Inflammation

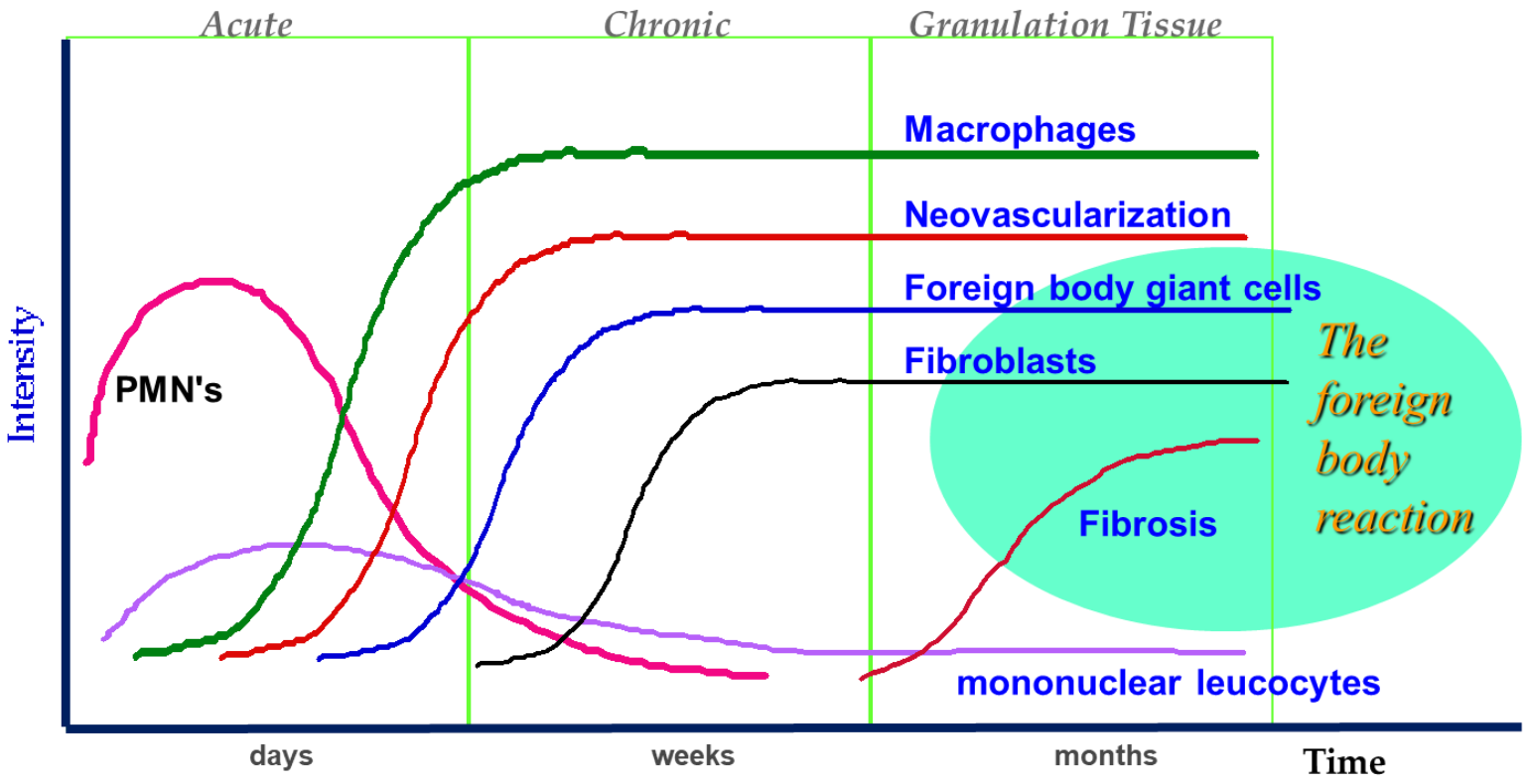
Normal response of the body to injury in vascularized tissue. When the injury is healed, the inflammatory process ceases.

Foreign Body Reaction

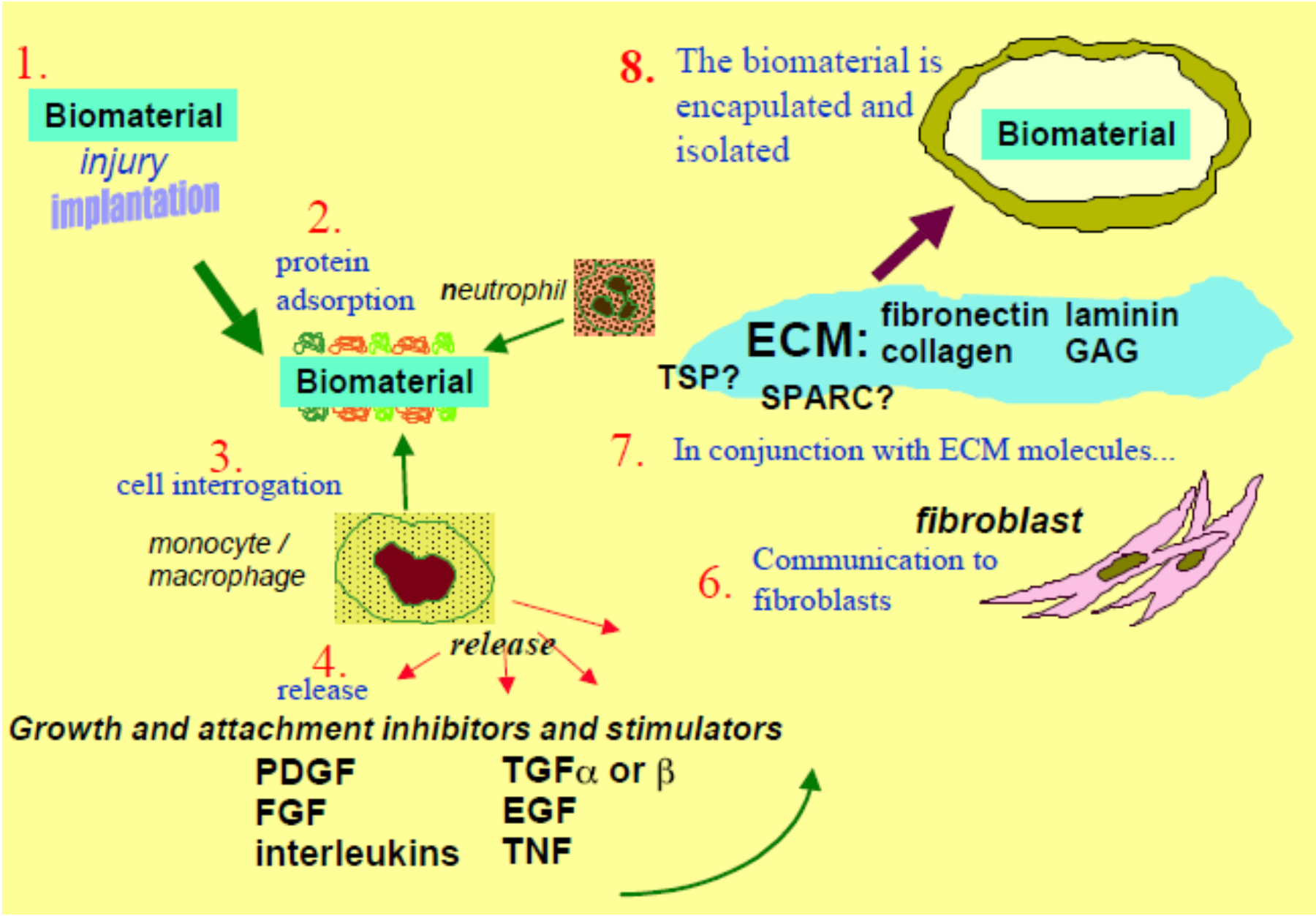
When the inflammatory reaction cannot be resolved, i.e., the body can't heal the "injury" (an implanted foreign object), the foreign body reaction is observed. This reaction is characterized by:

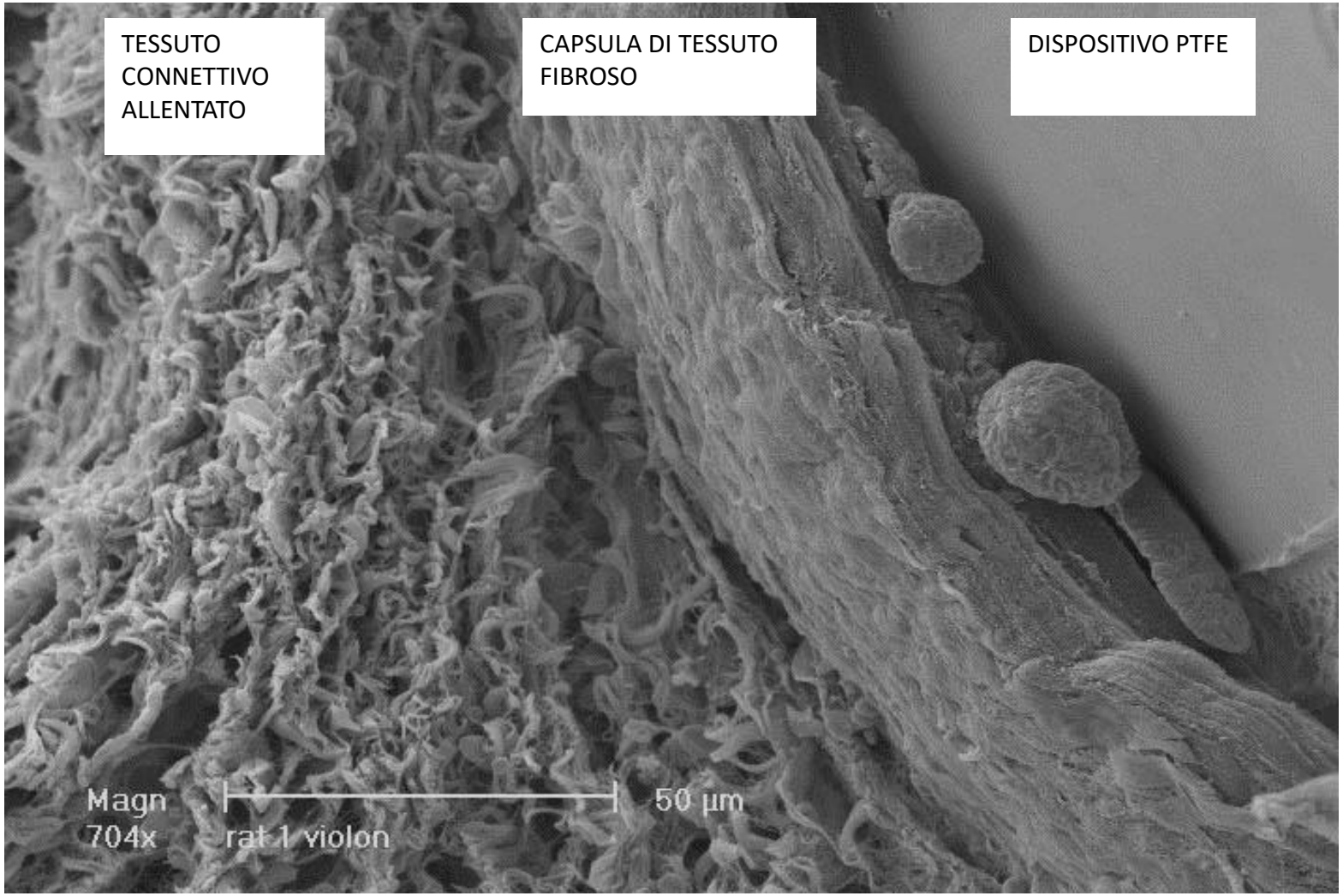
- foreign body giant cells
- a fibrous capsule
- mildly active inflammatory cells at the implant surface, even after years of implantation

temporal events in the inflammatory response
Foreign Body Reaction



Incapsulamento del biomateriale per reazione a corpo estraneo





Dispositivo sub cutaneo impiantato in topo dopo 6 settimane

Lo spessore della capsula dipende dal tipo di materiale
e dal movimento relativo all'interfaccia impianto/tessuto

