Nils Alwall - one of precursors of dialysis treatment

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ABSTRACT
Nils Alwall (1904-1986) came from a small village in southern Sweden. In 1923 he began his medical studies at the Lund University, to graduate in 1932. During his studies he conducted experimental work and in 1935 defended his doctoral thesis in pharmacology. In 1936 he was awarded the title of associate professor of pharmacology and started clinical practice combined with experimental research in the Department of Medicine at Lund. In 1940 Alwall obtained the position of assistant professor of practical medicine and in 1957 was promoted to professor of nephrology at the world’s first Department of Nephrology. His medical interests were many-sided but mostly related to kidney diseases and replacement therapy after the loss of renal function. From 1941 he worked on the construction of the vertical drum artificial kidney, tested mostly in rabbits, which also enabled ultrafiltration. The dialysis was first applied in September 1946 in a patient with severe uremia, and soon afterwards the first ward for artificial kidney therapy was established. Thenceforward Lund department became the leading center for treatment of acute and later also chronic renal insufficiency. Alwall was also the inventor of the arteriovenous shunt (1943-1948) and the pioneer in the use of renal biopsy (1943). He also inspired creation of the Gambro Company in Lund (1964) which resulted in construction of coil dialyzer (1966) and sheet single-use plate dialyzer (1967). Alwall was also involved in the founding of the International Society of Nephrology (1960), European Dialysis and Transplant Association (1964), and Swedish Society of Nephrology (1964), engaged at leading positions in these organizations, also after his retirement in 1971. He is an author and coauthor of 203 publications.

KEYWORDS: Nils Alwall, Dialysis Treatment, artificial kidney

Introduction
In the early 1940s three pioneers independently created artificial kidney apparatuses and applied them for treatment of renal failure. These pioneers were Willem Kolff (The Netherlands), Nils Alwall (Sweden) and Gordon Murray (Canada). Nils Alwall, (Figure 1) began experiments with dialysis in animals, mainly rabbits, in the early 1940s. Willem Kolff made similar attempts in patients since 1943. They first made contact in 1946. Alwall performed the first dialysis in a patient in September 1946 and Murray did that three months later. Earlier they both performed repeated animal experiments which actually delayed clinical attempts but contributed to a later success in subjects (1).

Nils Alwall – early education and young physician (2, 3)
He was born in October 7, 1904 as Nils Andersson in a small village (Figure 2) in southern Sweden. After public school his further education was supported by a childless uncle Jons. Already in the high school (where he had chosen a humanistic class with Greek and Latin) he was taking interest in technical aspects of the surrounding world and showed a gift of leadership. In 1923 he graduated from the high school, completed education at mathematics, physics and chemistry courses and in December the same year began medical studies at the University of Lund. He was active in the students’ federation, served as a secretary and executive vice-chairman.

Figure 1 - Nils Alwall, 1959.

Figure 2 - Nils Alwall’s family house in Kiaby, Southern Sweden, 1920s
In the health-promoting committee he implemented measures aimed at prevention and treatment of tuberculosis which was common at the time among medical students. Among other things, Nils arranged periodical radiological and ESR check-up sessions and reserved for convalescent students forty low-cost beds (US $ 450) in a nearby sanatorium. Nils took also an active part in organization of periodical students’ festivities (Swedish “carnivals”), the profits were used to supplement the sanatorium’s library. As an appreciated orator he was often invited to deliver an occasional speech. The summers of 1924 and 1925 he spent on army training in a medical unit, obtained driving license, and enjoyed riding a military motorcycle. With time, in 1942, he was promoted to the rank of captain in the medical units.

During the second year of his studies Nils became particularly interested in physiology and professor Torsten Thunberg offered him the assistant position, without salary but ensuring free accommodation at the attic of the Institute of Physiology. Nils stayed there for nearly four hard years, continuing his medical studies, conducting classes with students and engaging in his own experimental work. In 1927 Nils and his brother Edvin decided to change their family name from Andersson (regarded too common) to Alwall. In 1928 he published the results of the first experimental work, on the method of determination of dehydrogenase in rabbit blood. A year later he obtained the post of assistant at the Institute of Pharmacology, as before without payment, but with the privilege of free accommodation in a laboratory room and also access to experimental animals. Then he began his doctoral study on the role of dinitrophenol as a factor enhancing metabolism (and weight loss) in rabbits. After an internship in clinical departments (including one of obstetrics and gynecology where he had handled 50 deliveries), in the spring of 1932 he became a qualified doctor and started his work as a general practitioner in small villages in southern Sweden until 1934 (with annual salary of US $ 450). At the same time he continued his work on the doctoral thesis, which he defended in 1935. At the promotional ceremony of new doctors he delivered a speech in Latin, without using any written text. Afterwards he left for Pecs in Hungary, on invitation from his friend Geza Mansfeld, and there acquainted himself with experimental research with dogs. After return from Hungary he was appointed an associate professor in pharmacology, and in the autumn 1936 started his career in the Medical Clinic, University of Lund. Between 1928 and 1937 Nils Alwall published 17 articles, mostly experimental studies. However his interest focused increasingly on the clinical work. Although heavily burdened by the everyday clinical duties (up to 70 hours per week) he found time to play football, and took part in the university annual match; associated professors against the team of the vice-chairman of the student federation.

