolff, who put an undisputed mark on the history of organ-replacement devices by secretly inventing the first clinically functioning hemodialysis machine (in a Nazi-occupied Holland) and later in the United States leading the team that realized the first

implantable fully artificial heart. Besides offering a solid historical account, the book also describes the present revival of innovation in the artificial kidney field and contains valuable lessons for a broad variety of readers. Suitable for an audience ranging from medical professionals interested in technology and technologists interested in medicine, to patients and their families, as well as policy makers and research funding parties.

The review of this scientific/historic book was composed using the recommendations of Gupta for book reviews of scientific and technical books.<sup>1</sup> Additionally, the reviewer team, composed of a biomedical engineer, a dialysis patient, and a nephrologist, tried to distill some lessons that may be learned from the book.

## 2 | TEXT SAMPLE ABOUT “HEMODIALYSIS PATIENT 2”

On March 16, 1943, one of the sparsely available ambulances transports the twenty-nine year old domestic servant Janny Schrijver from Zwolle to Kampen. She is accompanied by her father, an elderly farmer. She had seen an ophthalmologist for the first time in Zwolle in December because her eyesight was deteriorating. The ophthalmologist referred her to internist Dhont in Zwolle and he determined that she was suffering from chronic nephritis (kidney inflammation) with uremia. However, her condition had taken a turn for the worse in the past few weeks. Janny Schrijver, a humble woman, did not know for sure what was wrong with her. She had simply kept on working until she literally dropped. At the time, Dhont is of the opinion that her kidney condition is far too advanced to have any hope of successful treatment and he sends her to Kolff and his artificial kidney as a last resource: it doesn't hurt to try.

Kolff sees her for the first time in the City Hospital, sitting upright in bed with a pillow against her back. She looks terrible, she is gasping for breath and complains that her heart rate is much too high and that she feels severe pressure on her chest. She is confused and the changes in her eye pupils suggest that she will soon go blind. Her blood pressure increases to 245/150 and Mieneke van der Leij determines that the urea content in her

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blood is 1.69 grams per liter, whereas a normal concentration is 0.15 to 0.45 grams. Kolff decides to put his artificial kidney to use for a second time. He hopes to acquire more experience by rinsing Janny's blood, to postpone her death or, *at best*, to achieve a temporary improvement. He takes Janny's father aside: 'Mr Schrijver, Janny's blood is contaminated. We want to remove some of her blood from her body, remove the contaminant with a machine and then put the blood back into her body. You may be present so you can be sure that nothing happens to Janny.'

The farmer looks at Kolff with a penetrating stare, but with fear in his eyes. He trusts Kolff because he is the first doctor who makes an effort to explain to him in normal terms just what is wrong with his daughter.

*'Are you sure that you can help Janny, doctor?'*

*'No. I can only do the very best I can.'*

*'We must call the vicar first,' Schrijver says.*

*'You can do whatever you need to do after that.'*

Vicar MD Gijsman from Kampen appears at Janny's bed at the end of the afternoon on March 17, 1943. As Janny slowly sinks into a state of unconsciousness, her family prays with Gijsman alongside her bed. When the vicar nods that the time has come, porter Andries Sijbrands wheels the patient to Kolff's room where the machine is ready and waiting. She is lying on a narrow bed, specially made for the dialysis procedure, because the regular hospital beds are too wide to pass through the narrow door of Kolff's consultation room. She is not aware of the activities around her, as she has meanwhile gone into a coma.

Kolff starts with an injection of heparin. When no exceptional reactions occur, besides shivering, he removes one hundred milliliters of blood from an artery in Janny's arm and lets the blood flow through the cellophane skin around the drum of the artificial kidney. The motor begins to hum as it rotates and the drum cleaves through the water in the rinsing tub with a soft gurgle. Twenty-two minutes later, the rinsed blood is returned to Janny Schrijver's arm via a vein.