The Kidneys

One major function of healthy kidneys is removal of the end products of protein metabolism. Every 24 hrs. they must remove:

~15 g of urea

~ 3 g of creatinine

~ 1 g of uric acid

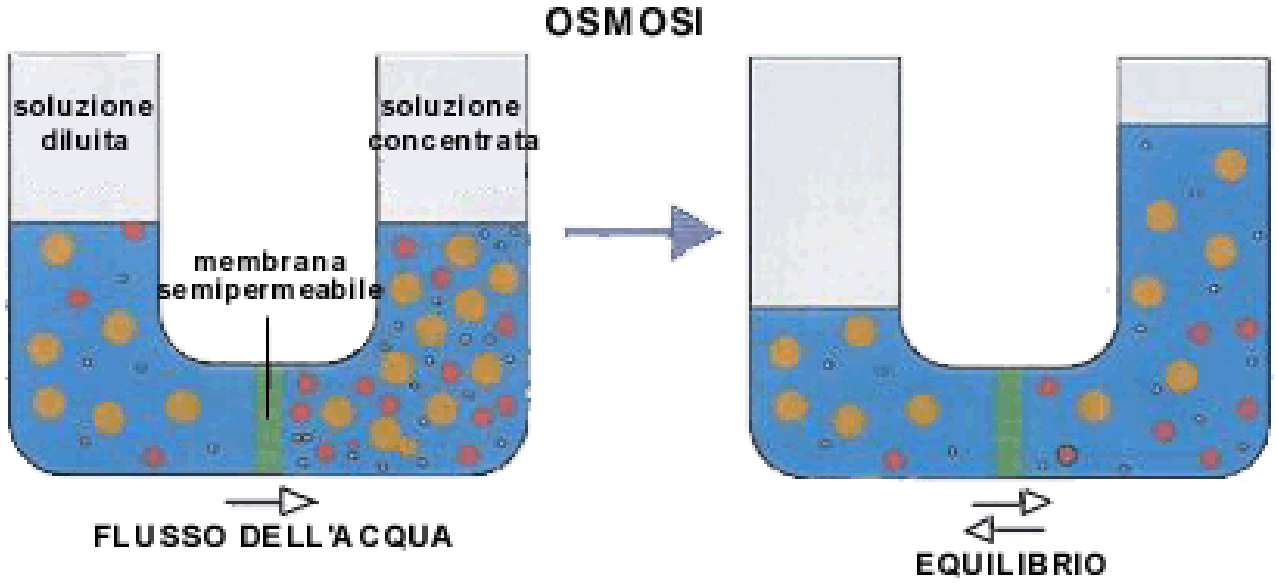
- The kidneys also balance electrolytes, remove fluid, and produce several hormones.

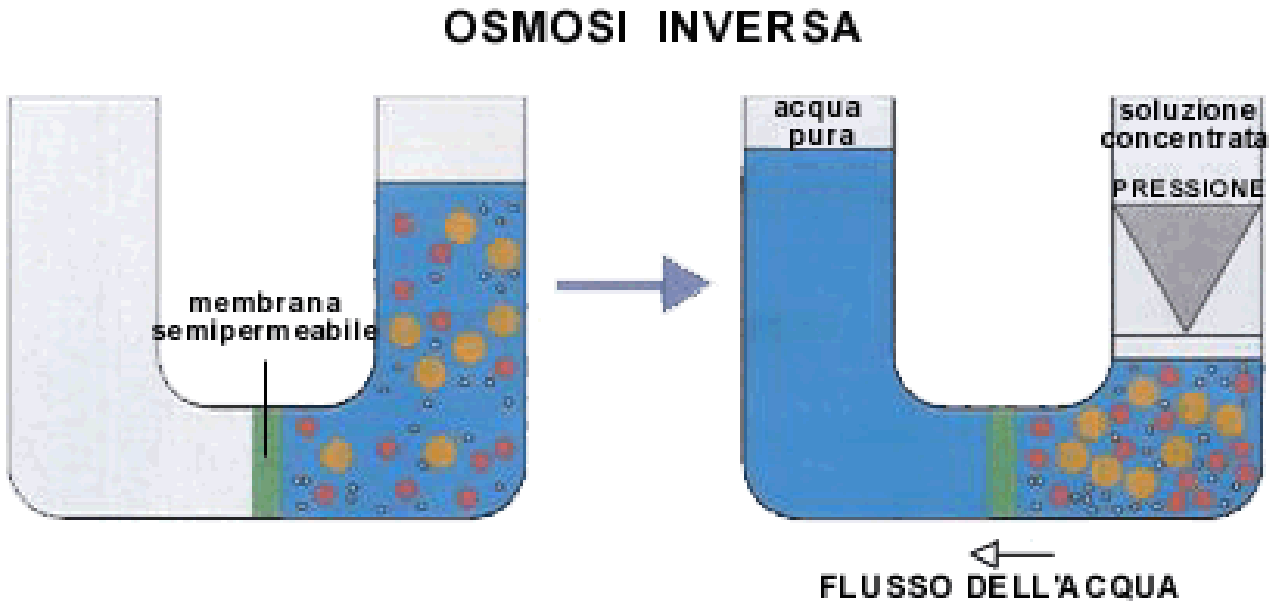
Mannekin-Pis
Brussels, Belgium

La **DIALISI** è un procedimento fisico con cui si separano una o più sostanze disciolte in un liquido, utilizzando una **membrana semipermeabile** che permette il passaggio selettivo di alcune molecole.

Il moto delle sostanze è di tipo diffusivo, dovuto, cioè, alla **differenza di concentrazione** dei soluti nel solvente nei due comparti, e cessa una volta raggiunto l'equilibrio. Tra solvente e soluto è importante il contributo dato dalla *pressione osmotica* (vedi **osmosi**).

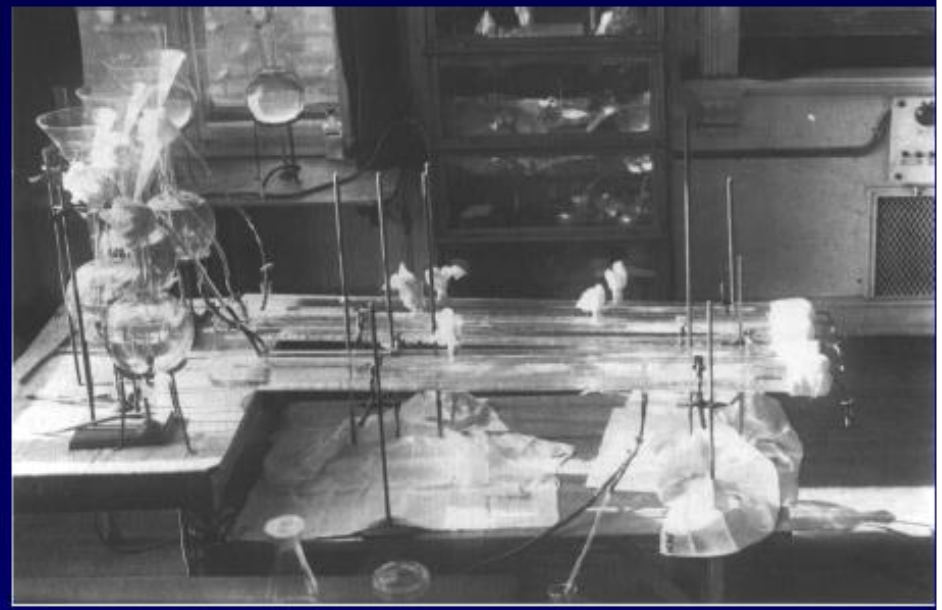
Anche il **gradiente di pressione** influenza il moto delle sostanze tra i due comparti, purché sia accettabile (o addirittura voluto, come in emodialisi) il passaggio di solvente dal comparto sottoposto a pressione maggiore all'altro.





Giessen 1924 – Georg Haas esegue la prima dialisi sull'uomo

Abb. 5 Glasbehälter mit Kollodiumschlauchpaar nach G. Haas.