The dream of the artificial kidney (3, 4)

At that time the treatment of patients with renal failure symptoms and edema was confined to low protein diet and almost prone positioning in bed, sometimes for many months. Nils was extremely moved by poor, if any, results of such treatment. This feeling of helplessness must have given rise to the idea of a need for a radical help, such as creation of an apparatus replacing the function of the damaged kidney – artificial kidney (AK). Alwall was then responsible for a 57-bed internal medicine ward and for teaching medical students; his position was assistant professor of practical medicine. Fortunately, new premises to accommodate small animals (rabbits) had been opened in the Clinic’s basement and in 1941 he received a regular scholarship for associate professor (US $ 1,400 per year) so he could devote a part of time to experiments with AK. They were performed usually after finished work at internal ward as to not disturb the patient’s care. In 1941-42 his experimental apparatus resembled the later introduced flat-plate dialyzer (dialysis filter). These results were never published because Alwall felt that the approach was not practical.

The next models of AK had a shape of a vertical drum of different sizes used in experiments since 1942 (Figure 3). After a single procedure the blood urea level was reduced by 20 to 30%, repeated dialysis could significantly prolong the animal’s life. Until 1953 almost 2000 rabbits were used in different experiments.

Figure 3 - Models of artificial kidney used in experiments with rabbits, 1941 – 1953. Height about 20 cm.

Glass cannulae and a small rubber tubes were used to get access to the artery and vein before the each dialysis and removed after the procedure. After several procedures vessels were damaged and further treatment was not possible. Repeated dialysis treatment required a more sophisticated approach and Alwall developed an arteriovenous shunt. Using already available heparin, patency of the arteriovenous shunts could be prolonged up to one week and maximally 7 dialyses in the same animal could be performed. These experiments with arteriovenous shunts were published in 1949 (5). This method of access to the vascular system was also used in patients but was later abandoned because of clotting and development of infection (6). The materials used were too primitive to obtain better results of shunts patency. Belding Scribner discussed with Alwall the problems with arteriovenous shunt in 1954, and visited Alwall’s Clinic in 1958; there is no doubt that they talked at length about the shunts. Scribner came to Lund again after the Congress in Geneva in 1960 (where he presented a new Quinton-Scribner shunt using PTFE – Teflon tubing) and brought a coil of a new material (Teflon) as a gift to Alwall.

In 1943-44 Alwall applied percutaneous renal biopsy (the first in the world) using the Iverson and Roholm needle for liver biopsy (7). Biopsy material was sucked into a syringe and sent for microscopic examination in Copenhagen. Alwall performed 13 renal biopsies but, unfortunately, the last patient went into shock, probably due to a reaction to the contrast medium, developed acute renal failure and died. After that Alwall discontinued the biopsies until 1950s. A report on all kidney biopsies done during the year 1943-44 was published in 1952 (8).

Modified and larger models of AK, suitable for use in large animals (dogs) and in patients were created in the workshops of the Institute of Physiology. Alwall covered the costs of production from his own pocket. In 1946 he received a grant of US $ 800 and could hire two assistants to help with animal experiments. This support was crucial for further investments required for improvement of the AK.
Alwall was prepared to carry out dialysis treatment in patients already in 1944. However, the head of the medical clinic, even though favorably disposed to the Alwall’s ideas, advocated patience and waiting for suitable circumstances. It was feared that the death of a patient during treatment would prevent the approval by the central health authorities of the entire dialysis program. In addition, the local colleagues were opposed to Alwall’s ideas and were reluctant to send the patients for dialysis treatment which they considered as very dangerous procedure.