The hours pass as Kolff repeats the procedure ten times until one liter of blood has been rinsed. The kidney team keeps a very close eye on the process: the blood pressure is monitored and the concentration of urea and other substances are checked regularly. The concentration of urea shows a slight decrease, but the improvement is again not worth mentioning.

The time-consuming experiment is repeated several times during the nights to come: the amount of rinsed blood per dialysis is increased step-by-step in the course of four treatments from 1.5 to 5.5 liters blood. While the first dialysis lasted twenty-two minutes, the last one takes more than six hours. Although the concentration of urea does not continue to increase, there are no visible improvements to Janny's condition. A problem then presents itself: the patient becomes

'overly punctured'. The number of new and usable arteries in her body through which blood can be tapped off and then led back is running out. Just when Kolff is toying with the idea of quitting for that reason, Janny's seriously too high blood pressure starts to go down. Very slowly, but surely.

It is evident from the tests that the team is continuously conducting that Janny Schrijvers's other organs are also being increasingly affected by her prolonged kidney disease. The uremia has been stable for the last fourteen days and the anticipated death of the patient has still not occurred. Kolff knows he is running out of time and so he takes the following next step: he stops removing blood from her body in fractions and connects Janny Schrijver directly to the artificial kidney. It is the 4<sup>th</sup> of April 1943 and the entire team is watching as the artificial kidney is uninterruptedly part of Janny Schrijver's bloodstream for the very first time. No extra complications are observed while the members of the kidney team take turns keeping watch at her bed. Then, what Kolff and his team have been hoping for finally happens: the urea concentration begins to drop. Kolff decides to keep on going and Janny is subjected to prolonged, uninterrupted dialysis four times in the next few days. A total of twenty liters of blood flow through the artificial kidney during the final treatment and the urea content in Janny's blood drops below 1 gram. This is when she wakes up from her coma.

Janny Schrijver is fully conscious and able to speak. She talks about her family at home and appears to be recovering. Two days later, however, the urea concentration begins to rise again and her condition deteriorates quickly. She is hastily connected to the artificial kidney, twenty liters of blood is rinsed for a second time and she again wakes up, only to collapse two days later again. Kolff brings his patient out of her coma a total of four times and her health subsequently worsens an equal number of times. On April 27, 1943, during the twelfth dialysis procedure, the nightmare scenario occurs: the artery through which the blood flows to the artificial kidney becomes so damaged during the preparation phase that the dialysis must be discontinued. Andries Sijbrands wheels her back to the ward for the last time as the kidney team looks on in silence. A despairing Mienke van der Leij determines that the urea concentration is quickly rising to 6.4 grams per liter. On May 4, 1943, Janny Schrijver, preceded by Jan Bruning and Gustav Boele, is the third patient whom Kolff sees die in his care.

But she is the first to have lived more than four weeks longer thanks to his artificial kidney.

When he arrives at the hospital to collect his daughter's body, Janny's father looks Kolff up. 'Doctor, you did everything that you could to try to save my daughter, I want to thank you for that. I want to know how much I owe you.'

Kolff initially refuses to accept any money, but Schrijver insists. The father insists so much that Kolff eventually gives in and charges him sixty guilders.

Schrijver pulls out his wallet, pays Kolff, shakes his hand again and leaves the hospital for Zwolle to bury his daughter.



### 3 | SOME REMARKS FROM THE REVIEWERS ON THE TEXT SAMPLE

The story of this treatment of patient 2—still 2 years before the big breakthrough with patient 17 as the first acute uremic coma survivor in 1945—contains several important elements:

