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ON THE OCCASION OF THE 45TH ANNIVERSARY SINCE THE FIRST-EVER CROATIAN DIALYSIS PERFORMED IN RIJEKA IN 1962

U PRIGODI 45. OBLJETNICE PRVE DIJALIZE U
HRVATSKOJ IZVEDENE U RIJECI 1962.

Milan Zgrablić*

SUMMARY

The first section of this review summarises the development of dialysis in Europe since its first successes in the early 20th century, reminding the reader, however, that it took fifty years to achieve clinical success. The first successful dialysis in the former Yugoslavia was performed in Ljubljana, Slovenia in 1959.

The review continues with the chronicles, documents, and quotations describing the preparations started in Rijeka in 1961 to set up dialysis in Croatia. On 17 June 1962 the first successful procedure was performed. At the time, Europe counted no more than 44 dialysis centres. The Rijeka team included four physicians and one pharmacist. The dialysis practice and results over the first decade were published in seven articles and reviews. Furthermore, the Sušak Hospital of Rijeka became the reference centre for the former Yugoslavia, educating new people for new dialysis centres all over the country. This well-organised dialysis team later provided sound foundation for kidney transplants; the first procedure was performed in the same hospital in 1971.

Key words: History of medicine, 20th century, dialysis, Rijeka, Croatia

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HISTORICAL REVIEW

The history of dialysis starts with the year 1912 when Abel, Rowentree, and Turner came to an idea to pass urea and other low-molecular-weight substances through a semi-porous membrane and eliminate them from the blood of experimental animals. They constructed an apparatus which they called the *artificial kidney*. This primitive device consisted of colloid tubes for blood that were immersed in saltwater solution. To avoid clotting, the blood was added hirudin. The success of this procedure varied greatly, to say the least. In 1915 Hass constructed a similar apparatus, but he used heparin instead, which meant less problems with blood clotting. Followed new inventions and improvements by Necheles in 1923, Lims and Nyril in 1926. A breakthrough came with Thailhimer in 1938 when he first introduced cellophane tubes. However, all these attempts remained at the experimental level, which does not diminish the merits of these scientist and their contribution to progress, taking of course into account the available technology at the time.

In 1943, Kolff made the major breakthrough with his apparatus, which was the first successfully used in a human the following year. It consisted of 30 m long cellophane tubes coiled about and hanging from a horizontally positioned drum, and the whole set was immersed in electrolyte solution. Heparinised blood from punctured artery was pumped back into the body circulation. Successful application of this apparatus in a human was later to earn Kolff the title of the *father of artificial kidney*, even though people who followed such as Murray, Alwall, Merrill, Battezzati, Taddei, and Caporale constructed more advanced apparatuses. All these devices were based on the same simple principle: the difference in the concentration of certain substances in blood and dialysate enabled their elimination from the organism through a semi-porous membrane.

TYPES OF DIALYSIS

Countless attempts to remove harmful substances from the organism led to the development of alternatives to the experimental artificial kidney. Eventually two types of dialysis have taken root: peritoneal and extracorporeal.

Peritoneal dialysis is a way to remove substances from the organism using a cannula which is introduced into the abdomen to take in or out the dialysate, while the peritoneum serves as the semi-porous membrane.

It was first applied in a human by Gardner in 1933, who used two cannulas.

At the beginning, the dialysate was saline, and then it was replaced by Ringer's solution with 5% glucose. The method with two cannulas, termed *continuous*, was revised in 1940 by Maxwell, who introduced only one cannula into the abdomen to serve as "inlet/outlet", and the method was termed *intermittent*. In 1946, Abbott and Shea added magnesium, phosphates and calcium carbonate to the dialysate. The advantage of peritoneal dialysis is that it does not need an apparatus to be performed, but the downside is that it takes long (between 12 and 24 hours), it is exhausting, and brings the risk of infection.