### Coming to clinical dialysis

At last it happened that an unconscious patient with terminal chronic renal failure and pneumonia was sent to the clinic from another hospital. The dialysis procedure was performed in the laboratory room on the night of 3/4 September 1946, it lasted 6 hours. The patient’s condition and the biochemical parameters improved: blood urea level decreased by 98 mg% to 320 mg% (53 mmol/L), approx. 45 g of urea has been removed from the body (Figure 4). However, the general condition was critical from the very beginning and he died of respiratory failure on the next day. Nevertheless, Alwall’s later conclusion was that this promising result of the dialysis procedure was a turning point on the way to implementation of this method of treatment in Lund (4).

Soon afterwards Alwall received US $ 1000 to adapt facilities in the clinic to the requirements of dialysis procedures. By December 1946 the construction of this world’s first dialysis department with a total area of 26 m² was completed. It consisted of two rooms, where one AK apparatus and a 100 L water tank were installed. In January 1947 dialysis treatment was used in the second patient, who survived further 15 years, and in February the same year the third patient was treated. These three cases were presented in a publication in the same year (9).

Throughout his work at the Institute of Physiology Alwall took great interest in the mechanism of edema formation. He emphasized on the status of hydration of patients, especially during the dialysis treatment, was a major novelty. Because of the increasing demand for AK, Alwall started the production of apparatuses made of hard rubber (ebonite), in cooperation with the rubber factory. These constructions were suitable to perform UF by creating negative pressure in the dialysate during dialysis procedure in rabbits and were used in patients between 1947 and 1949. However, they did not withstand steam sterilization and gradually underwent deformation. Therefore Alwall started cooperation with the steel factory in the town Avesta and AK made of stainless steel (Avesta model) were used since 1949 (3, 4). Subsequent models (altogether about 50 apparatuses were produced) underwent various modifications and were sold by Avesta factory to 17 countries in 1950s. By the end of 1960s they were still used in more than 40 dialysis centers in the world. The interest for dialysis treatment increased greatly after publication of 8 cases of dialyzed patients in *Lancet* 1948 (10) (Figure 5). The Clinic in Lund attracted attention worldwide and soon increasing number of doctors were coming to visit and take training. In 1948 Alwall was invited to London and Vienna with his staff and his apparatus to perform dialysis treatment in patients not suitable for transport to Sweden. In 1949 his annual salary was increased to US $ 4,000.

![Figure 4 - Nils Alwall during the first dialysis treatment in patient, September 1946.](image)

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Throughout his work at the Institute of Physiology Alwall took great interest in the mechanism of edema formation. He thought that also overhydration is responsible for the symptoms of uremia. Therefore quite early Alwall explored the possibility of applying dialysis to remove excess of water from the body (ultrafiltration, UF). At first in rabbits overhydrated 115% and later in patients he achieved significant UF by creating positive pressure in the extracorporeal blood channel or negative pressure in the dialysis fluid. In this way an UF of about 0.3 – 1.0 L/hour could be obtained. No other AK available at that time offered such possibility. Quite often Alwall’s patients urgently needed UF because of pulmonary edema (called by him “uremic lungs”), often secondary to the recommended Borst’s diet which involved fluid overload in anuric patients. To avoid complications (connected with blood pressure fall) during UF, since 1949 Alwall ordered strict control of bed-weight throughout the period of treatment and a special bed scale was constructed (6). Beginning from 1950 radiological chest control was performed frequently, sometimes every day. The weight of the patients hospitalized in the clinic was monitored daily. To the guests visiting the Alwall’s clinic the emphasis on the status of hydration of patients, especially during the dialysis treatment, was a major novelty.

In the subsequent year 1950 the dialysis department was expanded by addition of another room and the second AK was added. The preparation room was equipped with a big steam sterilizer and a large tank for the dialysate, 800 liters in capacity. Tap water was passed through the columns of a softener. Alwall already used the dialysate with reduced sodium chloride concentration at that time. As for the early 1950s these were extremely modern facilities and John Merrill, when on visit to Lund, called them “hotel class”.

Since 1954 in the guest book of the Clinic more than 450 inscriptions have accumulated, by visitors and trainee doctors from more than 40 countries of all continents. Alwall was also...
invited to various medical centers around the world to lecture on dialysis. He took part in many scientific congresses and symposia.

