The arteriovenous fistula and the history of a forgotten pioneer

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ABSTRACT

Objective: The radiocephalic arteriovenous fistula (AVF), first introduced by Dr Kenneth Charles Appell, allowed for the provision of hemodialysis for patients with chronic kidney disease (CKD) and remains a reliable method for vascular access today. The purpose of this study is to review the contributions that led to the development of the AVF. We describe the work of Dr Appell, whose procedure bypassed the need for repeated cannulation in achieving vascular access, transforming the management of patients with dialysis-dependent CKD.

Methods: A literature search was conducted by searching “arteriovenous fistula,” “history of surgery,” “hemodialysis,” “vascular access,” “chronic kidney disease,” “repeated cannulation,” and “Kenneth Charles Appell” on PubMed, Embase, and Web of Science. Only articles written in English were considered.

Results: Before the arteriovenous fistula, glass cannulae were used for vascular access, beginning with Abel’s ‘vividiffusion’ apparatus in animals and Haas’s experimental dialysis on humans. The use of glass cannulae was continued by Kolff, who transitioned from venipuncture needles to glass cannulae. However, these attempts were complicated by thrombosis, excessive bleeding related to heparin use, and damage to vascular access sites from repeated cannulation. Arteriovenous shunts, using polytetrafluoroethylene tubing, were an improvement from previous attempts at vascular access, but were prone to local bleeding, shunt occlusion, phlebitis, cellulitis, and rarely lasted more than a few months. To address these challenges, Dr Appell created an upper extremity AVF, allowing for the provision of maintenance dialysis without externalized devices, repeated cannulation, and extensive anticoagulant administration. Despite Dr Appell’s vision and pioneering contributions to vascular surgery, he has received little credit for his work.

Conclusions: The enormous contribution by Dr Appell in the development of the AVF that transformed the modern management of patients with CKD is recognized in this review of the history of vascular access surgery for hemodialysis. (J Vasc Surg Cases Innov Tech 2022;8:688-92.)

Keywords: Arteriovenous fistula; Hemodialysis; Vascular access; Surgical history; Chronic kidney disease

The progression of chronic kidney disease (CKD) to end-stage renal disease (ESRD), characterized by the inability of the kidneys to sufficiently fulfill their physiological function, requires urgent life-saving intervention. Today, the most common and effective course of treatment for ESRD is renal replacement therapy, which includes peritoneal dialysis, hemodialysis, and kidney transplantation. Of these modes of treatment, hemodialysis is the most common, and, in 2018, accounted for 86% of the 131,449 incident renal replacement therapy treatments in the United States.

Even though dialysis was successfully performed in a clinical context as early as March of 1943 in the Netherlands, using an artificial kidney device designed by Dr Willem Kolff, it was the advent of the arteriovenous fistula (AVF), which anastomoses the radial artery to the cephalic vein, that allowed the consistent and reliable provision of maintenance dialysis to patients with CKD. Before the introduction of the radiocephalic AVF, attempts to provide dialysis to patients with CKD involved venous and arterial cannulation at the onset of each session of dialysis and were challenged by excessive bleeding, complications at the access site, and an inability to access the peripheral vasculature due to repeated cannulation. Even today, more than 56 years after the AVF was performed, the procedure remains a relatively robust method of attaining vascular access for long-term hemodialysis. Despite the fact that recent findings have suggested the need for follow-up interventions to maintain the patency of the AVF in response to fistula maturation, which is characterized by reduced blood flow, limited clearance, and thrombosis, the procedure continues to be a relatively reliable method of attaining vascular access in patients requiring...
maintenance dialysis. As the global prevalence of ESRD rises, in large part due to the increasing ubiquity of type 2 diabetes, reliable vascular access in hemodialysis continues to be an essential component of the successful management of this condition.