Extracorporeal haemodialysis – or shortly *haemodialysis* – is a way to remove substances from the organism by pumping blood through a special apparatus called *artificial kidney*, using what were cellophane tubes back then. These cellophane tubes were immersed into a dialysate and served as the semi-porous membrane for the substances to be removed. This dialysis has proved far more practical than peritoneal, because it lasts much shorter (four to six hours), and patients find it more convenient, but it also requires the use of complex machines and trained staff to handle it.

DIALYSIS IN RIJEKA, THE FIRST EVER PERFORMED IN CROATIA

It took a while for the European dialysis centres to develop due to a number of professional and material difficulties. No wonder then that it took 15 years for dialysis to come to former Yugoslavia. The year 1959 saw the first use of Kolff's artificial kidney for haemodialysis in Ljubljana, Slovenia. Two years later (1961), the head of Urology of the Sušak Hospital in Rijeka, Dr Josip Zmajević, fully supported by the hospital's director Dr Ivo Mangan, managed to acquire a more advanced apparatus for haemodialysis, the first in Croatia.

It was a state-of-the-art Dogliotti-Battezzati-Taddei artificial kidney designed by the Turin University Hospital in 1958, but it was somewhat cumbersome to use. The apparatus consisted of two main parts. The first was a 120 x 60 x 40 cm box with two electrical pumps. One pumped blood into the cellophane tubes and back into the body and the other pumped the dialysate in the opposite direction from the tube flow. The second part was the *barrel* (a tub) holding 210 litres and measuring 75 cm in diameter that contained the dialysate and three double-walled Plexiglas cylinders.

Between the Plexiglas walls of each cylinder, seven meters of cellophane tubes were coiled to carry blood. The cylinders could be linked in series or in parallel, so that each could be accessed separately in case of emergency (if the tube broke or blood started to clot) without having to stop dialysis. Cellophane pores corresponded in size to those of the glomerules in the human kidney.

DIALYSIS PREPARATION AND PROCEDURE

For each type of dialysis preparations would take about 3-5 hours, including:

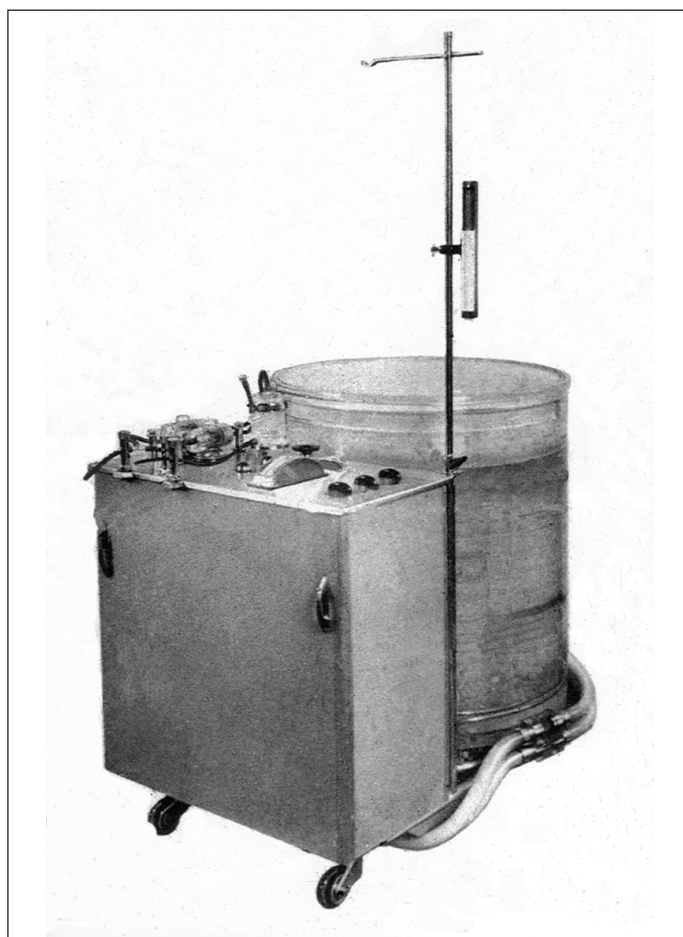
- gathering the team (four physicians, one pharmacist and two medical assistants)
- getting ready 1200 mL of blood matching in type and Rh factor, which meant collecting it from six to ten donors
- customizing the dialysate for each patient
- coiling three 7-metre cellophane tubes in the drums and connecting them
- setting up constant monitoring for the duration of dialysis.