Alwall believed that the methods of therapy current at the time: appropriate diet and bed rest, should be combined in selected cases with dialysis treatment. His contemporary colleagues were skeptical about such dialysis treatment in patients with renal failure but Alwall obtained unexpected support from surgeons who had to deal with many cases of postoperative acute renal failure, especially in the field of oral, abdominal and vascular surgery which ruled out the use of dietary treatment. There were also many cases of toxic kidney damage secondary to treatment with antibiotics. Many of these patients were transferred to Alwall’s clinic and dialysis treatment was applied in all such cases, including the patients on artificial ventilation (appropriate ventilator machine had been installed in the dialysis department). Not surprisingly, initially the mortality was very high so that instead of saying “the dialysed patient died” the expression “the patient was “alwalled” was ironically used.

Later, in the middle 1950s, the results of dialysis treatment were much better owing to the earlier admission to the dialysis department, before patient’s condition became critical, and this saying was abandoned. Alwall reported restoration of renal function after about 80 days of dialysis treatment. This was in discordance with the opinion that after 2 weeks the treatment of patients with anuria should be abandoned.

In 1949 Alwall performed the pioneering experiment of hemofiltration in a uremic rabbit, 2.1 kg in weight. During the 6-hours’ procedure 700 ml of fluid was removed and compensated by intravenous administration of electrolyte solution. For such treatment Alwall used the term of “exchangeable UF” and noticed that it gave a similar effect as dialysis (11). In 1952 he published the results of exchangeable UF treatment of barbiturate poisoning in rabbits. Suicide by barbiturate poisoning was frequent in the years 1940–1950 and in patients with barbiturate poisoning Alwall, as the first in the world, used dialysis treatment (12). Spectacular responses were observed with patients having come out of coma after dialysis and asking for a cup of coffee. In 1952 Alwall published a case of a recovery from excessive resistant edema in a patient with nephrotic syndrome and normal renal function. Strong diuretics were not available at that time. Over the period of 6 weeks Alwall performed three UF sessions without dialysis (called later isolated UF) and removed about 30 liters of edema fluid without compromising renal function (6, 11). His idea of hemofiltration was introduced by Lee Henderson into treatment of uremia in patients in 1967 and idea of isolated UF was introduced by Jonas Bergström into the clinic in 1976. In 1950 Alwall described also, as one of the first authors in the world, the clinical picture of diabetic nephropathy, and diabetic nephropathy in the absence of diabetes mellitus (13). Alwall was also the first clinician to draw attention to the nephrotoxicity of radiographic contrast media (14), in several cases he was forced to use dialysis treatment because of the so induced kidney function impairment.

The number of patients treated in Lund increased every year; they came from all over Sweden and from abroad. Initially, mainly the patients with acute renal failure were qualified for dialysis therapy however some patients with chronic renal failure were also treated. By 1961, 724 patients with acute renal failure and 351 with chronic renal failure (representing a 22% of all) had been treated with dialysis. A record survival rate in these chronic anuric cases was 186 days before Scribner’s shunt came to use (which gave an excellent testimony to the personal competence). In 1960 a regular dialysis program in patients with chronic renal failure was started in Lund and the requirement for disposable dialysis equipment became evident (3).
Then, in 1967, a fully disposable flat-plate dialyzer of Alwall’s type (Ad modum Alwall) was launched, the prototype weighed 7.5 kg. At this stage the construction team in Gambro was already numerous, consisted of people of various specialties and the Alwall’s role changed from that of a constructor to an investigator testing the new dialysis filters, providing comments and proposing amendments.

In 1968, the Department of Nephrology was moved to a new hospital building. The Clinical ward counted 42 beds, the dialysis department area was of about 1000 m². There were 14 bed sites, each equipped with a Gambro dialysis monitor (AK1). This dialysis facility was at that time the world’s second in size and in terms of the number of treatments just after the Swedish Hospital in Seattle under Belding Scribner.

Family life, pensioner, promotor

Alwall’s family life started quite late, because he was too much occupied with daily work. It was not until 1941 when, at the age of 37, he met Ellen Alströmer a 14 years younger cousin of a colleague. Ellen was by education English philologist and psychologist. The wedding was the same year and the marriage lasted 45 years. They had 3 children (born 1943, 1944 and 1947). Ellen was a great support and help to her husband owing to her knowledge of foreign languages. She had completed her doctoral studies and was active in her profession.