The development of hemodialysis to contemporary standards involved contributions from physicians, surgeons, and medical scientists around the world, each of whom incrementally improved the treatment to progressively mitigate its complications. In achieving reliable vascular access, a major and persistent challenge in the effective provision of hemodialysis, possibly the most significant innovation was made by a relatively unrecognized surgeon, Dr Kenneth Charles Appell (Fig 1). Despite pioneering the technique at the Veterans Administration (VA) Hospital in Bronx, New York, the procedure is often attributed, not to Appell, but to the internists Dr Michael J. Brescia and Dr James E. Cimino, who managed the patients Dr Appell operated on at the VA Hospital. In fact, the procedure is frequently referred to by the eponym “Brescia-Cimino fistula,” which excludes Appell, and thus fails to recognize his significant contributions to the technique. Seldom given credit for the procedure he developed, Dr Appell has proven to be a pioneer in vascular surgery due to his consequential work in improving vascular access in hemodialysis.

In this paper, we outline early challenges related to reliable vascular access for hemodialysis, describe advancements in hemodialysis and attempts to improve access, and describe the development of the AVF. We also discuss the pioneering work of Dr Kenneth Charles Appell, whose contributions to vascular surgery have resulted in significant improvements in the effectiveness and reliability of hemodialysis as a long-term treatment of ESRD.

**EARLY ATTEMPTS AT VASCULAR ACCESS AND THE USE OF GLASS CANNULAE**

Before dialysis was performed on human patients, in 1913, Dr John Jacob Abel created a “vividiffusion” apparatus, which consisted of two cannulae, one attached to an artery and the other to a vein, connected by a collodion tubing system containing serum or saline solution to allow for the diffusion of noxious substances. Building on Abel’s work on animals, Dr Georg Haas, a German physician, performed experimental dialysis on humans by using cannulae adjoined to the radial artery and the cubital vein. The cannulae were connected to a dialyzer that was constructed using three glass cylinders enclosing collodion tubes. Haas employed fractionated dialysis, a technique in which 400 mL of blood was withdrawn and dialyzed at a time, for a total of nine 30-minute courses of dialysis.

Haas’s efforts, which subsided as a result of limited interest in his work at the time, were continued by Dr Willem Kolff, who delivered 12 dialysis treatments to a 29-year-old female patient with congestive heart failure and uremic pericarditis. Although vascular access was initially achieved using venipuncture needles to withdraw blood from the femoral artery and reinfuse it into a vein, Kolff transitioned to the use of glass cannulae at separate arterial and venous cannulation sites. However, reliable access to the vasculature continued to cause problems for Kolff, whose technique of drawing blood from the radial artery using a glass cannula was time-consuming and caused significant complications, including thrombosis, which Kolff rectified by employing heparin. As Kolff describes in his 1965 paper, in which he details his early experiences with hemodialysis, he and his colleagues used a large amount of heparin, causing excessive bleeding in patients and obscuring vascular access. Unfortunately, Kolff’s difficulties with achieving dependable vascular access were compounded by the fact that drugs that known to reverse the effects of heparin, such as protamine sulfate, were not clinically safe to use at the time. Because these early attempts at dialysis involved the introduction and removal of glass cannulae during each procedure, each
subsequent dialysis damaged the vessels, hindering future access.\textsuperscript{16} The inability to gain vascular access without damaging the vasculature limited the use of hemodialysis to short periods of time.\textsuperscript{14}

**THE DEVELOPMENT OF ARTERIOVENOUS SHUNTS**

The next major advancement in vascular access came from the University of Lund in Sweden, where Dr Nils Alwall created an arteriovenous shunt by connecting arterial and venous cannulae using rubber tubes, coated with silicone, to prolong vascular access in hemodialysis.\textsuperscript{14} Like Kolff, Alwall employed heparin to maintain the patency of the shunt, but the length of patency was limited to a week or seven dialyses.\textsuperscript{16} Alwall’s method was discontinued because of a high risk of thrombosis and infection.\textsuperscript{14,15}