The dialysis itself lasted four to six hours, during which time the team had to:

- add heparin to inflowing blood to prevent clotting and add protamine sulphate to outflowing blood to prevent bleeding in the organism
- check blood urea, creatinine, electrolytes, and coagulation time every half hour, and check the dialysate for the quantity of removed urea, creatinine, and electrolytes (especially potassium) at the end of dialysis, monitoring throughout the flow through the drums for possible ruptures of the cellophane tubing, and monitoring the colour of dialysate for bleeds or clotting in the cellophane tubes that might stop the flow in the cylinder.

THE TEAM

The first Croatian team to work with the artificial kidney was assembled by the Sušak Hospital director Dr Ivo Margan in consultation with



The first Dogliotti-Battezzati-Taddei type artificial kidney of the Sušak Hospital
Prvi umjetni bubreg sušačke bolnice tipa Dogliotti – Battezzati –Taddei

the head of Internal Diseases Clinic professor Silvijo Novak and head of Surgery Dr Vinko Frančišković. The team included:

- Dr Jerko Zec (team leader), DSc, surgeon and professor at Rijeka University School of Medicine, head of the School's Dialysis Center, and since 1971 head of the Dialysis and Kidney Transplantation Centre (the first of the kind in Croatia!). He died in 1992.
- Dr Milan Zgrablić (team leader assistant), DSc, internist, later specialised in nephrology, lecturer at Rijeka University School of

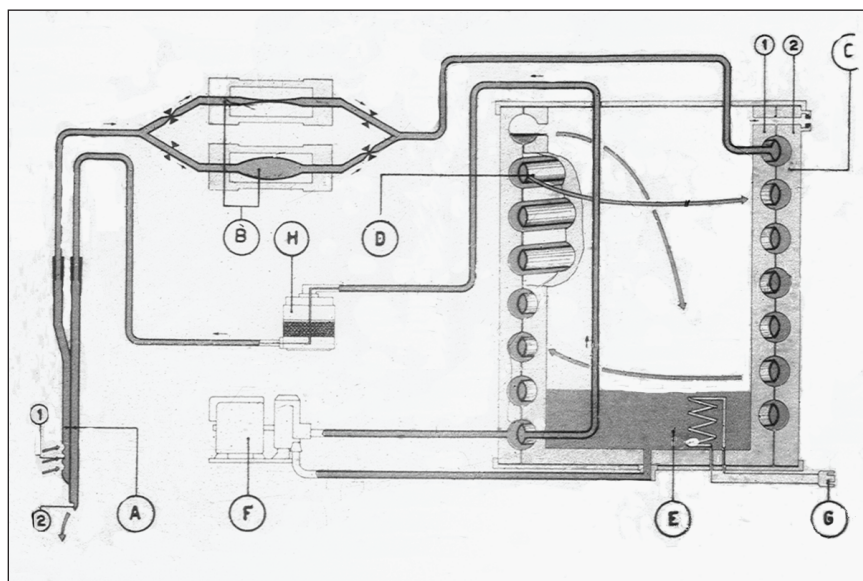


Diagram of the first artificial kidney of teh Sušak Hospital

Shema prvog umjetnog bubrega sušačke bolnice

Medicine, the founder of the School's Nephrology Dept. and of Nephrology ward within the Internal Diseases Clinic, head of peritoneal dialysis (also the first in Croatia!). He left the team in 1969, and retired in 1992.

