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History of the Science of Dialysis

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Key Words
Dialysis
History
Artificial kidney

Abstract
Thomas Graham (1805–1869), who is credited with seminal work on the nature of the diffusion of gases and of osmotic forces in fluids, can properly be called the father of modern dialysis. His apparatus to study the behavior of biological fluids through a semipermeable membrane clearly presaged the artificial kidney in clinical use today. In 1913, John Abel and coworkers reported the first application of the principles of diffusion to remove substances from the blood of living animals. Unaware of Abel's work, Georg Haas (1886–1971) performed the first human dialysis in the German town of Giessen in 1924. But it was not until 1945 that Willem Johan Kolff, working under extremely difficult wartime conditions in The Netherlands, achieved the first clinically successful hemodialysis in a human patient.

Thomas Graham, a Scotsman who lived from 1805 to 1869, can properly be considered the father of modern dialysis (fig. 1). Although a physical chemist, he performed seminal work in several areas of great importance to modern physiology: the discovery of the laws governing the diffusion of gases which we now call Graham's law, investigations of osmotic force, and the fractionation of biologic or chemical fluids by dialysis. Educated in Scotland, Graham studied chemistry much against his father's wishes. First a young professor at Anderson University in Glasgow, he was later appointed professor at University College, London, and in 1855 was made Master of the Mint, a position he held until his death in 1869.

During the years 1846 to 1861, he published a remarkable series of papers in the *Philosphical Transactions of the Royal Society*. In the first two, entitled 'The Motion of Gases' (fig. 2), he described the methods for separating gasses by diffusion, which were employed nearly a century later in the separation of uranium-235 from its heavier 238 isotope [1, 2].

In his 1854 Bakerian lecture entitled 'On Osmotic Force' Graham said, 'The expression of osmotic force has reference to the endosmose and exosmose of Dutrochet' [3]. The French-

Fig. 1. Thomas Graham, 1805–1869. [From ref. 15].

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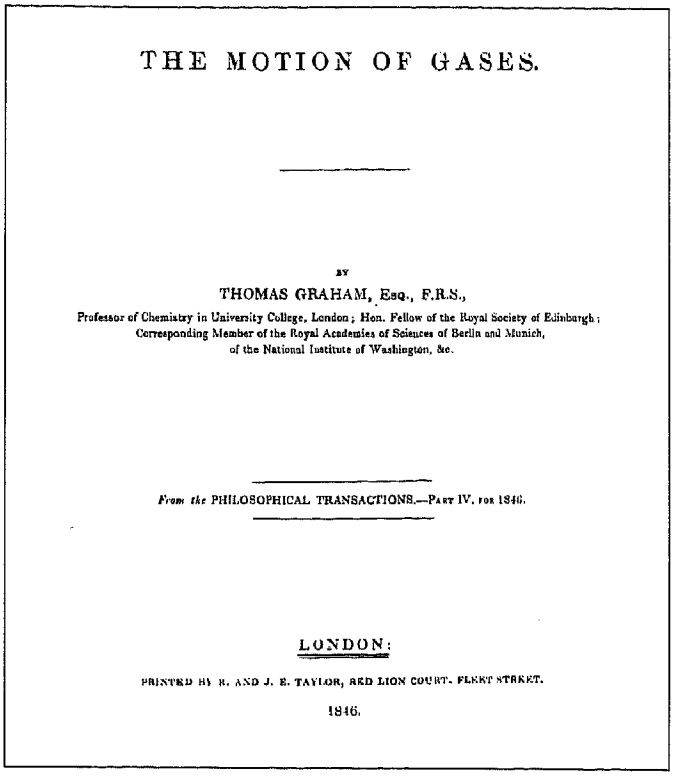

THE MOTION OF GASES.

BY

THOMAS GRAHAM, Esq., F.R.S.,

Professor of Chemistry in University College, London; Hon. Fellow of the Royal Society of Edinburgh; Corresponding Member of the Royal Academies of Sciences of Berlin and Munich, of the National Institute of Washington, &c.

From the PHILOSOPHICAL TRANSACTIONS.—PART IV. FOR 1846.

LONDON:

PRINTED BY R. AND J. E. TAYLOR, RED LION COURT, FLEET STREET.

1846.

Fig. 2. Frontispiece to 'The Motion of Gases' by Thomas Graham, 1846 [1].

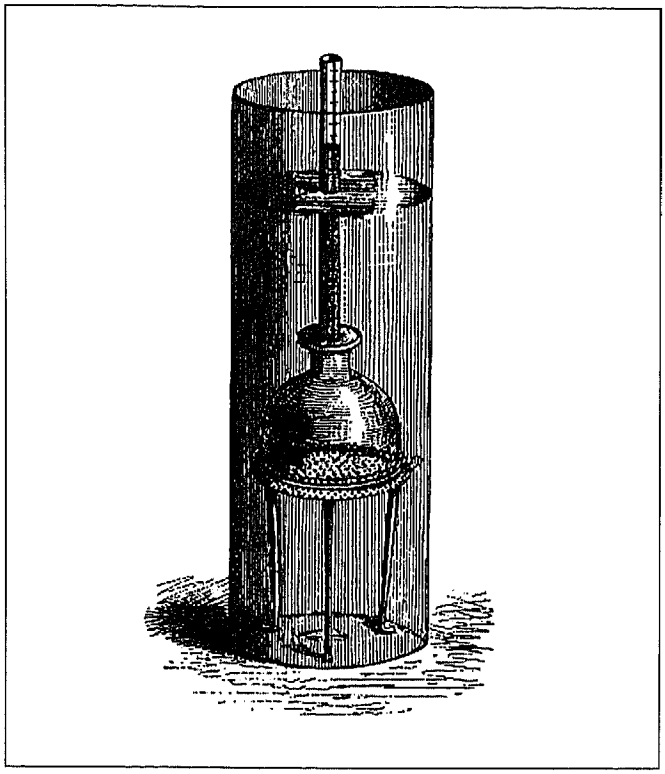

Fig. 3. Graham's apparatus for measuring osmotic pressure [3].