- It shows the crucial need for a better and repeatably usable vascular access (which was first solved in 1960 by doctor Scribner and technologist Wayne Quinton from Seattle, who jointly invented the arterio-venous shunt).
- It shows that a dedicated multidisciplinary team (doctor, nurse, laboratory, and technical support) can work miracles: Coming out of a uremic coma to regain clear consciousness (even for a limited time) was *a true miracle* in 1943!
- The repeated recovery episodes from coma clearly showed that Kolff was on the right track. Something that was vigorously pointed out by the patient's father, Mr Schrijver, who *therefore* insisted so much upon paying, because he thought it is crucial that the research would continue. And for that, being a farmer, he knew it needed funding! There's no harvest without the investment of seeding ...
- It also shows that perseverance is needed for success. It took 2 more years of further improvements by the team until the first patient anywhere in the world survived uremic coma from acute kidney failure thanks to Kolff's dialysis team: Patient 17, Mrs Sofia Schafstadt recovered on September 18, 1945. Would a modern ethical committee approve continuation of medical research during which 16 patients successively died?
- And this success (just after the liberation of Holland) by itself also teaches us another important lesson: Sofia Schafstadt was a Nazi-sympathizer, and very much hated by the majority of the Dutch population who had suffered so hard during the Nazi-occupation. Yet, Kolff stayed true to his Hippocratic oath and treated her to the best of his abilities. His medical care was apolitical. Even presidents from super powers might apply this example from Kolff to the advantage of their country, for example, by continuation of a government program to fight a disease, even if that program is connected to the name of a predecessor from an opposite political signature.<sup>2</sup> Diseases do not care about borders or political opinions; they target us all! Hence, jointly fighting diseases can help to unite mankind.

### 4 | OVERALL BOOK DESCRIPTION

Within the field of pioneers in Medical Technology there are quite some biographies but within the sub-domain of artificial organs the assortment is thinner, although the ASAIO History Committee has an excellent program to collect and

preserve such material.<sup>3</sup> In the context of the rising effort put into topics like organs-on-chip and regenerative medicine, it may be useful to learn from early pioneers like Kolff, similar as the professional education of nurses still applies lessons from Florence Nightingale.

The first version (Dutch language) of this book appeared in 2003, followed by updates in 2007 (English), 2011 (Dutch), and 2018 (Dutch) which were sponsored by the Dutch Kidney Foundation. The latest—here reviewed—English version is fully revised and extended with new material from released archives, as well as with progress on the field of kidney replacement therapies, after Kolff died in 2009. Translation into English was sponsored by imec, a not-for-profit international research hub for nano- and digital technologies.

The author Herman Broers is a professional scientific/historic journalist. He maintains close contact with the Kolff family until the present date and has been a key person in preserving the legacy of Dr Kolff, via the Kolff Foundation. The book is characterized by thorough research of original sources in archives around the world and numerous interviews with Kolff and people that worked with him. The author collected various perspectives on matters where controversies existed. The reader is provided with critically evaluated and well-digested material with appropriate references for further reading.

The book is easily accessible, and the readership that may enjoy (and likely profit from) the book, ranges from medical professionals interested in technology and technologists interested in medicine, to patients and their families, as well as R&D managers, policy makers, and research funding organizations.

The main rationale behind the book—preserving the memory of this true pioneer—is achieved well. Interestingly, the book *also* seems to achieve a transfer of the huge energy and drive of Dr Kolff. He was known for his motivational effect when interacting with people, but peculiarly enough the book also seems to further spread this *spark* and additionally describes how this *spark moved on* from Kolff's death in 2009 up to 2020. That alone makes it a must-read for anyone interested in artificial organs, from veteran to newcomer. An interesting mark of the book's success is also that within 6 months the first 2020 edition was nearly sold out and a second printing round was ordered by the Willem Kolff Institute in Groningen. Also remarkable is that the book has been presented to policy makers taking an interest in Kidney Health within both the European Parliament as within the American Congress.