Alwall’s bypass method was further developed by Quinton et al,\textsuperscript{16} who used polytetrafluoroethylene tubing instead of glass to forego the use of heparin in preventing thrombosis. Quinton et al\textsuperscript{16} created an arteriovenous shunt from the radial artery to the cephalic vein that was externalized from the body and could be replaced by a dialyzer during dialysis treatments. Importantly, during the insertion of the cannulae, this technique involved the creation of a subcutaneous tunnel to allow for the puncture wound to be created at a site away from the cannulation site, reducing the risk of infection in relation to previously described procedures (Fig 2).\textsuperscript{15} This reduced propensity for infection, coupled with the fact that heparin and other anticoagulants were no longer required, allowed for longer term vascular access. By the time Quinton et al\textsuperscript{16} wrote about their progress for the American Society for Artificial Internal Organs in 1960, they had successfully dialyzed each of their first six patients, two of whom required longer term dialysis and were able to receive treatment without repeated attempts to access the blood vessels.

Despite these promising results, the arteriovenous shunts developed during this period preceding the advent of the radiocephalic fistula continued to cause problems. Often referred to by the eponym “Quinton-Scribner shunt,” the polytetrafluoroethylene shunt, though a marked improvement from its predecessors, was associated with complications such as local bleeding, shunt occlusion, decreased blood flow,\textsuperscript{16} dislodgement of the external component of the shunt, and distal limb ischemia.\textsuperscript{5} Although the risk of infection was reduced by the use of the subcutaneous tunnel, phlebitis and cellulitis still occasionally occurred at the cannulation site, leading to an elevated risk of septicemia and pulmonary emboli.\textsuperscript{17} These external shunts also typically only lasted for several months.\textsuperscript{17} To address the need for a method to attain high flow vascular access with minimal complications, a more reliable solution was still needed.

**THE ARTERIOVENOUS FISTULA AND THE CONTRIBUTIONS OF DR KENNETH CHARLES APPELL**

Driven by the prevalence of external shunt complications, physicians and surgeons at the VA Hospital in Bronx, New York, began exploring ways to use a fistula to connect arterial and venous blood in the forearm, instead of an external shunt.\textsuperscript{17} Before the creation of the AVF, Cimino and Brescia\textsuperscript{18,19} explored the use of simple percutaneous venipuncture to replace externalized shunts. Their procedure involved percutaneously accessing a forearm vein using a 12- to 16-gauge needle, connecting the needle to an artificial Kolff twin-coil kidney, and returning the dialyzed blood through another needle, most often to a vein in the ankle.\textsuperscript{18} Brescia and Cimino\textsuperscript{18} ensured that the veins remained patent using a sphygmomanometer, placed proximally to the puncture site, to apply approximately 70 mm Hg of pressure. Initial success was obtained using this procedure in patients who were overhydrated to achieve a state of hypervolemia,\textsuperscript{19} in order to meet the minimum blood flow of 200 to 400 mL per minute required for effective dialysis.\textsuperscript{18} However, the use of percutaneous venipuncture was limited by an inability to maintain adequate flow levels for extended periods of time in patients who were not hypervolemic.\textsuperscript{19}

The external arteriovenous shunt predated Appell’s attempts to use it to achieve reliable vascular access for maintenance dialysis. Appell was initially reluctant to create an internal fistula to replace the externalized Quinton-Scribner shunt due to the existence of clinical evidence that AVFs were associated with increased heart rate and cardiac output, hypertension, and heart failure.\textsuperscript{9,20,21} These concerns were assuaged when Appell encountered a 1961 Mayo Clinic report that detailed outcomes of a new procedure that involved the anastomosis of the femoral artery to the femoral vein in children with stunted limb growth.\textsuperscript{9,22} By creating an internal fistula, surgeons at the Mayo Clinic were able to improve blood flow and bone growth at the femur, while minimizing the hemodynamic and physiological changes that were previously described in the literature.\textsuperscript{9,12} In cases where heart rate and blood pressure did, in fact, increase,
surgeons were able to revert patients back to normal levels by ligating the fistulas. With growing confidence in the ability of hemodialysis patients to tolerate an autogenous AVF, Appell started the process of developing his procedure.