Tab. 2 Georg Haas. Seine Schriften zur Hämodialyse

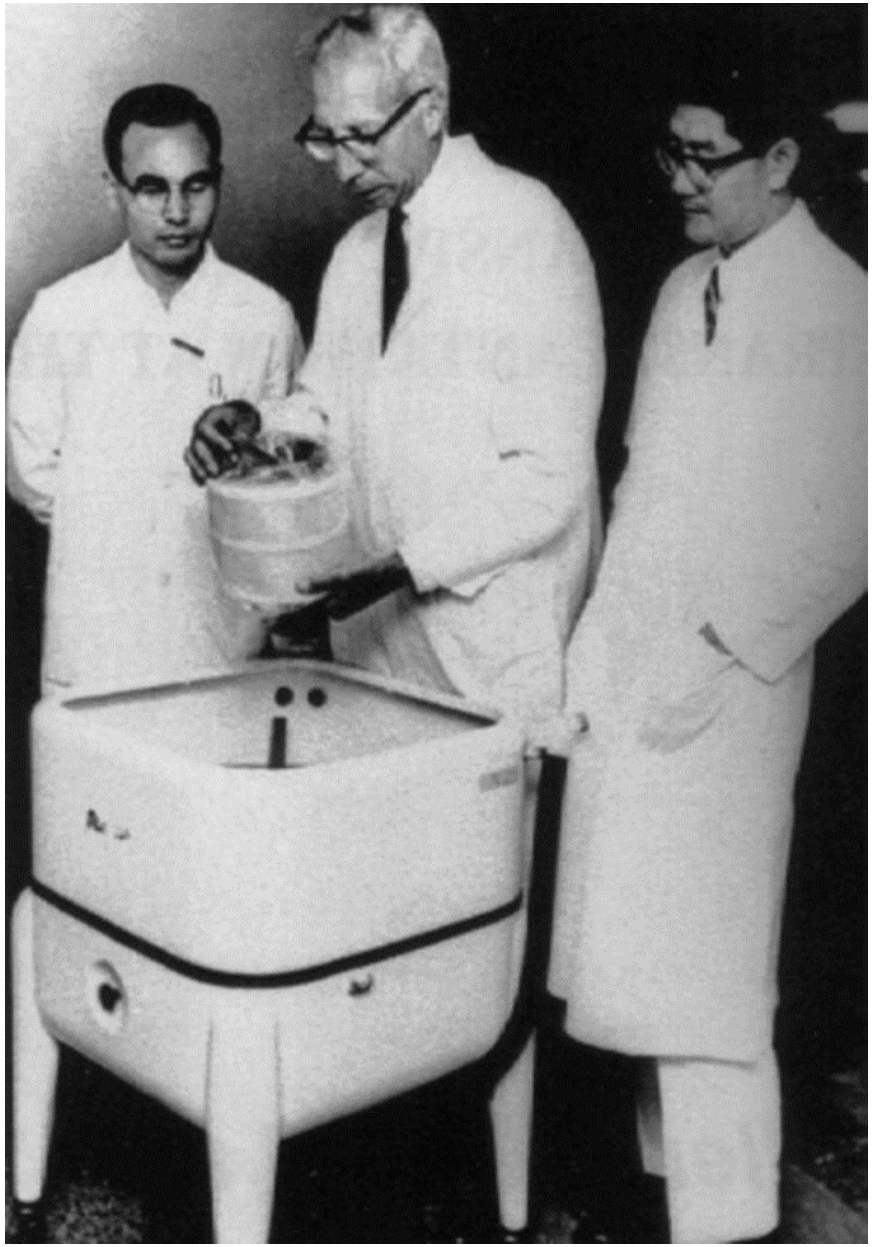
1923	Dialysieren des strömenden Blutes am Lebenden. Klin Wschr, Jhg. 2, Nr. 41, 1888, 1923
1925	Versuche der Blutauswaschung am Lebenden mit Hilfe der Dialyse. Klin Wschr, Jhg. 4, Nr. 1, 13–14, 1925
1926	Über den Versuch der Blutauswaschung am Lebenden mit Hilfe der Dialyse. I. Mitteilung. Archiv für Experimentelle Pathologie und Pharmakologie, 116, H. 3/4, 158–172, 1926
1927	Über Versuche der Blutauswaschung am Lebenden mit Hilfe der Dialyse. II. Mitteilung. Archiv für experimentelle Pathologie und Pharmakologie, 120, H. 5/6, 371–386, 1927
1928	Über Blutwaschung. Klin Wschr, Jhg. 7, Nr. 29, 1356–1362, 1928

The Artificial Kidney

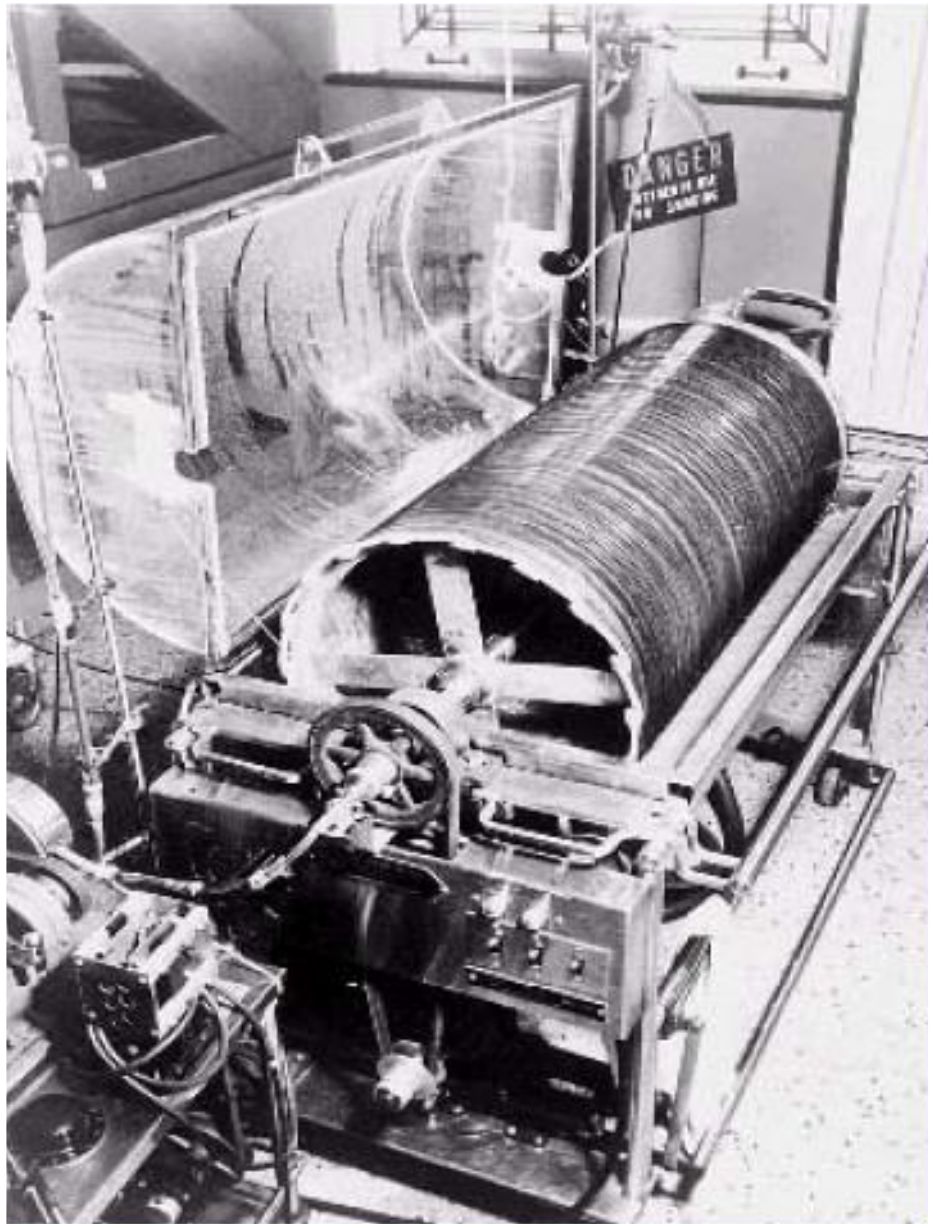
Kidney failure, through history, was a sentence to an unpleasant death lasting about a month. In 1910, at John Hopkins University (Baltimora, USA), the first attempts to remove toxins from blood were made by J.J. Abel. The experiments were with rabbit blood, and it was not possible to perform this procedure on humans.

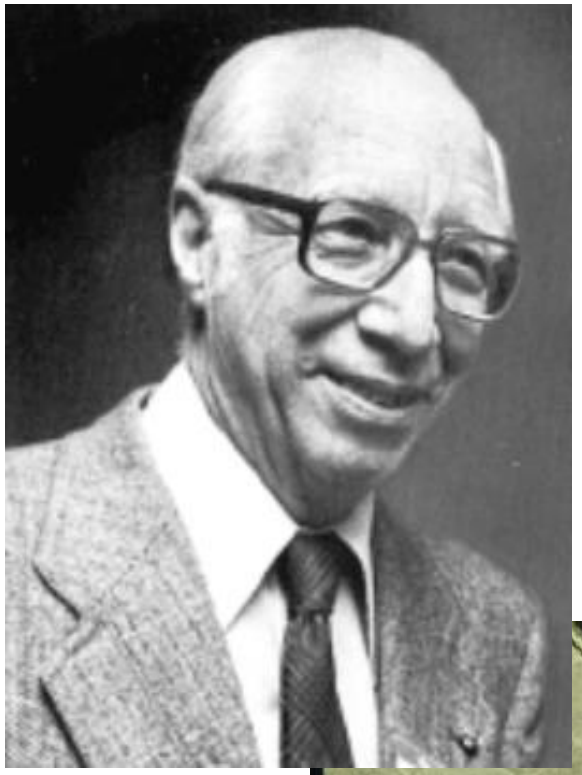
In 1924 George Haas performed the first dialysis experiments on humans.

1943, in Nazi-occupied Holland, Willem Kolff, a young physician, built a drum dialyzer system from a 100 liter tank, wood slats, and 130 feet of cellulose sausage casing tubing as the dialysis membrane. Some successes were seen in saving lives where before the outcome was only one unpleasant. Kolff took his ideas to USA and in 1960, at the Cleveland Clinic, developed a “washing machine artificial kidney”.

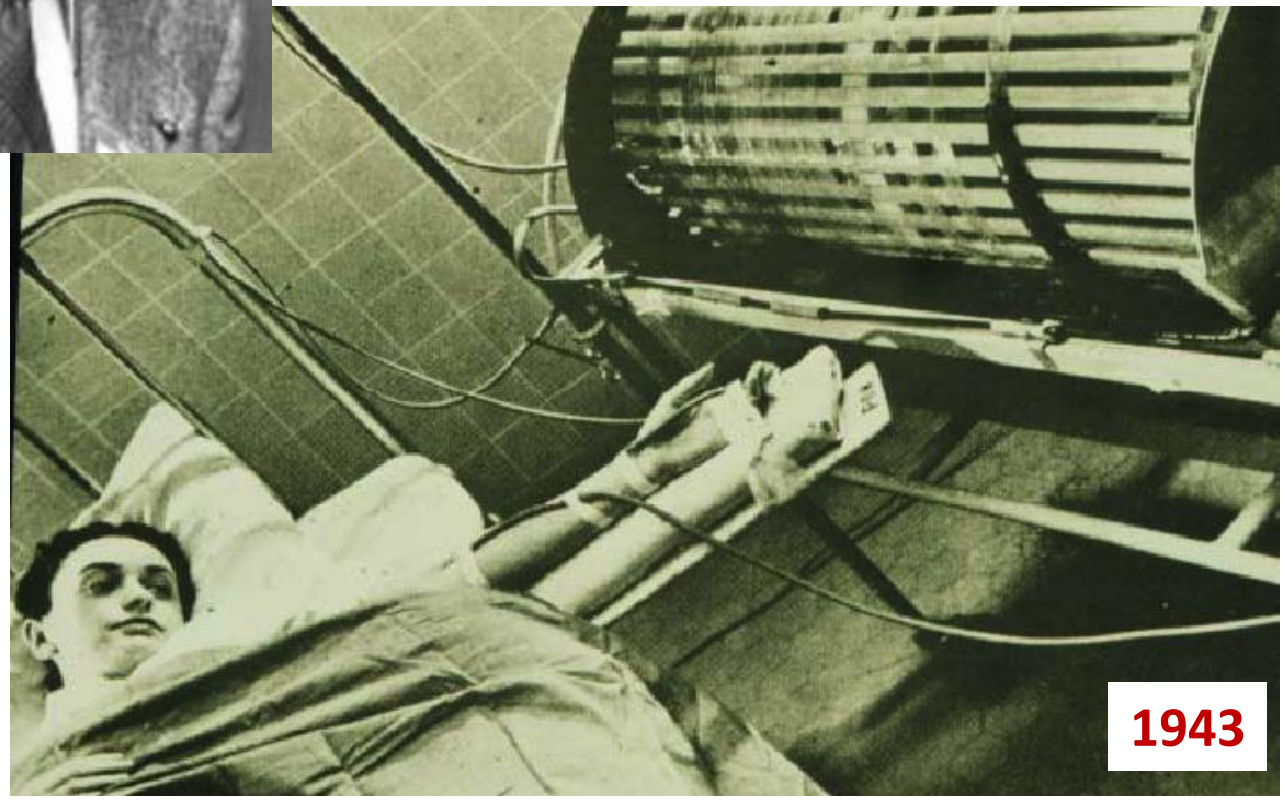


Willem Kolff (center) and the washing machine artificial kidney.