- *Dr Dasen Razmilić*, surgeon, later specialised in urology, took additional training in Germany in 1966, assistant head and *oberartz* at the Urology Clinic in Heilbronn until 1984 when he returned to the Surgery Clinic of the Sušak Hospital in Rijeka. After the demise of Dr Zec in 1992, he took over the Dialysis and Transplantation Centre. Retired since 1997.
- *Dr Milan Prica*, DSc, internist, later specialised in gastroenterology, professor at Rijeka University School of Medicine, founder of the School's Gastroenterology Dept. and head of Gastroenterology ward of the Internal Diseases Clinic. Left the team in 1964. Died in 1996.
- *Davor Smokvina*, MPharm, pharmacist, later assistant lecturer at Rijeka University School of Medicine, founder of the modern

Clinical Laboratory in Rijeka and head of Laboratory Services of the Clinical Hospital Rijeka. Retired since 1992.

- Ankica Tomljanović, theatre nurse, full and active dialysis team member.

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Service des Maladies Métaboliques
et Rénales

Professeur J. TRAEGER
Médecin Adjoint : Docteur D. FRIES

Lyon, le 12 juin 1965

Docteur Milan ZGRABLIĆ

Cher Ami,

Voici le nom et l'adresse du fabricant de l'appareil d'hémodialyse :

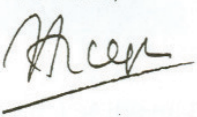
SWEEDEN FREEZER Manufacturing company
Seattle Artificial Kidney supply division
3401 - 17th Avenue West
SEATTLE 99
Washington, U.S.A.

Le nom et l'adresse du représentant, en Hollande, est

Robert HILEKEP
9, Sarphatistraat
AMSTERDAM, Hollande

Les appareils de perfusion sont des appareils fabriqués par la Maison
BRAUN en Allemagne. Le représentant en France est les Etablissements ROUCAIRE.
Etablissements ROUCAIRE
21, rue des Favorites
PARIS 15^e

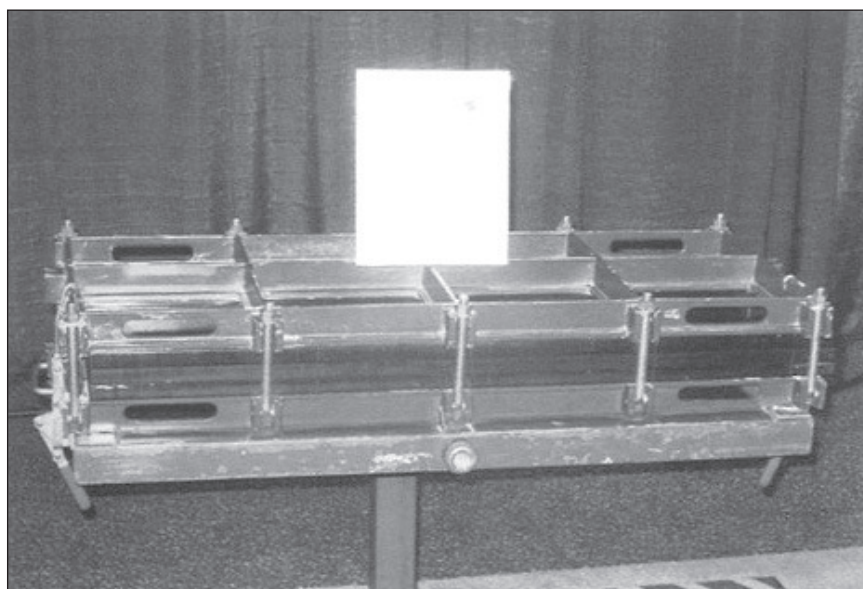
J'ai été très heureux de vous rencontrer à Zagreb et je vous prie de
croire à mes sentiments très amicaux.

Pr. J. TRAEGER,


H. C. L. N° 84 83 - 2-1965

Correspondence between professor Trager and Dr Zgrablić about the Kill dialyser

Korespondencija prof. Trager – dr. Zgrablić o Killovu dijalizatoru



Kill dialyser

Killov dijalizator

This team visited the Ljubljana Dialysis Centre and received additional dialysis training abroad; Jerko Zec and Davor Smokvina went to Padua, Italy, and Milan Zgrablić to Lyon, France.