man, René Joachim Henri Dutrochet lived from 1776 to 1847. His classic work about endosmosis and exosmosis described the process by which water passes through a semipermeable membrane from one side to another. Graham, in his Bakerian lecture, explicitly distinguished between diffusion when two solutions are carefully layered upon one another and what occurs when the two solutions are separated by a semipermeable membrane. His apparatus (fig. 3) was a small bell jar, the mouth of which was covered by an animal membrane supported by a perforated metal plate, filled with the solution to be studied and topped with a glass capillary tube. Thus assembled, it was immersed in a glass cylinder filled with water. He measured the osmotic pressure generated by a variety of solutes and solutions and rejected Dutrochet's hypothesis that the osmotic pressure was due to the capillarity of the tube in which it was measured. Graham shared his speculations on the occurrence of osmotic movement in physiologic processes. He stated, 'Chemical osmose appears to be an agency particularly well adapted to take part in the animal economy. It is seen that osmose is peculiarly excited by dilute saline solution such as animal juices really are.' His definition of osmosis as 'the conversion of chemical affinity into mechanical power' still remains scientifically valid and powerful.

Fig. 4. Statue of Thomas Graham in George Square, Glasgow, Scotland.

In Graham's 1861 paper to the Royal Society, 'Liquid Diffusion Applied to Analysis', he provided the original distinction between colloids and crystalloids [4]. He explained that a variety of inorganic salts, sugars, and alcohols have high diffusibility and belong to the more volatile class, which he named crystalloids. In contrast, a comparatively fixed class of chemi-

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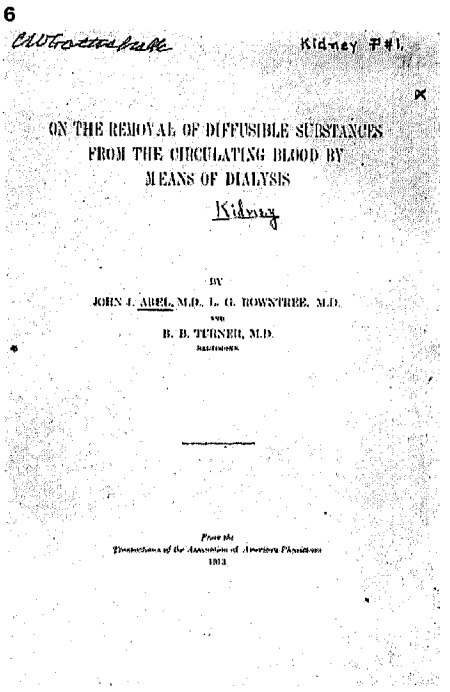


ON THE REMOVAL OF DIFFUSIBLE SUBSTANCES FROM THE CIRCULATING BLOOD BY MEANS OF DIALYSIS

Kidney

BY

JOHN J. ABEL, M.D., L. G. ROWNTREE, M.D.

AND

B. B. TURNER, M.D.

Fig. 5. John Jacob Abel, 1857–1938. [From ref. 15].

Fig. 6. Abel, Rowntree, and Turner's initial report on experiments with their vivi-diffuser [5].

cal substances such as starch, gum, albumin, gelatin, and animal extractive matters are unable or very slow to crystallize or diffuse. He wrote:

> The plastic elements of the animal body are found in this class. As gelatine appears to be its type, it is proposed to designate substances of this class as *colloids*, and to speak of their peculiar form of aggregation as the *colloidal condition of matter*. Opposed to the colloidal is the crystalline condition. Substances affecting the latter form will be classified as *crystalloids*. The distinction is no doubt one of intimate molecular constitution.

Graham introduced the concept of the semipermeable membrane by pointing out that the fluidity of gelatinous colloids permits them to become a medium for liquid diffusion. He described several simple experiments in which two different solutions were separated by very thin sheets of letter paper impregnated with starch. The paper was indented to form a cavity which could be filled with an aqueous solution of sugar and gum arabic and then laid upon the surface of a basin of pure water. Twenty-four hours later the water below contained sugar but no gum arabic. Graham wrote:

> I may state at once what I believe to be the mode in which this takes place. The sized paper has no power to act as a filter. It is mechanically impermeable, and denies a passage to a mixed fluid as a whole. Molecules only permeate the system and not masses. The molecules are moved by the force of diffusion ... It may perhaps be allowed to me to apply the convenient term *dialysis* to the method of separation by the method of diffusion through a system of gelatinous matter.

Graham did not coin the word dialysis but gave it a new and its still current meaning. Previously, dialysis meant a dissolution of the strength or weakness of the limbs, coming from the Greek, to part asunder. It is not surprising that the work of this paper earned him the title 'Father of Modern Dialysis' and that he was honored with the erection of his statue in Glasgow (fig. 4).