Willem Kolff



DIALISI OGGI

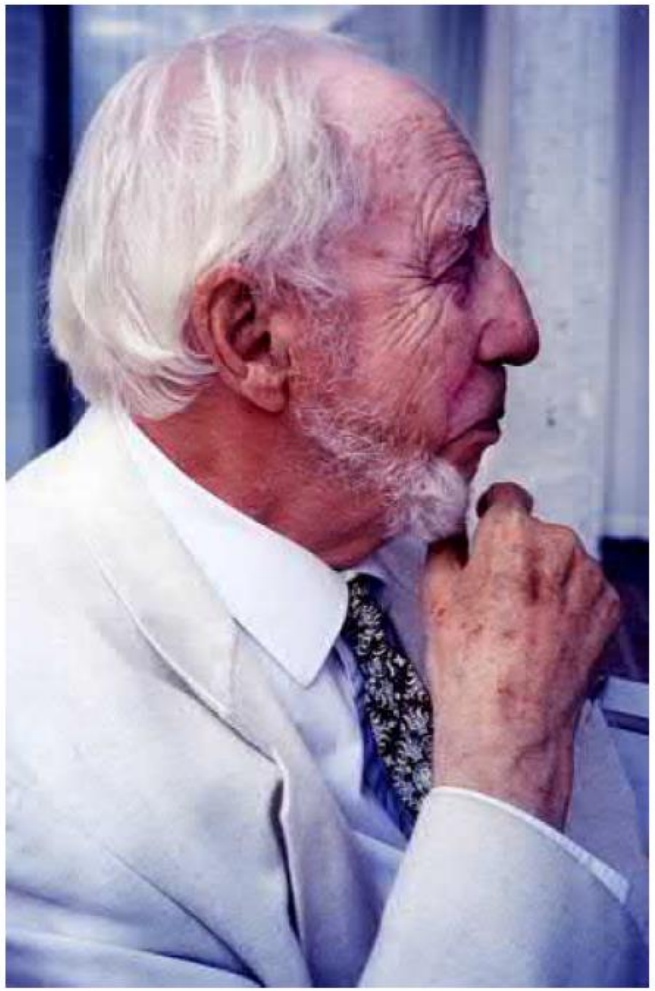
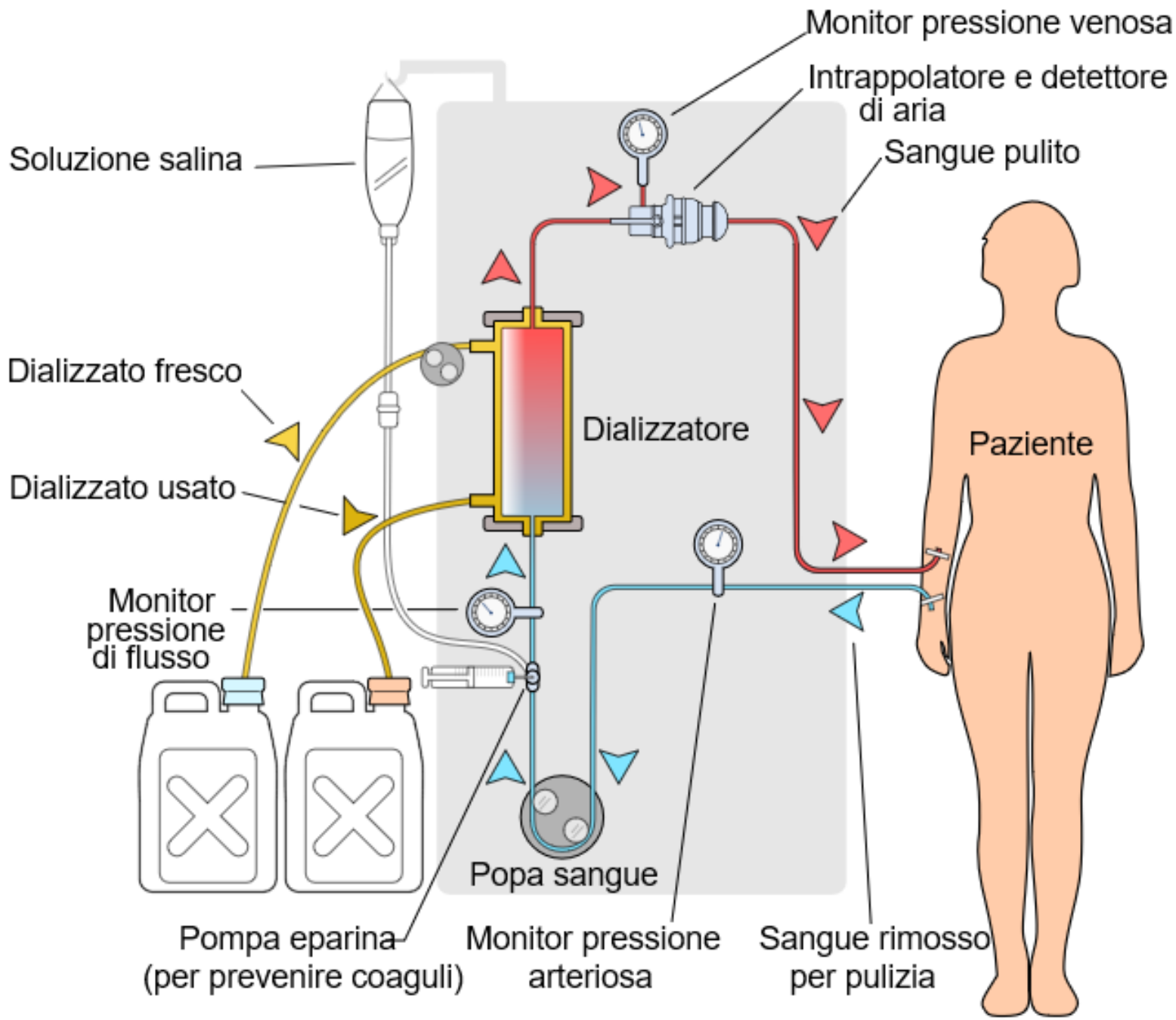
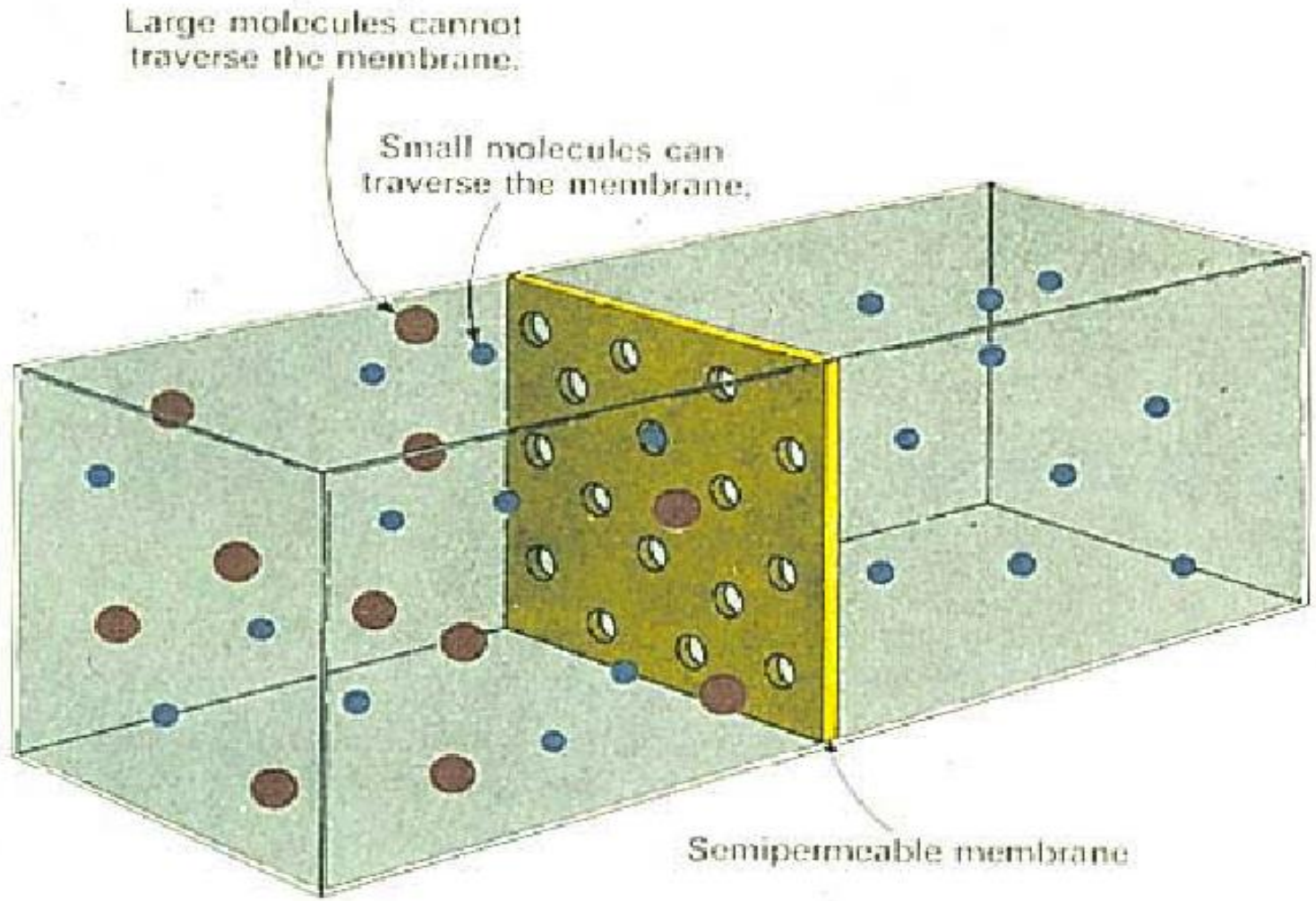


Figure 1.1.2.4 Dr. Willem Kolff at age 92. (Photograph by B. Ratner.)


Monitor pressione venosa
Intrappolatore e detettore di aria
Sangue pulito
Soluzione salina
Dializzato fresco
Dializzato usato
Dializzatore
Paziente
Monitor pressione di flusso
Popa sangue
Pompa eparina (per prevenire coaguli)
Monitor pressione arteriosa
Sangue rimosso per pulizia

Separation of molecules on the basis of size by dialysis

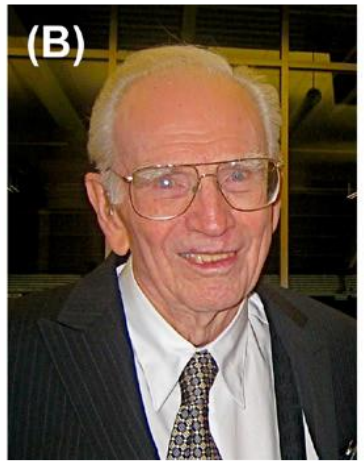


Major advances in kidney dialysis were made by Dr. B. Scribner (Univ. of Washington, Seattle, USA), who devised a method to routinely access the bloodstream for dialysis treatments. Prior to this, after just a few treatments, access sites to the blood were used up and further dialysis was not possible.

