UNDERSTANDING HEMODIALYSIS
THE INVENTION, DEVELOPMENT, AND SUCCESS OF THE ARTIFICIAL KIDNEY
Hemodialysis – from the early days to today

Historical basis of hemodialysis

Hemodialysis

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HEMODIALYSIS – FROM THE EARLY DAYS TO TODAY

The first signs of uremia within the human body are an indication that the kidneys are no longer performing or are unable to completely fulfill their function. The Greek origin of the word shows that the knowledge of the condition is much older than the ability to treat this life-threatening problem.

It was not until the 1940s that researchers finally established a scientific basis advanced enough to support the first therapeutic trials. The discoveries and inventions of dedicated doctors and scientists are to thank for the advances that have cleared the way for continuous technological improvement over the decades.

This brochure looks at the development of hemodialysis and the artificial kidney (dialyzer) – inventions that help secure the life and quality of life of millions of hemodialysis patients worldwide.
Acute and chronic kidney failure, which can lead to death if untreated for several days or weeks, is an illness that is as old as humanity itself. In early Rome and later in the Middle Ages, treatments for uremia included the use of hot baths, sweating therapies, bloodletting, and enemas. Current procedures for the treatment of kidney failure include physical processes such as osmosis and diffusion, which are widespread in nature and assist in the transport of water and dissolved substances.

The first scientific descriptions of these procedures came from the Scottish chemist Thomas Graham, who became known as the “Father of Dialysis.” At first, osmosis and dialysis became popular as methods used in chemical laboratories that allowed the separation of dissolved substances or the removal of water from solutions through semipermeable membranes. Far ahead of his time, Graham indicated in his work the potential uses of these procedures in medicine.

Today **hemodialysis** describes an extracorporeal procedure, or procedure outside the body, for filtering uremic substances from the blood of patients suffering from kidney disease. The actual purifying process, which requires the use of a semipermeable membrane, is based on the seminal work carried out by Graham, Fick, and others.
HEMODIALYSIS

Hemodialysis is the process of cleaning blood outside the body, and involves taking blood from a blood vessel and passing it through a synthetic filter, known as a dialyzer. The blood is cleaned in the dialyzer before being returned to the body, which is why the dialyzer is also referred to as an “artificial kidney.” The process is controlled by a dialysis machine, which pumps the blood around the circuit, adds in an anticoagulant, and regulates the cleaning process, among other things. Hemodialysis usually takes around three to six hours and is performed at least three times a week, usually in a dialysis center.

Instead of being treated in a dialysis center, patients may be offered the option of receiving treatment in their own home environment. Various types of home dialysis give patients the opportunity to make their treatment part of their everyday life.
THE EARLY DAYS OF DIALYSIS

The first historical description of this type of procedure was published in 1913. Abel, Rowntree, and Turner “dialyzed” anesthetized animals by directing their blood outside the body and through tubes of semipermeable membranes made from Collodion, a material based on cellulose. It is impossible to say for sure whether Abel and his colleagues intended to use this procedure to treat kidney failure from the start. There is no doubt, however, that dialysis treatment today continues to use major elements of Abel’s vividiffusion machine.

Before the blood could be routed through the “dialyzer,” its ability to clot or coagulate had to be at least temporarily inhibited. Abel and his colleagues used a substance known as hirudin, which had been identified as the anticoagulant element in the saliva of leeches in 1880.