DEVELOPMENT AND MILESTONES

As early as 1962, the team made experimental dialyses in nine dogs with a high degree of success. On 17 June 1962, the first haemodialysis in a uraemic patient was performed at the Sušak Hospital Surgery Clinic – the first ever in Croatia!

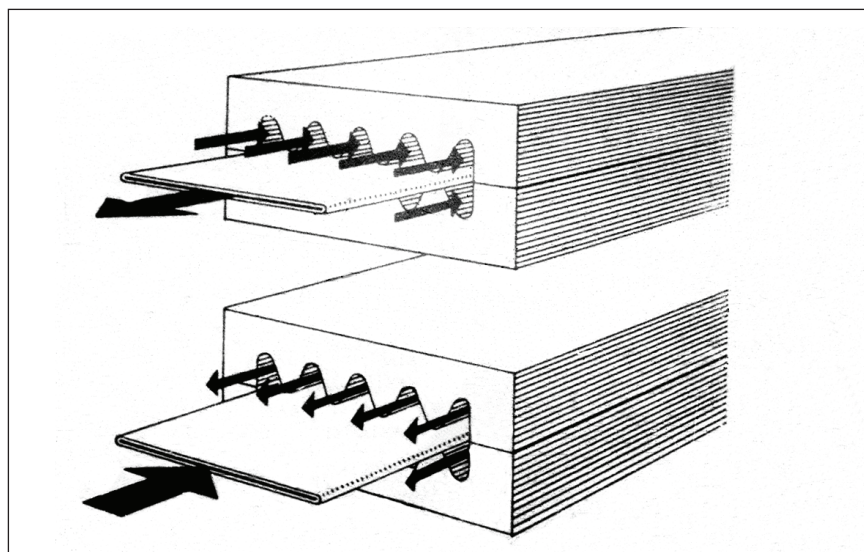
According to later classification, it was the so-called *single-session* or *acute dialysis* that lasted six hours. The dialysis was led by Dr Jerko Zec, and the physicians Boško Čorak and Nikola Zaninović connected the apparatus to the patient's saphenous vein. In the early period, only these acute dialyses were performed.

After the successful start of the dialysis team, on 20 September 1962, hospital director Dr Ivo Margan sent an elaborate letter to all healthcare institutions in Croatia informing them about the possibility to treat renal insufficiency by haemodialysis.

No later than the New Year's Eve of 1963, the first 12-hour peritoneal dialysis was performed in a uraemic patient at the Sušak Hospital Surgery Clinic under the supervision of Dr Jerko Zec. Again the first of the kind in Croatia! Dr Igor Pakušić introduced the cannula into the patient's abdomen. Later peritoneal dialyses were performed at the Internal Diseases Clinic and were led by Dr Milan Zgrablić, who was assisted by physicians Zdravka Kolacio and Mira Sever-Prebelić.

In July 1964, Dr Milan Zgrablić brought from Lyon the so-called Quinton-Scribner AV shunt, a U-shaped, Teflon-coated silastic tube for arteriovenous connection. Difficulties with supply of this shunt were overcome after a brief correspondence between Dr Zgrablić and professor J. Treger from Lyon. With its first successful use in 1965., the shunt restored the dominance of haemodialysis over peritoneal dialysis.

After some practice, the shunt made it possible to perform the first Croatian multi-session dialysis in a patient suffering from chronic renal insufficiency. Not only did this save the lives of patients, but it also improved their quality of life. Again, the procedure was led by Dr Jerko Zec. This success is particularly worth the mention, as only 44 dialysis centres provided multi-session dialysis in Europe at the time, and had the capacity to treat no more than 1600 patients altogether.



Cross section of the Kill dialyser

Shema (prerez) Killova dijalizatora

After the Lyon experience, another novelty was introduced in 1966; it was the Kill dialyser which significantly simplified haemodialysis and increased its modes of use. It consisted of two-layer, finely corrugated 80x50x10 cm Plexiglas panels with two-layer cuprophane PT 125 membranes placed between them. Their major advantage was that the space between the membranes did not have to be filled up with blood before dialysis, that is, donated blood was no longer necessary. This procedure was run by Dr Jerko Zec and Dr Milan Zgrablić.