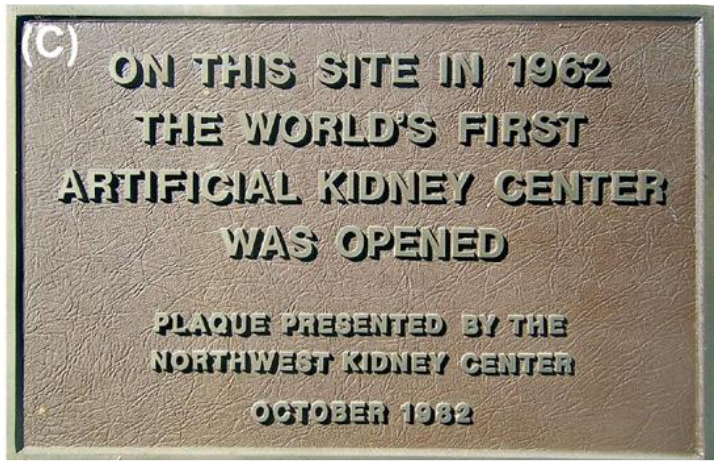
After seeing the potential of dialysis to help patients, but only acutely, Scribner tells the story of waking up one night with an idea to gain easy access to the blood, a shunt implanted between an artery and vein that emerged through the skin as a "U." Through the exposed portion of the shunt, blood access could be readily achieved. When Dr. Scribner heard about the new plastic, Teflon®, he envisioned how to get the blood out of and into the blood vessels. His device, built with the assistance of W. Quinton, used Teflon tubes to access the vessels, a Dacron® sewing cuff through the skin, and a silicone rubber tube for blood flow.

PTFE	PET	PDMS
TEFLON	DACRON	SILASTIC

Belding Scribner



Wayne Quinton



Plaque commemorating the original location in Seattle of the world's first artificial kidney center.

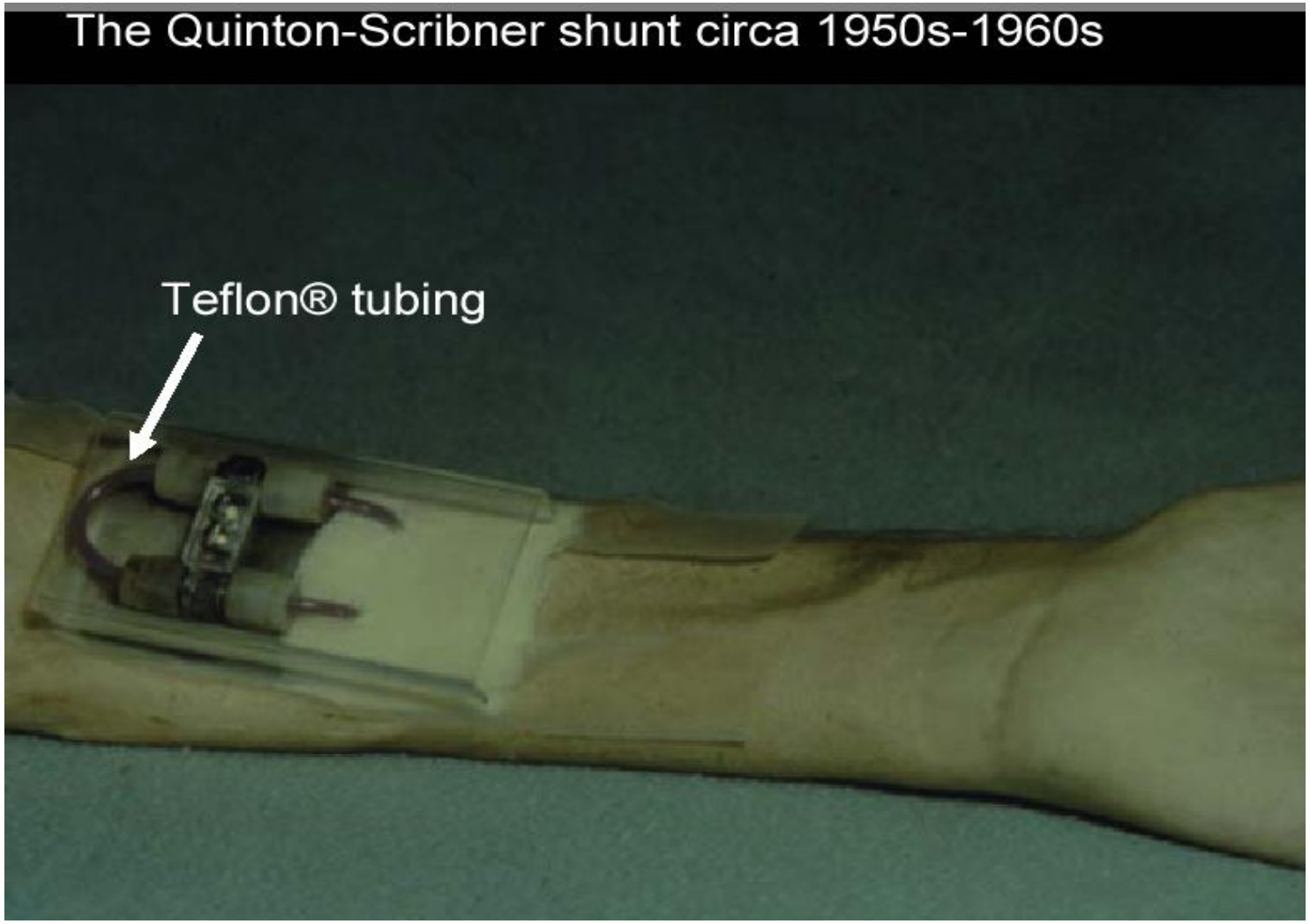
The Quinton– Scribner shunt made chronic dialysis possible, responsible for more than a million patients being alive today. Interestingly, Dr. Scribner refused to patent his invention because of its importance to medical care.

Additional important contributions to the artificial kidney came by Chem. Eng. Prof. Les Babb (Univ. of Washington) who, working with Scribner, improved dialysis performance and invented a proportioning mixer for the dialysate fluid. The first dialysis center was opened in Seattle making use of these important technological advances. The early experience with dialyzing patients where there were not enough dialyzers to meet the demand.

Prima dell'invenzione della **fistola di Cimino-Brescia**, l'accesso vascolare utilizzato per la dialisi era lo shunt di Scribner, un tubicino in teflon esterno all'arto che metteva in comunicazione arteria e vena mediante un tip terminale rigido fissato chirurgicamente su ciascuno

dei vasi.

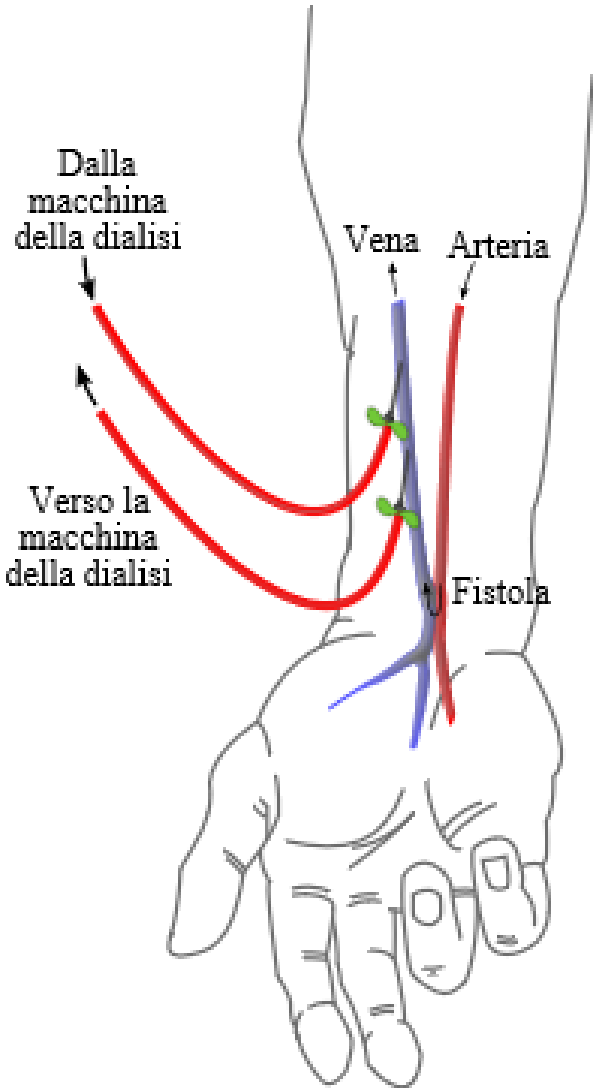
Durante la dialisi il sangue arterioso era così messo in comunicazione con il circuito di dialisi, mentre fra un trattamento e l'altro si ripristinava la comunicazione artero-venosa collegando i rami dello shunt.