A German doctor by the name of Georg Haas, from the town of Giessen near Frankfurt am Main, performed the first dialysis treatments involving humans. It is believed that Haas dialyzed the first patient with kidney failure at the University of Giessen in the summer of 1924, after performing preparatory experiments. By 1928, Haas had dialyzed an additional six patients, none of whom survived, likely because of the critical condition of the patients and the insufficient effectiveness of the dialysis treatment. The Haas Dialyzer, which also used a Collodion membrane, was built in a variety of models and sizes.
Haas, like Abel, also used hirudin as the anticoagulant in his first dialysis treatments. However, this substance often led to massive complications arising from allergic reactions because it was not adequately purified and originated from a species very distant from humans. In the end, Haas used **heparin** in his seventh and final experiment. Heparin is the universal anticoagulant in mammals. This substance caused substantially fewer complications than hirudin – even when it was insufficiently purified – and could be produced in much larger amounts. Following the development of better purification methods in 1937, heparin was adopted as the necessary anticoagulant, and continues to be used today.
In fall 1945, Willem Kolff, of the Netherlands, made the breakthrough that had stubbornly eluded Haas. Kolff used a rotating drum kidney he had developed to perform a week-long dialysis treatment on a 67-year-old patient who had been admitted to hospital with acute kidney failure. The patient was subsequently discharged with normal kidney function. This patient proved that the concept developed by Abel and Haas could be put into practice and thus represented the first major breakthrough in the treatment of patients with kidney disease.

The success was partially due to the technical improvements in the actual equipment used for the treatment. Kolff’s rotating drum kidney used membranous tubes made from a new cellulose-based material known as cellophane that was actually used in the packaging of food. During the treatment, the blood-filled tubes were wrapped around a wooden drum that rotated through an electrolyte solution known as “dialysate.” As the membranous tubes passed through the bath, the laws of physics caused the uremic toxins to pass into this rinsing liquid.
THE ROTATING DRUM KIDNEY

Examples of the Kolff rotating drum kidney crossed the Atlantic and arrived at the Peter Brent Brigham Hospital in Boston, where they underwent a significant technical improvement. The modified machines became known as the Kolff-Brigham artificial kidney, and between 1954 and 1962 were shipped from Boston to 22 hospitals worldwide.

The **Kolff-Brigham kidney** had previously passed its practical test under extreme conditions during the Korean War. Dialysis treatment succeeded in improving the average survival rate of soldiers suffering from post-traumatic kidney failure and thus won time for additional medical procedures.

*Acute dialysis during the Korean War (1952)*

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HOSPITALS WERE EQUIPPED WITH MODIFIED ARTIFICIAL KIDNEYS FROM BOSTON BETWEEN 1954 AND 1962.
DIALYSIS AND ULTRAFILTRATION

One of the most important functions of the natural kidney, in addition to the filtering of uremic toxins, is the removal of excess water. When the kidneys fail, this function must be taken over by the artificial kidney, which is also known as a dialyzer.

The procedure by which plasma water from the patient is squeezed through the dialyzer membrane using pressure is termed ultrafiltration.

In 1947, Swede Nils Alwall published a scientific work describing a modified dialyzer that could perform the necessary combination of dialysis and ultrafiltration better than the original Kolff kidney. The cellophane membranes used in this dialyzer could withstand higher pressure because of their positioning between two protective metal grates. All the membranes were in a tightly sealed cylinder so that different pressure ratios could be generated.

Nils Alwall in 1946 with an early model of the dialysis machine.
By proving that uremic patients could be successfully treated using the artificial kidney, Kolff sparked a flurry of activity around the world to develop improved and more effective dialyzers. The “Parallel Plate Dialyzer” evolved as the most significant development of this period. Rather than pumping the blood through membranous tubes, this dialyzer directed the flow of dialysis solution and blood through alternating layers of membranous material. This development began with the first Skegg-Leonards dialyzer in 1948, and reached its technological peak in 1960 with the presentation of the Kiil dialyzer from Norwegian doctor Fredrik Kiil. These dialyzers were the predecessors of modern plate dialyzers.

Just as the technology of dialyzers continued to develop, so too did the scientific principles regarding the transport of substances across membranes, and these principles were applied specifically to dialysis. This work enabled scientists to develop a quantitative description of the dialysis process and allowed the development of dialyzers with clearly defined characteristics.
Vascular Access and Chronic Dialysis

Belding Scribner made a breakthrough in this field in 1960 in the United States with the development of what would later become known as the “Scribner shunt.” This new method provided a relatively simple means of accessing a patient’s circulatory system that could be used over a period of several months, meaning patients with chronic kidney disease could, for the first time, be treated with dialysis. The shunt was on a small plate that would be attached to the patient’s body, for example on the arm. One Teflon cannula was surgically implanted in a vein and another in an artery. Outside the body, the cannulae were joined in a circulatory short circuit – hence the name “shunt.” During dialysis, the shunt would be opened and attached to the dialyzer. Further development brought the introduction in 1962 of improved shunts made entirely from flexible materials.