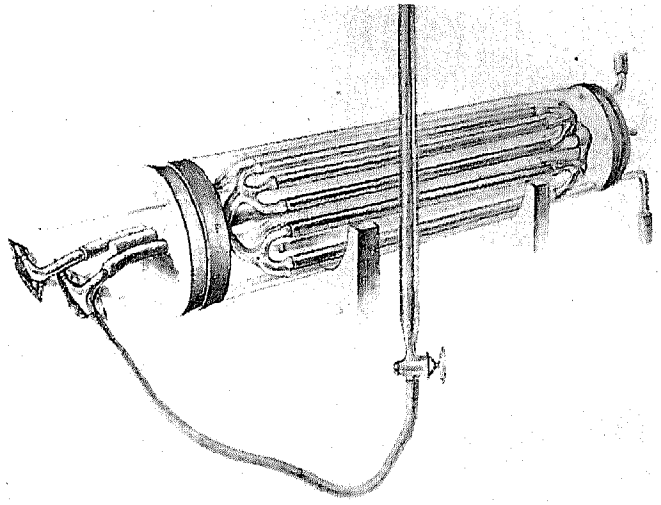
Although Graham was a pure chemist, he speculated on the possible physiologic roles of colloids in animals:

> It may be questioned whether a colloid when tasted, ever reaches the sentient extremities of the nerves of the palate, as the latter are probably protected by a colloidal membrane, impermeable to soluble substances of the same physical constitution.

He also speculated that the mucous coating of the stomach may protect the mucosa from secreted hydrochloric acid.

The first scientists to actually apply the principle of diffusion to the removal of substances from the blood of living animals were John J. Abel (fig. 5), Leonard Rowntree, and B.B. Turner. Their papers published some 52 years after Graham's make no reference to him. Abel described their preliminary results at the annual meeting of the Association of American Physicians in Washington DC in 1913 (fig. 6):

> There are numerous toxic states in which the eliminating organs of the body, more especially the kidneys, are incapable of removing from the body, at an adequate rate, the natural or unnatural substances whose accumulation is detrimental to life. In the hope of providing a substitute in such emergencies, which might tide over a dangerous crisis, as well as for the important



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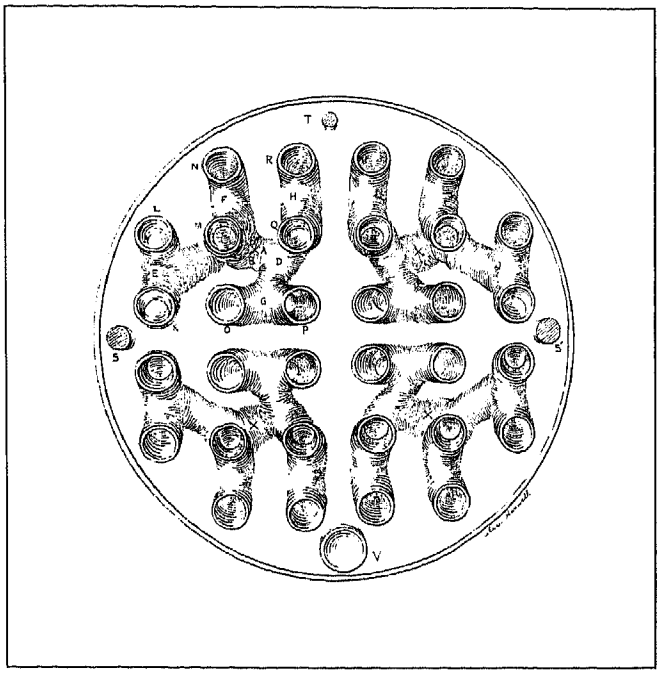

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Fig. 7. Vivi-diffusion apparatus of Abel, Rowntree, and Turner with 16 celloidin tubes [6].

Fig. 8. Cross-section of Abel, Rowntree, and Turner's vivi-diffusion apparatus with 32 celloidin tubes [6].

information which it might be expected to provide concerning the substances normally present in blood, ... a method has been devised by which the blood of a living animal may be submitted to dialysis outside the body, and again returned to the natural circulation without exposure to air, infection by microorganisms, or any alterations which would necessarily be prejudicial to life. The process may be appropriately referred to as *vivi-diffusion* [5].

Abel and colleagues did not use their vivi-diffusion apparatus on humans, but they were clearly thinking of its potential application in cases of poisoning or other causes of acute renal failure. Further, they understood that the dialysate could be used to study materials collected from the blood of living animals.

In two papers published in 1914 Abel, Rowntree, and Turner gave a much more detailed account of their apparatus which they called an *artificial kidney* [6, 7]. This was, to our knowledge, the first use of the term artificial kidney and the results obtained with it. They wrote:

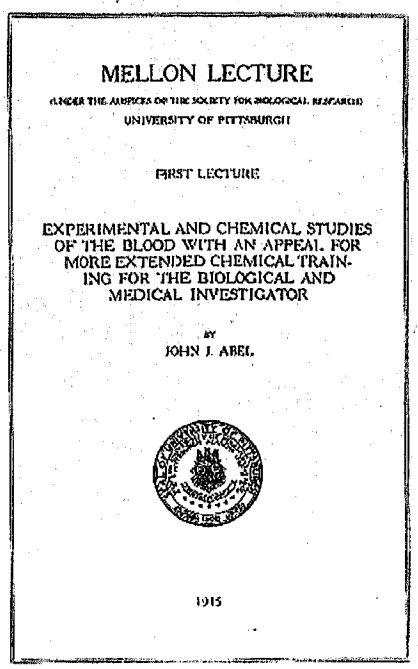
The apparatus constitutes what has been called an artificial kidney in the sense that it allows the escape of diffusible components of the blood, but it differs from the natural organ in that it makes no distinction between these constituents, the rate of their elimination being presumably proportional to the coefficients of diffusion. It will be shown, however, that any given constituent of the blood, as urea, sugar, or sodium chloride, can be retained in the body by a simple expedient when so desired.