In May 1967, Dr Zec introduced another major improvement; he replaced the old external AV shunt with a subcutaneous AV connection called “Brescia-Cimino AV fistula” launched in 1966. With the acquisition of a new, smaller MacNeill-Collins dialyser, the hospital became a modern dialysis centre that trained new people for dialysis centres opening all over the country. This new centre counted seven dialysis beds for chronic patients and two beds for acute treatment for all types of renal failure. The first head of the centre was Dr Jerko Zec.

In 1971, the team of the Sušak Hospital Surgery Clinic, led by professor Vinko Frančičković, successfully performed the first kidney transplant procedure in Croatia and former Yugoslavia, and from that point on, the dialysis centre also served as the prep stage for kidney transplants.

DISSEMINATION OF KNOWLEDGE AND ACHIEVEMENTS

The pioneering efforts, and later valuable experience of the first Sušak Hospital dialysis team were the key reasons that the hospital and its Dialysis Centre over the first ten years of activity became the source of knowledge and training for other hospitals of the former Yugoslavia, and particularly Croatia, including Zagreb. The Sušak Dialysis Centre trained hundreds of physicians and other medical staff, and Sušak physicians would often open new dialysis centres all over the country, training their staff on the spot.

The team as a whole or its members would present their experiences and successes in a number of scientific and professional meetings and published a total of seven papers [1-7].

This first team also raised a new generation of highly trained professionals who continued and broadened the scope of the Dialysis and Transplantation Centre.

CONCLUSION

All of the above had to be said while there are still live witnesses of what was going on, who can make sure that future records do not misinterpret or neglect these facts.

The success of the first team of nearly a half a century ago was a remarkable scientific and professional contribution to the development of medicine in Croatia, one of team's achievements being nearly 100% success rate in the treatment of uraemia, once a lethal condition. Since then, dialysis had developed into a preparatory stage for kidney transplant, being the only method for the organ transplant from a dead or live donor.

17 June 1962 should be written in gold letters in the history of medicine, not only of the Rijeka hospital or the town, but also of the entire nation and southeast Europe. This date is not only a historical milestone, but also a turning point for thousands of patients who have been given new life. All the more so as the entire Europe counted no more than 44 dialysis centres at the time (today there are over 600) and that the Sušak centre in no way lagged behind them. Moreover, without these achievements in dialysis there would have been no room for yet another important milestone in the history of the Sušak Hospital Surgery Clinic – kidney transplant, the first performed by a new team in 1971.

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SAŽETAK

U prvome dijelu prikaza autor rezimira razvoj dijalize u Europi od prvih pozitivnih rezultata s početka XX. stoljeća te podsjeća da se njezina uspješna klinička primjena postiže tek pedesetak godina poslije. Prva dijaliza na prostorima bivše Jugoslavije izvedena je 1959. u Ljubljani.

Slijede prisjećanja popraćena relevantnim dokumentima i citatima o pripremama za primjenu dijaliza u Hrvatskoj, koje su započele u sušačkoj bolnici u Rijeci 1961., a prva dijaliza izvedena je 17. lipnja 1962. godine. U to doba u Europi su postojala samo 44 centra za dijalizu. Riječku ekipu sačinjavala su četiri liječnika i jedan farmaceut. O radu i rezultatima tijekom prve dekade djelovanja objavljeno je sedam članaka i prikaza. Uz to, sušačka bolnica u Rijeci postala je i referalni centar za tadašnju državu, u kojem se educiralo osoblje za nove centre iz cijele zemlje. Uspješno organizirana služba dijalize bila je poslije i preduvjet usvajanja transplantacije bubrega, koja je isto tako prva uspješna u Jugoslaviji izvedena 1971. u istoj bolnici.

Ključne riječi: *povijest medicine, XX. stoljeće, dijaliza, Rijeka, Hrvatska*