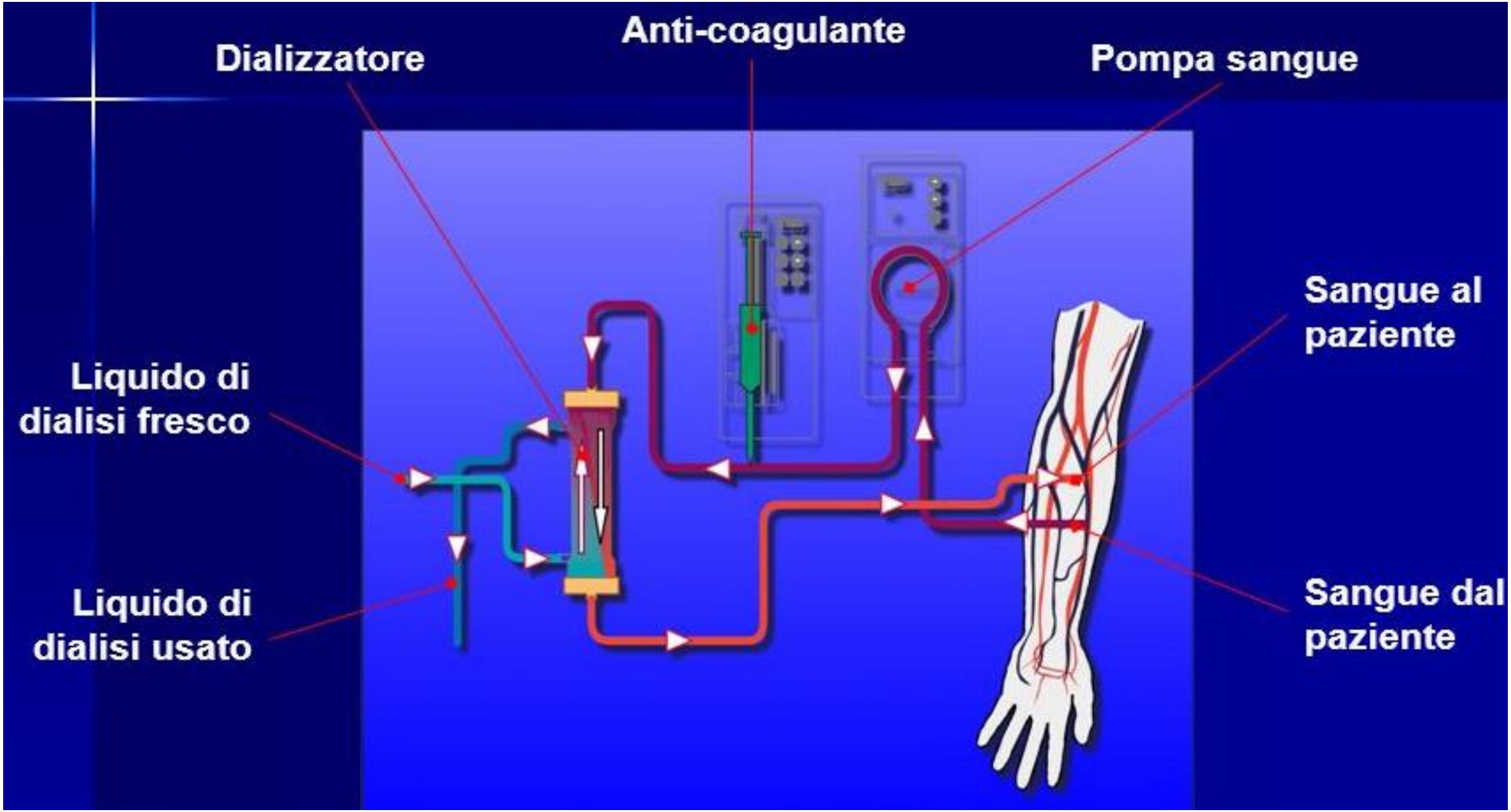


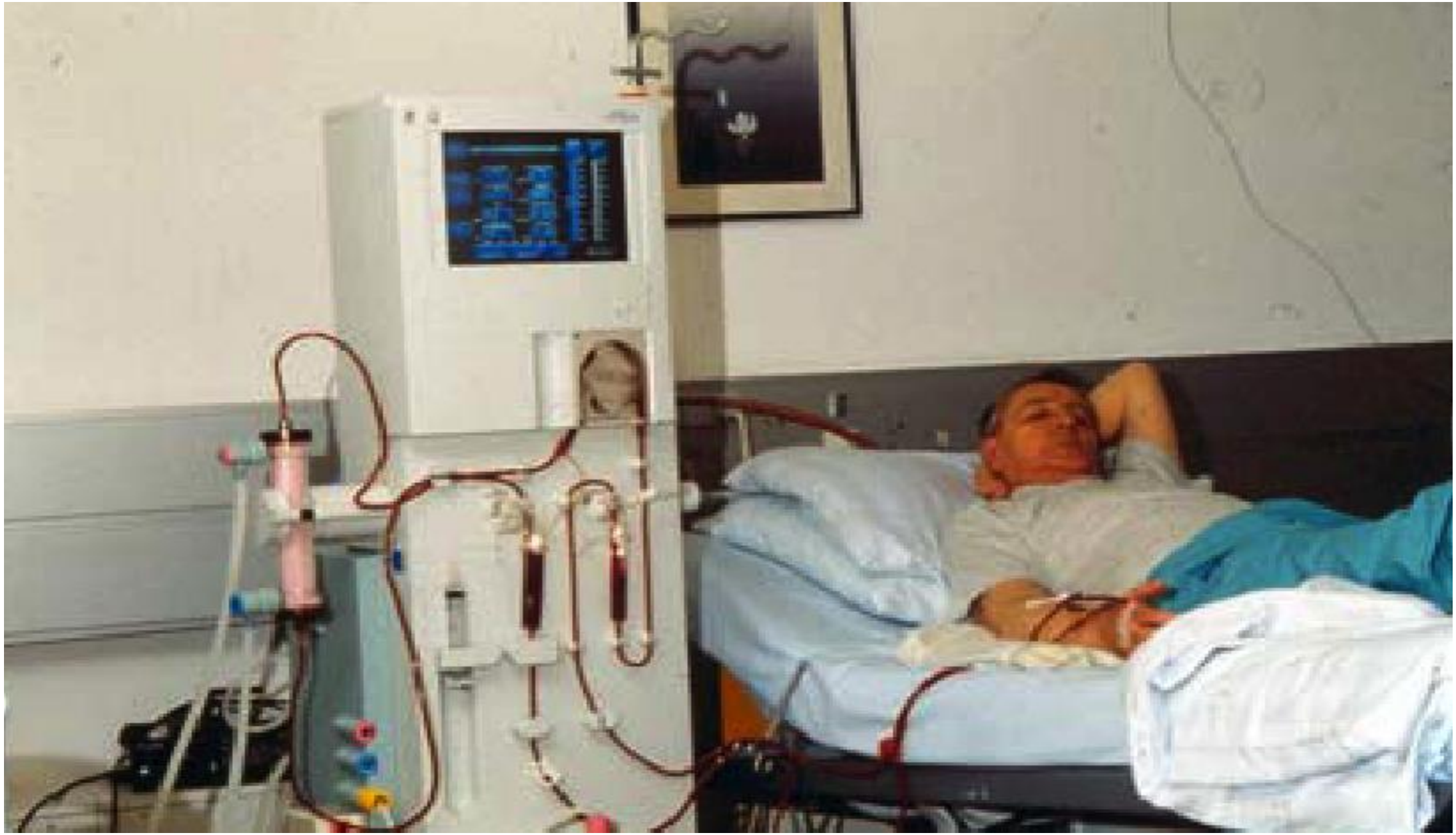
I dispositivi, però, avevano breve durata a causa di complicanze quali trombosi, infezioni e emorragie importanti dovute al cedimento improvviso di uno dei capi.

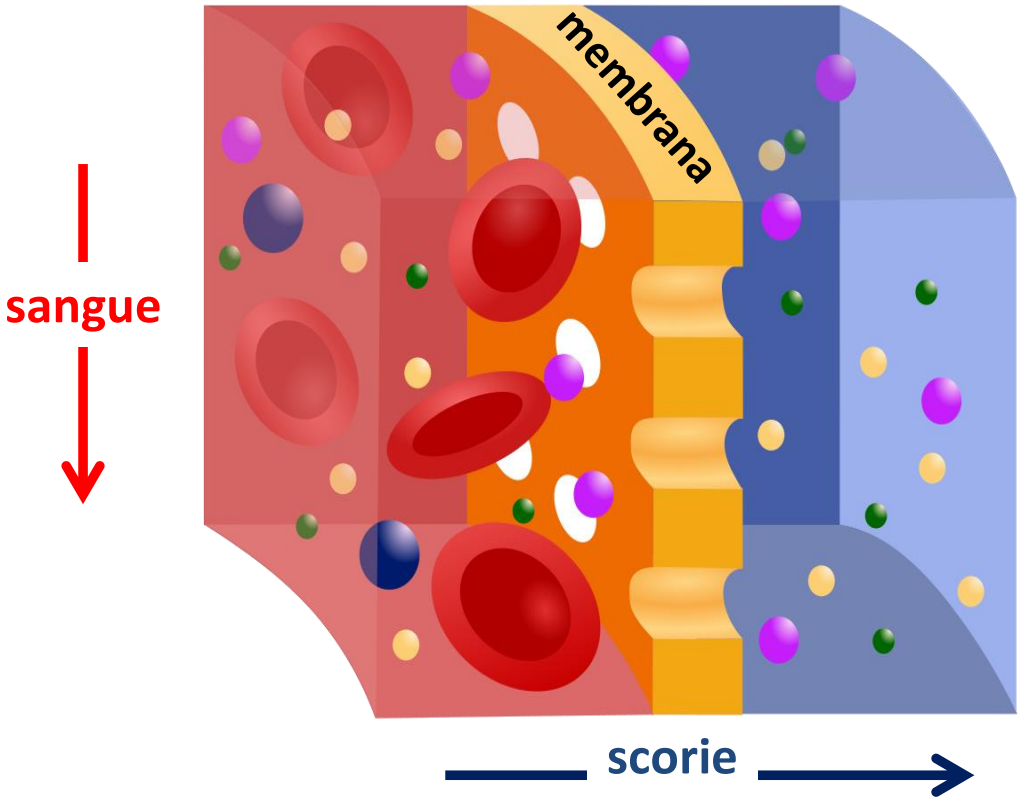
La **fistola artero-venosa** o **arterovenosa,** nota come **fistola di Cimino-Brescia**, è un accesso vascolare per emodialisi ottenuto per via chirurgica fra un'arteria e una vena, allo scopo di deviare sangue arterioso ad alta pressione nel sistema venoso ad alta capienza per ottenere flussi ematici adeguati ad effettuare la dialisi. Le fistole arterovenose ottenute chirurgicamente funzionano poiché rappresentano vie di minore resistenza per il sangue proveniente dall'arteria, rispetto al letto capillare caratterizzato da alte resistenze. Ciò permette di raggiungere alti valori di flusso ematico in vena. Rispetto alle protesi vascolari, le fistole chirurgiche presentano meno rischi di complicanze come la stenosi, e in generale di fallimento.