This simple expedient, of course, was an alteration in the composition of the bath fluid, no different from what is done today.

Their vivi-diffusion apparatus was made of celloidin tubes immersed in a dialysate bath housed in a glass jacket (fig. 7). In anesthetized animals, an arterial cannula was connected to the apparatus and blood was returned via another cannula to a vein. Arterial pressure drove the pumpless system, not unlike clinical dialysis 25 years ago. Anticoagulation was achieved with hirudin, a natural anticoagulant from leeches. The very high price of hirudin, US$ 27.50/g in 1914, just enough for two experiments, forced them to prepare their own leech extracts. Heparin had not yet been discovered.

Abel, Rowntree, and Turner explored ways of minimizing the volume of blood in the system and achieving maximum surface area for diffusion in their device, 'This can be obtained either by using very small tubes, or by flattening a larger tube until the opposite surfaces nearly touch.' It is amazing to realize that over 80 years ago these investigators had developed the concepts for the hollow fiber and plate dialyzers that are currently used in dialysis units. For large dogs, they used a vivi-diffuser, shown in figure 8 in cross-section, with 32 celloidin tubes, each 8 mm in diameter and 40 cm long.

Most of their experiments were with dogs, a few with rabbits, all performed under general anesthesia. In two animals they demonstrated rapid and complete recovery after several hours of dialysis. Other experiments were designed to demonstrate the ability of the artificial kidney to remove foreign substances such as salicylic acid, which they chose because of its moderate diffusibility and simple colormetric determination. In the summary of their paper they state, 'directions in which the method may be utilized, both for the study of problems in physiological chemistry and as a promising therapeutic agent, have been indicated.'



MELLON LECTURE

UNDER THE AUSPICES OF THE SOCIETY FOR BIOLOGICAL RESEARCH
UNIVERSITY OF PITTSBURGH

FIRST LECTURE

EXPERIMENTAL AND CHEMICAL STUDIES OF THE BLOOD WITH AN APPEAL FOR MORE EXTENDED CHEMICAL TRAINING FOR THE BIOLOGICAL AND MEDICAL INVESTIGATOR

BY
JOHN J. ABEL

1915

9

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Fig. 9. Reprint of Abel's address at the dedication of the Mellon Institute, University of Pittsburgh, 1915 [8].

Fig. 10. Georg Haas, 1886–1971 [From ref. 15].

At the dedication of the Mellon Institute of the University of Pittsburgh in 1915 (fig. 9), Abel summarized their studies not only with the artificial kidney, but also with plasmapheresis which they were conducting simultaneously [8]. This historically oriented and engrossing paper reviewed the ancient practice of cupping and bloodletting, practised since the time of Hippocrates. Abel recognized that withdrawal of whole blood compromised its oxygen-carrying capacity; thus he proposed separating the plasma from the cellular elements so that red cells could be returned to the patient. The commencement of World War I limited the supply of the anticoagulant hirudin made from leeches in France, and because extracts of leeches from other sources were very toxic, Abel and his colleagues were forced to abandon this field of investigation and the potential use of the artificial kidney in humans. Their vision of clinical application of their techniques was extinguished by war.

Not surprisingly, other investigators immediately utilized Abel's vivi-diffuser for their own research. von Hess and McGuigan published a paper entitled 'The condition of the sugar in the blood' in the September 1914 issue of the *Journal of Pharmacology and Experimental Therapeutics* [9]. The two groups were well aware of each other's work. To avoid clotting, von Hess and McGuigan created pulsatile blood flow through the celloidin tubing. They improved the efficiency of the process by mixing the dialysis fluid in order to overcome the unstirred layer effect. Their work demonstrated that blood sugar was in simple solution rather than being bound to protein as has been hypothesized previously.

The year 1914 witnessed yet another early application of dialysis. MacCallum, Lambert, and Vogel were interested in the relationship between tetany and the calcium concentration of the blood [10]. Because they were unable to reduce the blood calcium in intact dogs by dialysis, they turned to studies of isolated limbs which they alternately perfused with normal blood or with blood that had been dialyzed to lower its calcium concentration. Limbs perfused with dialyzed, low-calcium blood became hyperexcitable and responded to nerve stimulation with tetany; these effects were promptly reversed by perfusion with normal blood.

The credit for performing the first human dialysis belongs to Georg Haas who lived from 1886 to 1971 (fig. 10). For most of the first half of the 20th century he worked in the small German city of Giessen, north of Frankfurt. Despite interruption of his research by World War I, he managed to develop a dialyzer (fig. 11) suitable for work with dogs and rabbits [11]. Haas was unaware of Abel's earlier work until 1925, but like Abel, he

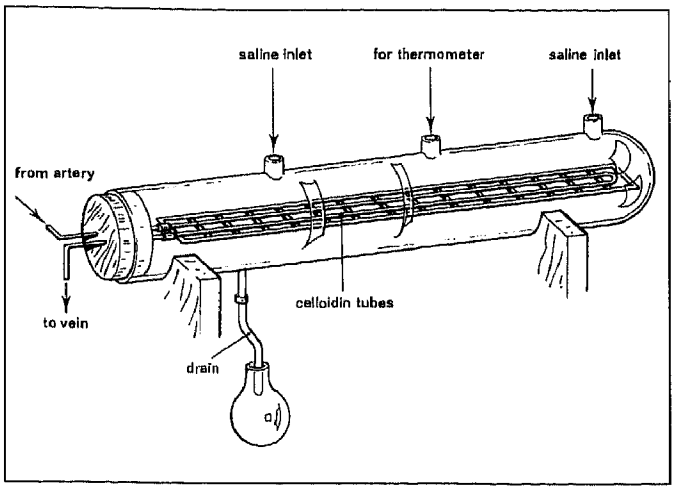


Fig. 11. Diagram of Haas' dialyzer [11].