The potential cardiovascular complications associated with AVFs were not the only barriers of the implementation of the AVF. As Cimino and Brescia detail in their 1994 historical summary of the creation of the fistula, the team at the VA Hospital were also concerned about the possibility of reduced blood flow to the distal parts of the arm, when a radiocephalic fistula was created proximally. To address this concern, they decided to employ the Allen test, a technique initially created to assess ulnar artery thromboangiitis obliterans, before surgery to create the fistula, in order to determine whether there was sufficient blood flow through the palmar arches to compensate for impeded radial artery circulation. Radial artery blood flow was also maximized by using side-to-side anastomosis, a technique that maintains circulation distal to the anastomotic site.

The radiocephalic AVF was not immediately successful. In February of 1965, 1 year before Appell’s first documented success, his initial attempt resulted in insufficient blood flow in the fistula and thrombosis, due to the use of an insufficiently sized vein and the improper preparation of the patient before the procedure, causing hypovolemia and hypotension. Appell reattempted the procedure in 1966, this time using the cephalic vein on the radial aspect of the wrist to ensure adequate circulation through the fistula. The first successful iteration of the AVF involved administering local anesthesia, performing a 3-cm transverse incision in an area approximating the location of the radial pulse, and mobilizing the radial artery along with a nearby vein, using no. 00 silk loops. Then, smaller incisions, ranging from 0.3 to 0.5 cm, were made longitudinally on both of the mobilized vessels, followed by a side-to-side anastomosis, using running no. 0000000 arterial silk. Of the 16 patients under the care of the hemodialysis team at the Bronx VA Hospital, a radiocephalic fistula was successfully created in 13, and, as of July of 1966, these patients had received 800 (110 months-worth) total dialyses. By creating an upper extremity fistula, Appell managed to attain reliable vascular access and adequate blood flow without an external device or the use of anticoagulants.

The procedure gained widespread recognition after the team’s publication in the New England Journal of Medicine (Fig 3), the lead authors of which were Brescia and Cimino. As a result, the method was most attributed to the pair of internists who published the findings, whereas Appell, the surgeon who pioneered the fistula and performed the first successful surgery, received little recognition. To this day, the procedure is widely known by the eponym “Brescia-Cimino fistula,” whereas Appell’s contributions have remained little more than a footnote.

More recent studies have identified complications associated with the AVF, such as aneurysm, thrombosis, hand ischemia, carpal tunnel syndrome, endocarditis, bacteremia, reduced patency, dyspnea, and pulmonary hypertension. However, these sequelae are uncommon, and the AVF, introduced in the 1960s, remains the standard method of achieving long-term vascular access in patients with ESRD. This remarkable innovation represents a milestone in vascular surgery, and it was made possible by the contributions of many pioneering surgeons and researchers, including Dr Kenneth Charles Appell, whose work, though seldom recognized, has proven to be instrumental in the modern-day treatment of ESRD.

CONCLUSIONS

Before the conception of the AVF, the provision of maintenance dialysis to patients with ESRD was inhibited by the depletion of cannulation sites due to repeated attempts to gain vascular access. Limited to short periods of time, hemodialysis was unable to become a dependable and effective way to prevent mortality associated with renal failure. Many procedures preceded the AVF, but it was the adoption of an internal fistula to an upper extremity location by Dr Kenneth Charles Appell in the Veteran Administration Hospital in Bronx, New York, that transformed vascular access, by avoiding the need for repeated cannulation and minimizing complications. Through his elegant procedure, the underappreciated surgeon improved the quality of hemodialysis provided to patients around the world for decades to come.
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