Kolff himself formed a living transatlantic bridge, and his biography now does the same: We highly recommend a great video speech of EU-Parliament member Hilde Vautmans on this.<sup>4</sup>

Although the title is appropriate, it does not reveal an additional important aspect that we might call the *secret weapon* of Kolff, namely the contributions of his wife Janke



Kolff-Huidekoper. Not only was she a highly intelligent woman that sacrificed her own career perspective and for decades supported her husband by running the family life. She also was his earliest and most consistent sponsor until a point where she could not bear it anymore and divorced at an age of 88 years, while both had closely stuck together through a terrible war and a demanding emigration.

The major lessons that can be learned from this book are creepily consistent with a great review article about the science of science (abbreviated as “SciSci”) by Fortunato *et al* from which review we cite a few passages here<sup>5</sup>:

- *The value proposition of SciSci hinges on the hypothesis that with a deeper understanding of the factors behind successful science, we can enhance the prospects of science as a whole to more effectively address societal problems.* The reviewed book provides valuable (mostly timeless) insights in do's and don'ts for researchers in the field of artificial organs.
- *The successful combination of previously disconnected ideas and resources that is fundamental to interdisciplinary research often violates expectations and leads to novel ideas with high impact.* Kolff excelled in combining ideas, materials, methods, and talented people from various disciplines to create amazing progress. His first dialysis machine for example, was built from a bath-tub, cellophane sausage skin, a sewing machine motor, a rotating water seal from a model-T Ford engine, and aluminium scavenged from a crashed plane. Kolff recruited help from people in unconventional ways: Because of his interest and drive to help with the artificial kidney, the Kampen hospital porter Andries Sijbrands received full training to assist the doctor during autopsies
- *Nevertheless, evidence from grant applications shows that, when faced with new ideas, expert evaluators systematically give lower scores to truly novel or interdisciplinary research proposals.* If his wife Janke would not have sponsored the artificial kidney project, it never would have succeeded. The elite of the Dutch post-war medical profession regarded Kolff's machine as a useless toy, until it came back after maturation within the USA.
- *Scientists who left their country of origin outperformed scientists who did not relocate, according to their citation scores.* Although Kolff had to start from scratch again at the bottom, his emigration to the USA (in 1950 not a very easy project) put him into the ecosystem that he needed. Also here, the financial reserves<sup>2</sup> of his wife Janke were essential, and without that this move might likely have failed.
- *It is not the institution that creates the impact; it is the individual researchers that make an institution.* The Kolff biography clearly highlights this indeed.
- *Given that scientists fail more often than they succeed, knowing when, why, and how an idea fails is essential in our attempts to understand and improve science. Such studies*

*could provide meaningful guidance regarding the reproducibility crisis and help us account for the file drawer problem. They could also substantially further our understanding of human imagination by revealing the total pipeline of creative activity.* This is one of the core factors of Kolff's success: With his team he meticulously recorded all experimental results, performed autopsies on deceased patients and figured out solutions. By creating an environment where lessons could be learned and solutions could be polished long enough, clinically useful results were achieved.


- *It would benefit science if curiosity, creativity, and intellectual exchange — particularly regarding the societal implications and applications of science and technology — are better appreciated and incentivized.* This recommendation very well complements with what—quoting the book—Utah University president Chase Peterson said when addressing the press about the first successful human artificial heart implant in 1982: *Every university needs a Kolff to add with a wink: But not more than one ...*

The book approaches the subject in a serious journalistic and historical manner, but with a touch of humor here and there, which makes for pleasant reading. The selection, treatment, and arrangement of topics is well chosen. Reliability of facts is excellent and completed by a very well organized and thorough bibliography. The soft-covered book is nicely illustrated with interesting photographs and has a pleasant writing style. Printing quality is fine, with a generous font size across 336 pages.

For further reading (besides the book itself), we recommend an open access article by Ren *et al* that puts the work of Kolff within a broader context of fellow pioneers in the history of medical technology.<sup>6</sup>

## AUTHOR CONTRIBUTIONS

Fokko P. Wieringa (corresponding author) drafted the first concept of the manuscript, Henning Søndergaard and Stephen Ash both performed a critical revision of the manuscript.

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