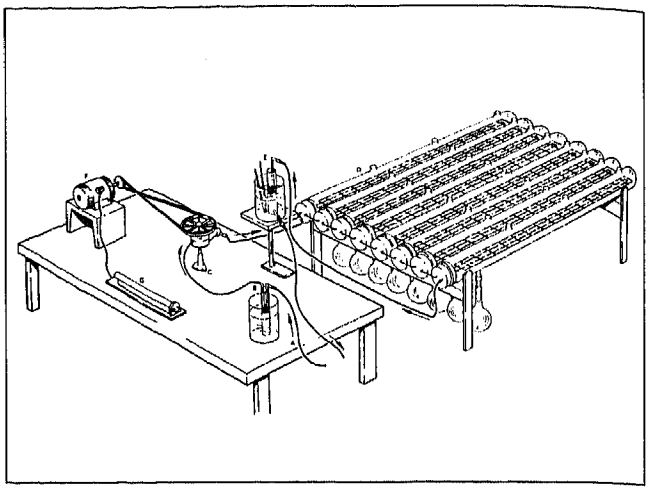


Fig. 12. Diagram of battery of dialyzers used by Haas in experiments on dogs [11].

used celloidin for dialysis tubing and hirudin for anticoagulation, with which he initially had problems with toxicity. Figure 12 is a diagram of the dialyzer Haas used in dog experiments.

In the January 1925 issue of *Klinische Wochenschrift*, Haas proposed that the dialysis methodology and hirudin application had become sufficiently reliable to employ the procedure on humans with uremia [12]. The issue then was less the efficacy of dialysis quantitatively, but rather one of safety and reliability of the technology. The first dialysis in a human lasted only 15 min. Vascular cannulas were inserted into the left radial artery and antecubital vein under local anesthesia. The patient suffered no untoward effect from the surgery and the procedure was free of disruption or complication. Haas calculated from measurements of indican concentration in blood and dialysate that 150 ml of blood had been cleansed. Thus, the first dialysis of a human, ineffective as it was for the benefit of the patient, was performed 73 years ago in October of 1924!.

On February 18, 1925 Haas dialyzed a second patient, a uremic boy, shown in figure 13, for 35 min and, in 1926, four additional patients, employing hirudin as the anticoagulant in all. The necessarily short dialysis time presumably coupled with low blood flows and small dialysate volumes prevented the dialyses from having any significant therapeutic effect.

In a lecture to the Giessen Medical Society in January of 1928, Haas detailed the results of three blood cleansings, as he termed them, in two patients with chronic uremia [13]. By then, heparin had become available. He performed both continuous and fractionated dialysis, the latter a procedure in which blood withdrawn from the patient was heparinized, dialyzed and then returned to the patient. Clinical improvement was only temporary. Haas concluded his lecture with this comment:

> There have indeed only been three cleansings on a grand scale up to now – and I know that one swallow still doesn't make a summer – but despite the limited number of observations, I have already gotten the distinct impression that it is worth the effort to continue along the path taken.

But Haas did not continue along that path, apparently because of a lack of support from his medical community.

The history of clinical hemodialysis is a tale of technological advancements. First heparin replaced the toxic and expensive hirudin. Next, cellophane tubing supplanted celloidin tubes. William Thalheimer, working in the Manhattan Convalescent Serum Laboratory in New York City, compared exchange transfusion with dialysis in previously nephrectomized, heparinized dogs [14]. With an Abel-type of artificial kidney, he used cellophane sausage casings instead of celloidin. Both modalities of therapy lowered the blood urea nitrogen (BUN) in these animals which led Thalheimer to suggest that they might be clinically useful for treating patients with acute renal failure but he did not pursue the project.

Willem (Pim) Johan Kolff (fig. 14) may be considered the major contributor to the management of uremic patients with the use of the artificial kidney. His achievements are all the more remarkable considering that Kolff and his colleagues worked under extraordinarily difficult conditions in The Netherlands during World War II. His fellow countryman, William Drukker, has provided a fascinating, dramatic and detailed account of Kolff's work during the military occupation of Holland in his excellent chapter on 'The History of Dialysis' in the book *The Replacement of Renal Function by Dialysis* edited by our beloved, deceased colleague, Jack Maher [15].

While working in the Department of Medicine at the University of Groningen, Kolff, distressed by not being able to assist a young patient dying of uremia, performed some simple experiments with cellophane tubing to study the dialyzability of urea. This was in the spring of 1940, and as we know, Germa-

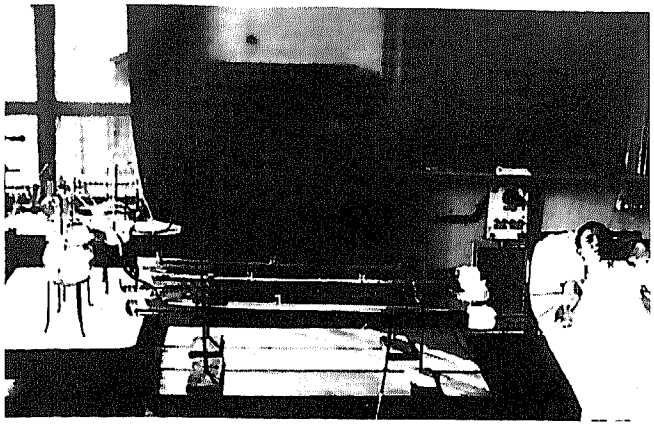


Fig. 13. Photograph of the second human dialysis performed by Haas, February 18, 1925. [From ref. 15].