Still, the most decisive breakthrough in the field of vascular access came in 1966 from Michael Brescia and James Cimino. Their work remains fundamentally important to dialysis today. During a surgical procedure, they connected an artery in the arm with a vein. The vein was not normally exposed to high arterial blood pressure and swelled considerably. Needles could then be more easily placed in this vein, which lay beneath the skin, to allow repeated access. This technique lowered the risk of infection and permitted dialysis treatment over a period of years. The arteriovenous (AV) fistula remains the access of choice for dialysis patients, and some AV fistula implanted more than 30 years ago are still in use today.

This development allowed the long-term treatment of patients with chronic kidney failure. In the spring of 1960, Scribner implanted a shunt in American Clyde Shields, in Seattle. Shields became the first chronic hemodialysis patient, and the dialysis treatments allowed him to live an additional eleven years before dying of cardiac disease in 1971.
These successes provided a fertile basis for the world’s first-ever chronic hemodialysis program, which was established in Seattle in the following years. At that time, Scribner and his team refrained from seeking patent protection for many of their inventions and innovations to ensure swift distribution of their life-saving techniques for dialysis patients.

The development of improved methods for accessing blood vessels meant that patients with chronic kidney disease could be offered effective treatment for the first time. However, in the early 1970s, a dialysis treatment lasted around twelve hours and was very expensive, due to the high outlay for materials and the treatment itself. As a result, not all kidney patients could access this life-saving therapy. In the United States, for example, committees decided on how the small number of treatment slots should be allocated – a matter of life-or-death decision-making.
MODERN HEMODIALYSIS

After the early successes in Seattle, hemodialysis established itself as the treatment of choice worldwide for chronic and acute kidney failure. Membranes, dialyzers, and dialysis machines were continuously improved and manufactured industrially in ever-increasing numbers. A major step forward was the development of the first hollow-fiber dialyzer in 1964. This technology replaced the until-then traditional membranous tubes and flat membranes with a number of capillary-sized hollow membranes. This procedure allowed for the production of dialyzers with a surface area large enough to fulfill the demands of efficient dialysis treatment. Over the years that followed, thanks to the development of appropriate industrial manufacturing technologies, it became possible to produce large numbers of disposable dialyzers at a reasonable price. Today, dialyzers are made from entirely synthetic polysulfone, a plastic that exhibits exceptionally good filtering efficiency and tolerance for patients. They are still based on these technologies.

* A dialyzer incorporates up to 20,000 hollow fibers

* The walls of the hollow fibers in a dialyzer are only 0.035 mm thick
State-of-the-art dialysis machines also monitor patients to ensure critical conditions can be detected at an early stage and treated. They feature efficient monitoring and data management systems and have become more user-friendly over recent years. A growing number of the latest generation of dialysis machines also utilize computer-controlled machines, online technologies, networking, and special software.

As the clinical use of hemodialysis became increasingly widespread, scientists were better able to investigate the unique attributes of patients with chronic kidney disease. In contrast to the early years of dialysis presented here, the lack of adequate treatment methods or technologies is no longer a challenge in the treatment of kidney patients. The present challenges stem rather from the large number of patients requiring dialysis treatment, the complications resulting from years of dialysis treatment, and a population of patients that presents demographic as well as medical challenges; a population whose treatment would be unimaginable, were it not for the pioneering work presented here.
Fresenius Medical Care is the world’s leading provider of products and services for patients with kidney disease, millions of whom are undergoing dialysis treatment. We look after hundreds of thousands of dialysis patients in our global network of dialysis centers. Fresenius Medical Care is also the leading provider of dialysis products such as dialysis equipment and dialysis filters. Additionally, in the field of Care Coordination, the company is expanding its portfolio of supplementary medical services related to dialysis.

Further information about our company and the history of dialysis can be found online at:

www.freseniusmedicalcare.com