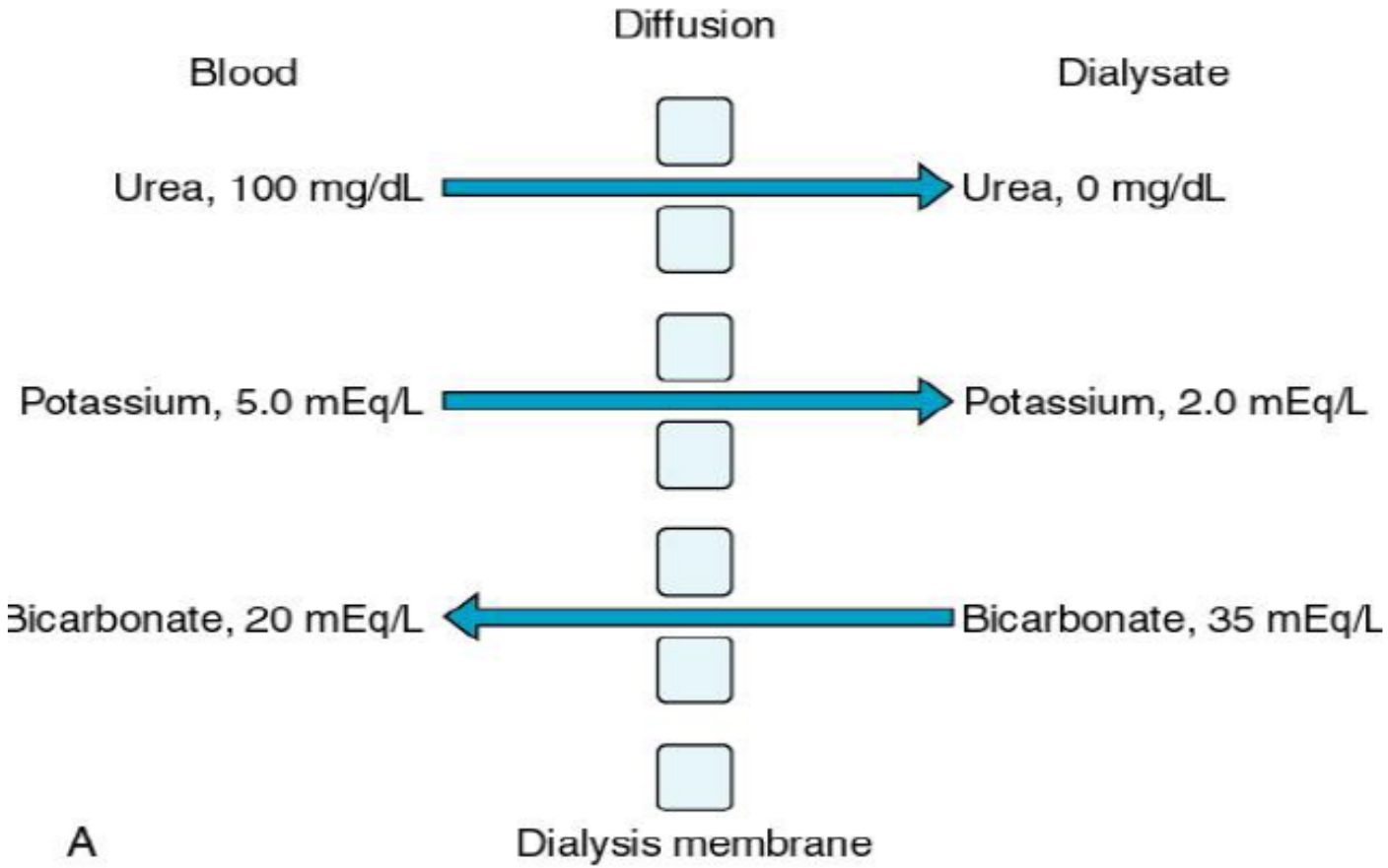
Nel 1966 i medici James E. Cimino e M. Brescia, in collaborazione con il chirurgo vascolare K. Appel, realizzarono con successo la prima fistola artero-venosa tra l'arteria radiale e la vena cefalica del polso, con un'anastomosi tipo latero-laterale, ovvero la parete laterale dell'arteria con quella della vena. Per garantire una buona efficienza di dialisi il flusso ematico deve essere compreso fra 300 e 500 ml/min. Flussi più bassi determinano dialisi inefficiente, più elevati possono dare sovraccarico cardiaco, con possibile insufficienza cardiaca in soggetti predisposti. Entro 15-30 giorni dopo l'intervento chirurgico la vena subisce profonde modifiche strutturali, con ispessimento della parete e dilatazione del vaso, spesso non uniforme, e con rimodellamento del sistema venoso dell'arto. Il vaso così modificato può essere incannulato con aghi di calibro fra 15 e 17 gauge.



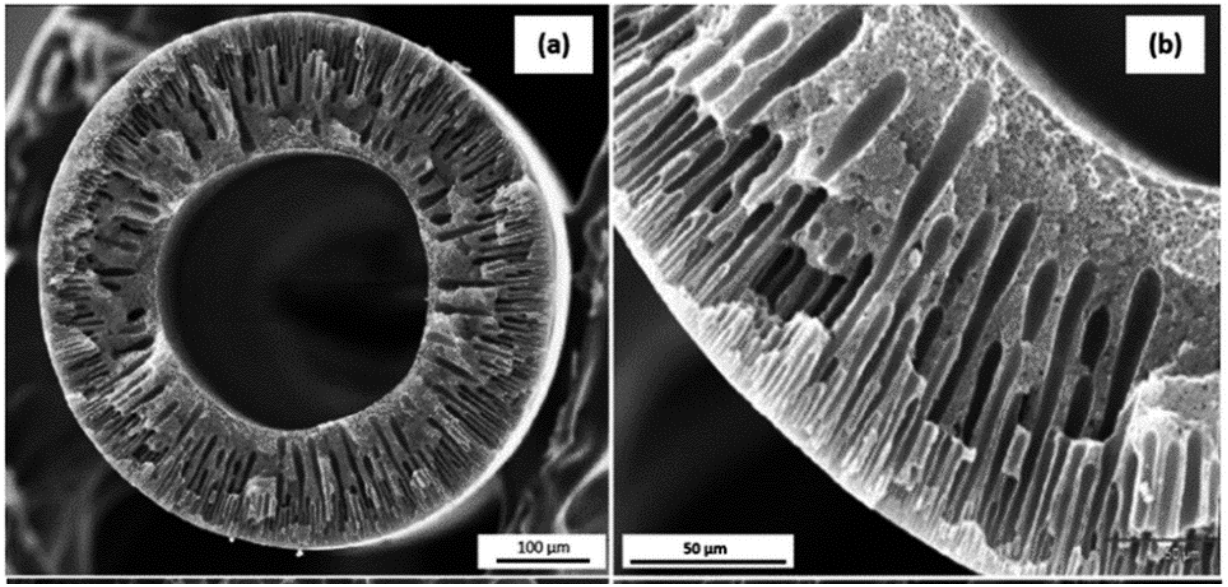

Dializzatore
Anti-coagulante
Pompa sangue
Liquido di dialisi fresco
Liquido di dialisi usato
Sangue al paziente
Sangue dal paziente



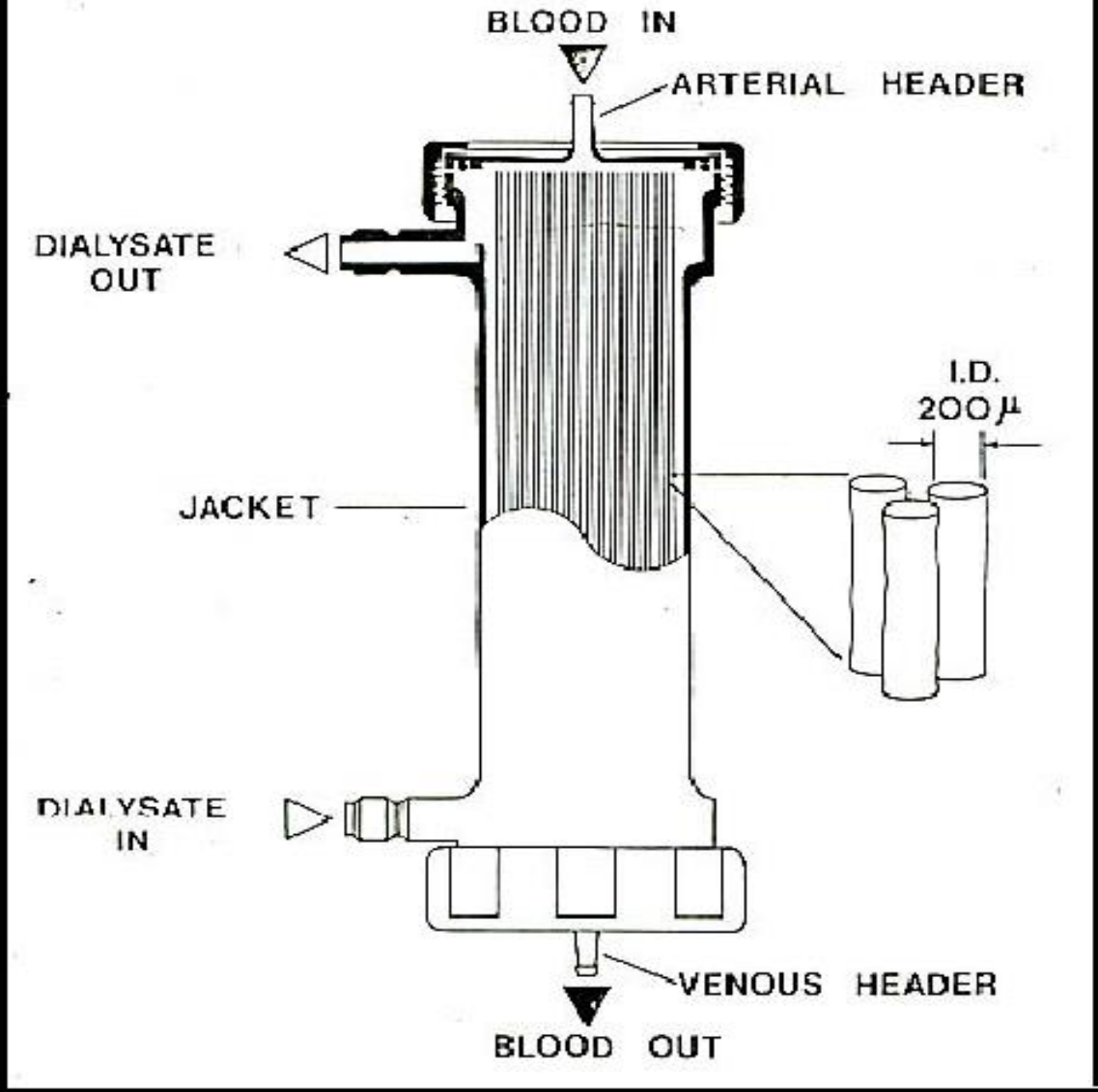

membrana
sangue
soluzione dialisi
scorie


Diffusion
Blood
Dialysate
Urea, 100 mg/dL
Urea, 0 mg/dL
Potassium, 5.0 mEq/L
Potassium, 2.0 mEq/L
Bicarbonate, 20 mEq/L
Bicarbonate, 35 mEq/L
A
Dialysis membrane