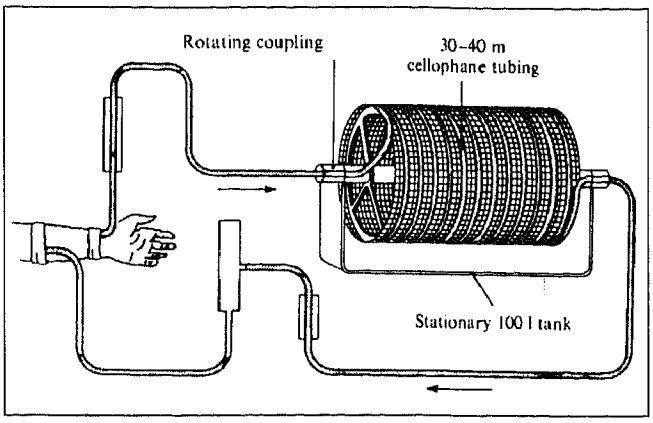


Fig. 15. Flow diagram of Kolff's rotating artificial kidney. [From ref. 15].

Fig. 14. Willem ('Pim') Johan Kolff, MD, PhD, 1979. [From ref. 15].

ny invaved The Netherlands on May 10, 1940. Kolff immediately decided that he must leave Groningen, and moved to the small town of Kampen where he remained throughout the war. There, with the help of an engineer, Hendrik Berk, he designed and constructed the rotating artificial kidney. Figure 15 shows the flow diagram of the rotating drum which was covered with cellophane tubing and partially submerged in a tank of dialysis fluid. Figure 16 is a picture of the original dialyzer.

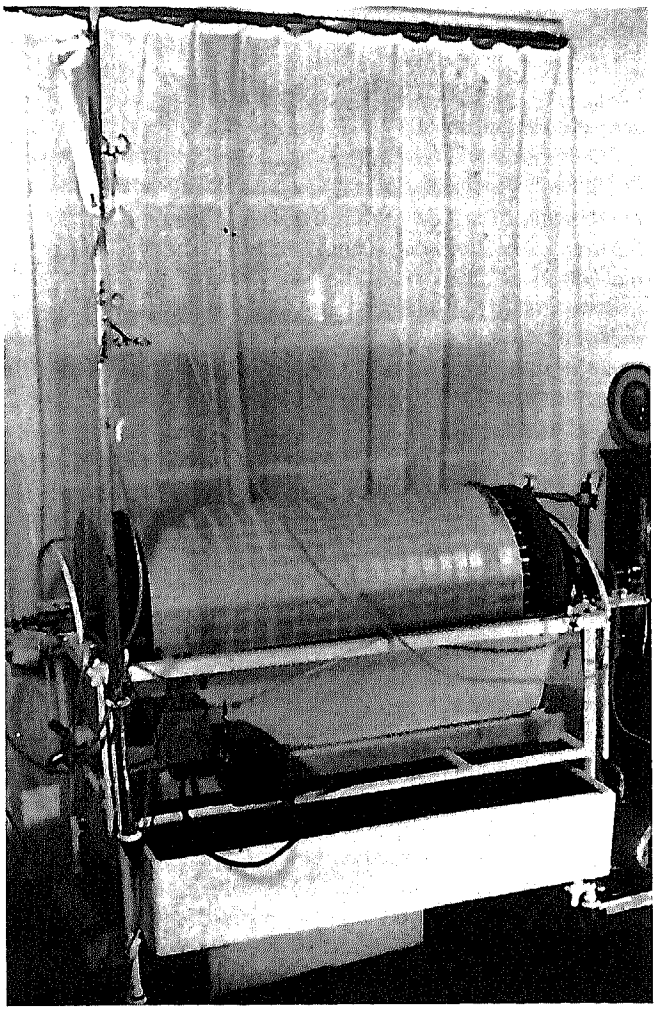
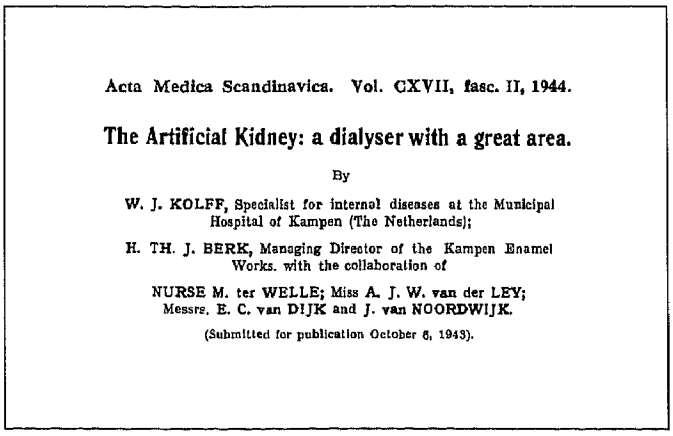


Fig. 16. Kolff's original rotating artificial kidney used for dialyzing his first patient. [From ref. 15].



Acta Medica Scandinavica. Vol. CXVII, fasc. II, 1944.

The Artificial Kidney: a dialyser with a great area.

By

W. J. KOLFF, Specialist for internal diseases at the Municipal Hospital of Kampen (The Netherlands);

H. TH. J. BERK, Managing Director of the Kampen Enamel Works. with the collaboration of

NURSE M. ter WELLE; Miss A. J. W. van der LEY; Messrs. E. C. van DIJK and J. van NOORDWIJK.

(Submitted for publication October 6, 1943).