Nils Alwall retired in 1971, in accordance with the Swedish regulations at the age of 67, and had been assigned a retirement office in the hospital. He was involved in didactic, journalistic and scientific activities until the middle 1980s. He was also leading a group working on the epidemiology of pyelonephritis and hypertension in the population of approx. 5000 people in Southern Sweden. Moreover, he worked as a consultant in nephrology in the outpatient clinic in Malmö in the years 1973-1984. He worked also as a legal representative of patients with kidney diseases and his interpellations regarding insurance and reimbursement of organ’s donor, covering of the dialysis costs for patients staying abroad, reimbursement of the family care costs, preventive health tests or providing treatment outside own province – had all been approved. In 1965 Alwall established the Museum of the History of Medicine at the University of Lund.

Alwall was politically engaged in Social Democratic Party health activities, at that time the ruling party in Sweden. During many years he was president of the Institute of Adult Education where periodically he held popular science lectures. He served as scientific adviser on nephrology and as a chairman in the committee for the need and organization of renal care in Sweden during many years. He was also involved in the creation of International Society of Nephrology (ISN, founded in 1960) where he held leading positions (vice-president, president-elect, president, past-president) in the years 1969-1981, and of the European Dialysis and Transplant Association (EDTA founded 1964), serving as member of the board (1964-1967) and president (1970-1971). He founded the Swedish Society of Nephrology (1964) and was its chairman (1964-1971). His efforts led to creation of an official subspecialty of kidney diseases in Sweden (1964). The idea of a registry of renal replacement therapy within the EDTA was based on the Alwall’s register from the years 1946-1964. At the inauguration of Gambro Laboratory in Lund (given the name of Alwall Laboratory) in January 1985 (Figure 7) he said: “I feel like a helmsman who has sailed to the shore and wishes the crew good luck in the further sailing”.

The last public performance was as late as in October 1985 when he had a lecture on the history and development of dialysis at the ISAO congress in Chicago (16) and presented his own data from 1964 which had estimated the need for renal replacement therapy at a rate of 80 new patients/million population/year: this was close, to the present day estimations. A two months later he became ill, stopped driving the car. He arrived at the hospital where a young doctor wrote in Alwall’s chart: “he claims to be a retired professor of urology”. So short is public memory.

Alwall died suddenly the day after his admission, on February 2, 1986, of heart attack, and his ashes rest in the Lund cemetery. His last words to his bird-fan wife Ellen were: “Did you see the robin?”

Final remarks

Let us have a look backwards at the 72 years’ history of the development of dialysis treatment in medicine. Since the late 1970s there was an abrupt development of dialysis in the world. Strenuous Alwall’s efforts to increase the number of dialysis departments in Sweden (with present population of 9 million) led to opening of new dialysis units: 19 units with 98 dialysis sites were available in 1972, 32 units in 1982, and 65 units in 2016, with 4,000 patients with chronic renal failure treated with dialysis and another 5000 living with transplanted kidney.
Especially in the early decades, the Alwall’s role was enormous: he was a doctor extremely devoted to patients, an organizer, designer, scientist, and social activist at the same time. Alwall believed that any treatment, also dialysis, should be equally accessible to everyone. This humanitarian approach could be observed in his relations with patients: their good was always of primary concern, and the same attitude was demanded of his subordinate doctors. He never gave up, even though the help in his activities offered by his contemporaries was rather limited. Quite often he had to struggle against negative opinions expressed by recognized experts in nephrology who were ill-disposed to his ideas, and also had to cope with financial limitations. He published, alone or together with his collaborators, 203 scientific papers, without counting those written in Swedish. To resume, he was a man endowed with a vision of the future regarding further development of dialysis and kidney transplantation. Nobody was able to foresee as well as did Alwall the growing incidence of chronic renal failure secondary to diabetes mellitus, hypertension, congestive heart disease, chronic vascular disease, application of contrast media and antibiotics and other drug toxicities. The lack of dialysis facilities was a shock to politicians controlling allocation of funds for the development of health service.

Nils Alwall was a prominent figure in nephrology and medicine, he educated generations of doctors, 31 physicians received the degree of doctor of medicine (17), not only those from internal medicine (nephrology) but also specialists in radiology, surgery, and infectious diseases. This illustrates the scale of the challenge to various fields of medicine in connection with kidney disease, and of the attempts to meet it. Thanks to his personal talents, entrepreneurship, hard work, determination and humanistic approach Alwall was able to effectively promote his idea and vision of the crucial role of dialysis in the treatment of patients with renal failure, and to open the way to kidney transplantation.

Thanks to his work, thousands of patients with kidney diseases have had longer and more dignified life. It was not surprising that in Sweden he was given the nickname of “Man of Miracle”.

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