Hollow Fiber Artificial Kidney
HFAK

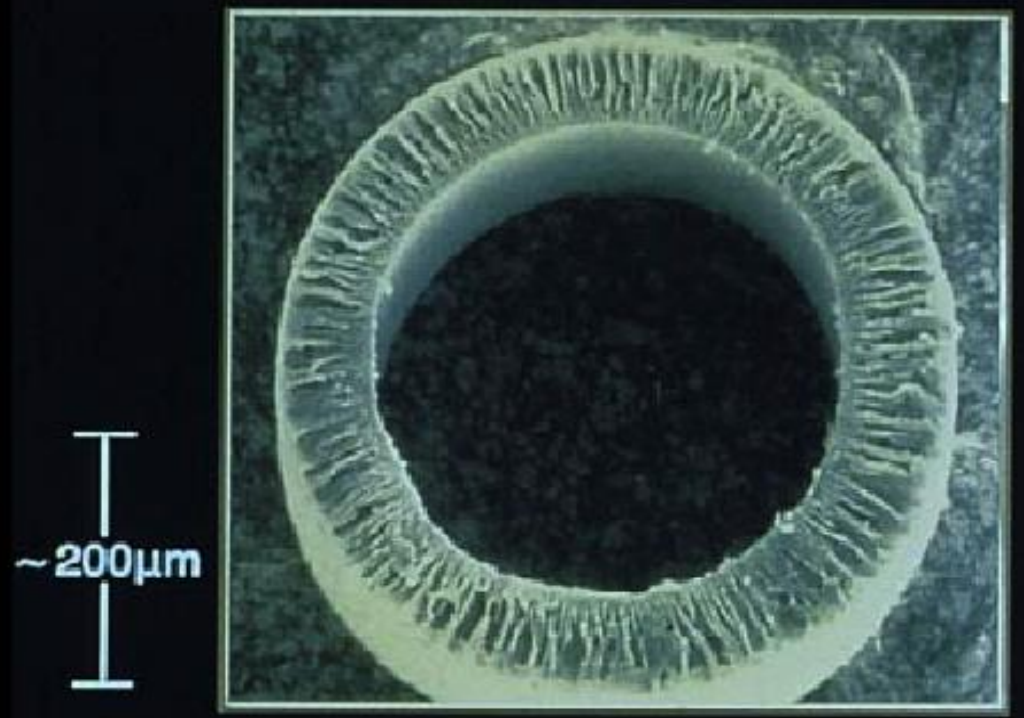


Schematic operation of HFAK



PERMSELECTIVE MEMBRANE

Inner Skin, Wall, Outer Surface



HOLLOW FIBER MADE OF CELLULOSE ACETATE

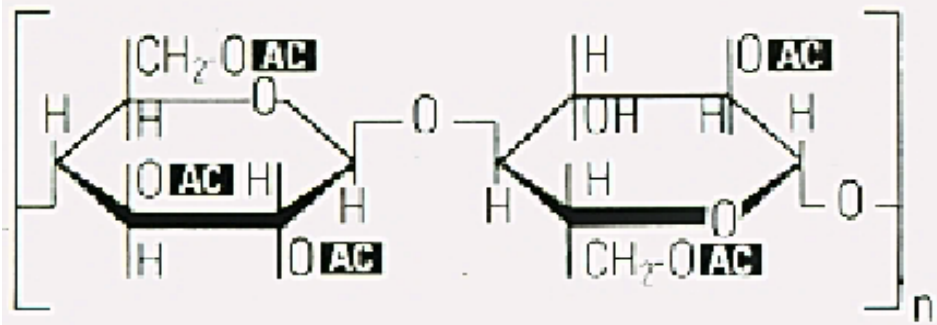
The hollow fiber artificial kidney (HFAK) with Cellulose Acetate hollow fibers, circa 1970s-1980s

Cellulose Acetate

ENKA Cellulose Acetate membranes were particularly developed specifically for plasma fractionation, hemo-filtration and high-flux dialysis.

Figure 17

Structural formula



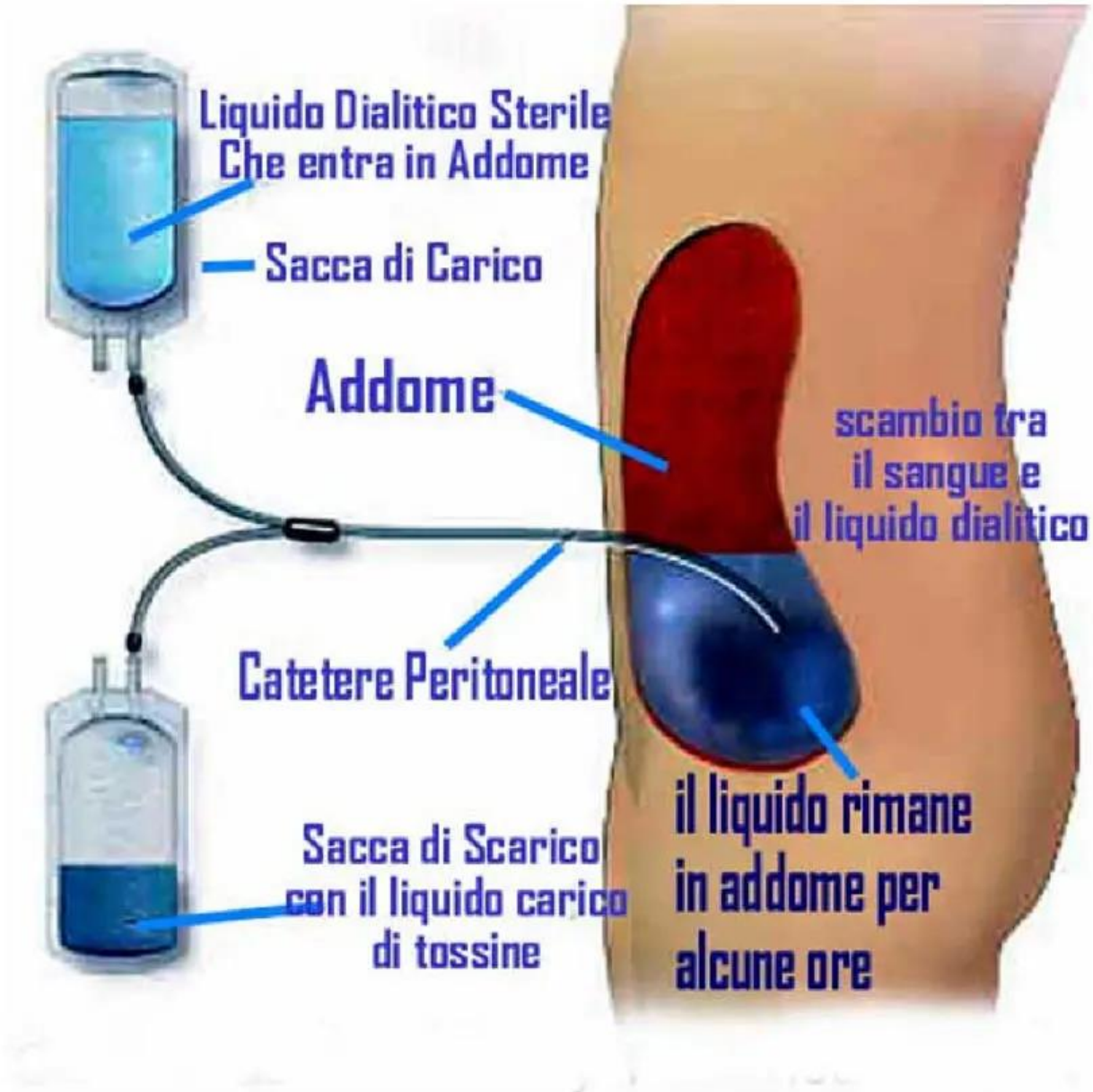
This is the polymer used to form thin skin, hollow fibers for the HFAK.

PMMA and polysulfone /polyethersulfone membranes are utilized nowadays

- Psu = Polisulfone (Fresenius Medical Care, Asahi, Toray ecc.)
- PMMA = Polimetilmetacrlato (Toray)
- EVAL = Poletilene polivinil alcool (Kuraray)
- PAN = Poliacrilonitrile (Hospal AN69)
- PEPA = Poliestere Polimero Alloy (Nikisso)
- PC = Policarbonato (Gambro)
- PA = Poliamide (Gambro)
- PAES = Poliamide S™ (Gambro)
- PES = Polietersulfone (Membrana: DIAPES)

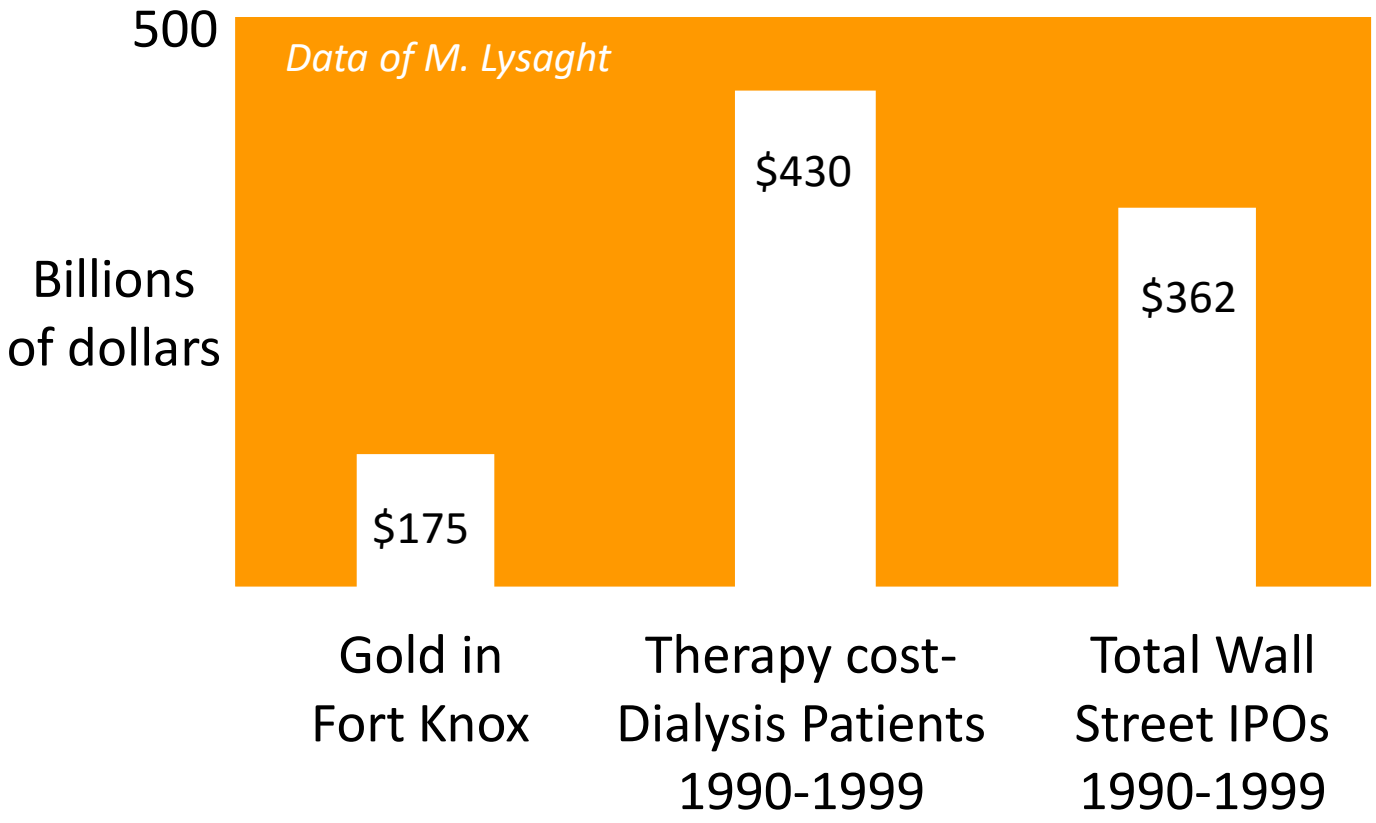
Dialisi peritoneale

1) Liquido dialitico entra in peritoneo
2) Il liquido si carica di scorie azotate
3) Il liquido è rimosso
4) Il liquido è rimpiazzato con nuovo liquido
5) Il processo ricomincia



World Maintenance Dialysis Cost - 2000

The nineties



Biomaterials in dialysis Silicones polyurethane, Teflon cellulose polysulfone