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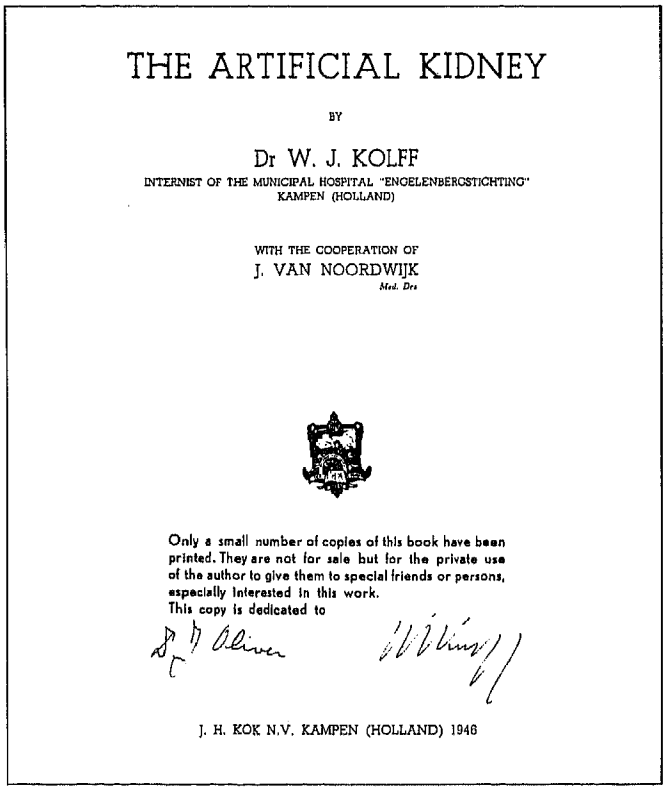

THE ARTIFICIAL KIDNEY

BY

Dr W. J. KOLFF

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WITH THE COOPERATION OF

J. VAN NOORDWIJK

Med. Dr.

Only a small number of copies of this book have been printed. They are not for sale but for the private use of the author to give them to special friends or persons, especially interested in this work.
This copy is dedicated to

J. H. KOK N.V. KAMPEN (HOLLAND) 1946

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Fig. 17. Title of the initial report by Kolff and colleagues on the use of the artificial kidney [16].

Fig. 18. Cover of Kolff's shortened English version of his use of the artificial kidney, 1946 [18].

Their paper entitled 'The Artificial Kidney: A Dialyzer with a Great Area' [16] (fig. 17) was published in early 1944 in *Acta Medica Scandinavica*. Their first patient had been dialyzed just 8 months before. They continued to improve and use their apparatus until the last year of the war. Detailed descriptions of the design and construction of the dialyzer and full clinical reports on the first 15 patients were published in a 200-page book in 1946 [17]. Although none of the patients survived, most underwent autopsy, permitting Kolff to discuss the likely cause of death of each one. Shortly thereafter, Kolff published an abbreviated English version of his Dutch book (fig. 18) [18]:

> Only a small number of copies of this book have been printed. They are not for sale but for the private use of the author to give them to special friends or persons especially interested in this work. This copy is dedicated to Dr. J. Oliver, signed W.J. Kolff.

In the last chapter of this book, Kolff wrote, 'I did not for one moment doubt that sooner or later a patient would come into our hands of whom it might be said 'he is cured, and without the artificial kidney he would have died."

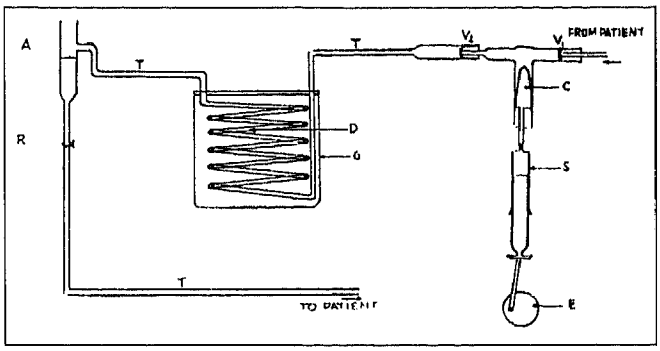
He realized his dream when a 67-year-old woman and, ironically, a Nazi collaborator during the war, was admitted to the surgical service on September 3, 1945. In the setting of acute cholecystitis, jaundice, and near anuria, she was treated with sulfathiazide for two-and-a-half days. By the end of a week, her BUN was 185 mg/dl and potassium 13.7 mEq/l! On September 11 she was dialyzed for 11.5 h. Sixty grams of urea were removed; the BUN fell to 56 mg/dl and the potassium to 4.7 mEq/l. Her clinical condition and sensorium had improved markedly following several hours of dialysis. Several days later she entered the polyuric phase of acute renal failure and recovered completely.

In contrast to his enthusiasm for the use of dialysis for acute renal failure, Kolff stated:

> Chronic nephritis is no indication for treatment with the artificial kidney, though an acute exacerbation of a chronic uremia might be an indication in some cases. An acute uremia, whatever the cause may be, is an indication for treatment with the artificial kidney as soon as it immediately threatens the patient's life.

This was written in 1946.

The events of World War II limted communication between scientific laboratories in different nations. During the years that Kolff was working in Kampen, a Canadian group in Toronto was developing an artificial kidney to the point of clinical usefulness [19]. Neither knew of the other's work. Gordon Murray and Edmund Delorme, both surgeons, and Newell Thomas, an undergraduate chemistry major, constructed an artificial kidney in the basement of Murray's house with US$ 8,000 of his own money, a not insubstantial sum in 1946. Their development of an artificial kidney sprang from Murray's earlier work in which he transplanted kidneys into nephrectomized, hepa-



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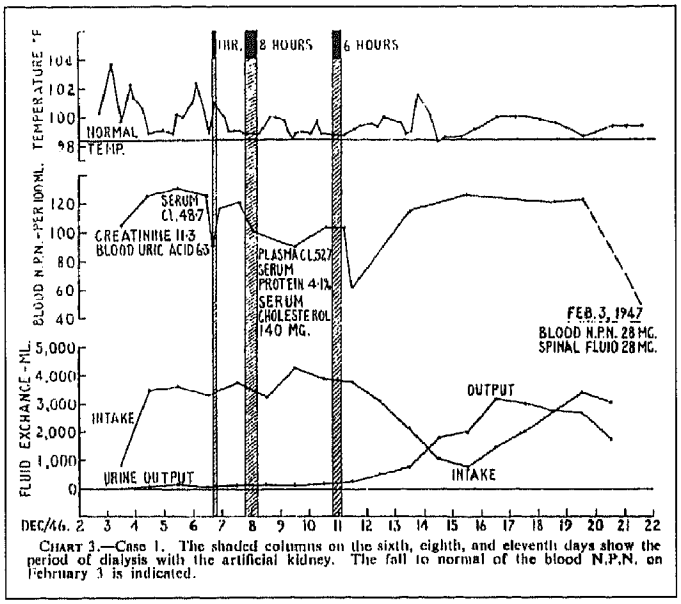

CHART 3.—Case 1. The shaded columns on the sixth, eighth, and eleventh days show the period of dialysis with the artificial kidney. The fall to normal of the blood N.P.N. on February 3 is indicated.

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Fig. 19. Diagram of Murray's artificial kidney [19].

Fig. 20. Clinical chart of the first patient dialyzed by Murray et al., December, 1946 [19].

rinized animals to clear their blood of toxic substances. Murray was a talented but controversial figure. He was an imaginative, innovative surgeon with great technical skills. But he was also a loner, suspicious and secretive in dealing with his colleagues. Although he has even been accused of misrepresentation of data, he certainly deserves credit for being a pioneer in the clinical use of heparin and for developing many new surgical techniques, including vein grafting. He performed the first heart valve transplant, placing a cadaveric aortic valve into a young man dying of aortic insufficiency. Few know that he invented an artificial kidney which he used in 1946 to perform the very first renal dialysis in North America. Although their work received considerable attention at the time, it is now largely forgotten. Murray, Delorme and Thomas briefly presented their work in two short earlier papers, but their story is best told in the Alexander Simpson-Smith lecture delivered by Murray at the Hospital for Sick Children, Great Ormond Street, London on July 11, 1949 [19].

Aware of the work of Abel and Thalheimer, they constructed an apparatus in which the dialysis membrane made of sausage tubing was wrapped around a wooden reel (fig. 19). A wire mesh compressed the sausage tubing in order to improve the surface-to-volume ratio. The blood was anticoagulated with heparin and pumped through the system with a rubber tambour inflated and deflated by the action of a piston syringe. Because the suction created by the pump prevented use of a surface vein as a blood source, they inserted a catheter through the femoral vein high into the inferior vena cava. Blood was returned into a peripheral vein. Their unsophisticated understanding of salt and water physiology was revealed in their initial use of pure water as bath fluid. But they perservered until they made a well-tolerated Ringer-like buffer solution. Their first attempts at creating renal failure in dogs with bilateral nephrectomies failed because the animals became uremic and ill too quickly. In typical surgical fashion, they solved the dilemma by transplanting the dog's ureters into the small bowel. Within several days the animals were azotemic, but still healthy enough to endure the procedure in which they could test the efficacy of the dialyzer and quantitate the removal of nonprotein nitrogen (NPN). They express their insight and vision in the following sentence, 'The NPN level in the blood varies greatly in the above state and is a less reliable guide to the efficiency of the dialysation than is the NPN measurable in the dialysate removed during the test run.' Thus, in 1949, Murray realized that NPN served only as a surrogate for uremic toxins in the blood.

He stated that dialysis 'obviously can function only as a temporary measure' in his detailed description of three patients treated with the apparatus. The first patient to receive hemodialysis in North America was a comatose young woman with seizures and acute renal failure seen 9 days following an attempted abortion. The first dialysis, performed on December 6, 1946, was terminated after only 1 h because of severe chills. Recall that the dialysate was not warmed nor was the sterility of the system ensured. Thirty-six hours later she tolerated 8 h dialysis, and then 6 h of dialysis 3 days later. Shortly thereafter urine flow resumed and she eventually recovered completely (fig. 20).

Murray concludes:

> There has been survival in about 50% of the patients treated. Those who succumbed were found on the whole to have had chronic kidney disease and even though the purification of the blood was accomplished satisfactorily, they relapsed into a uremic state.

Fig. 21. Kolff in front of the statue of Thomas Graham, Glasgow, 1979.

We are not told how many patients he treated. Nor do we know why they stopped using their artificial kidney. Perhaps, as surgeons, they pursued other interests. By that time, Kolff's rotating-drum-design artificial kidney had been distributed to several hospitals in both Europe and the United States.

You may ask yourself why we have chosen to close this history of hemodialysis with the first successful clinical applications. Put quite simply, our inclination has always been to honor the idea rather than the modification and perfection of the concept. Do we praise the Wright brothers or the engineers who designed 747 airplanes? And so we close with a picture of Professor Kolff (fig. 21), who was the first to translate successfully the basic scientific ideas into a clinically effective methodology. He stands here before a statue of Thomas Graham, to whom we are indebted for the concepts that were ultimately to become the foundation of modern dialysis.

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