BIOMATERIALI
PER IL CARDIOVASCOLARE

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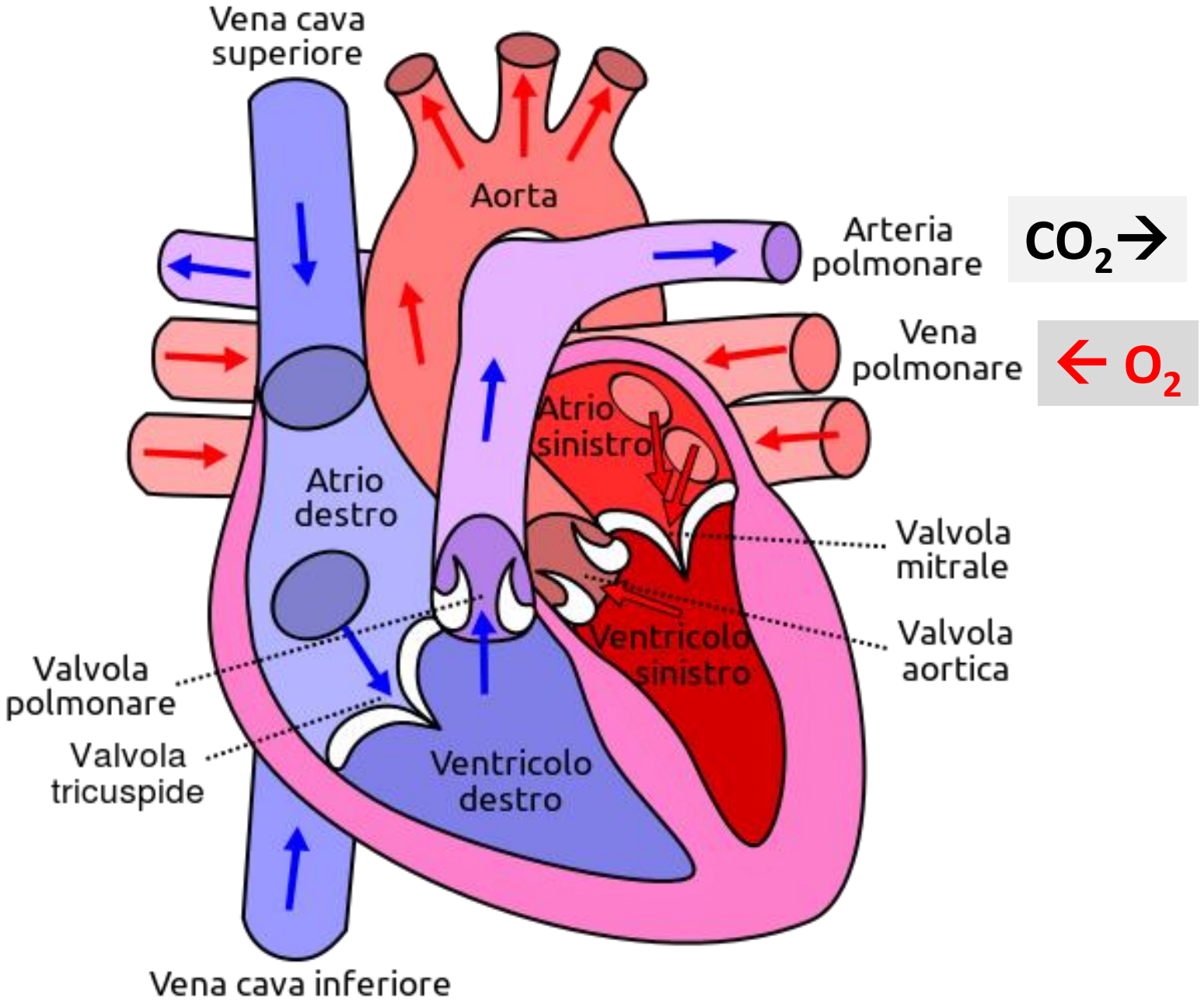
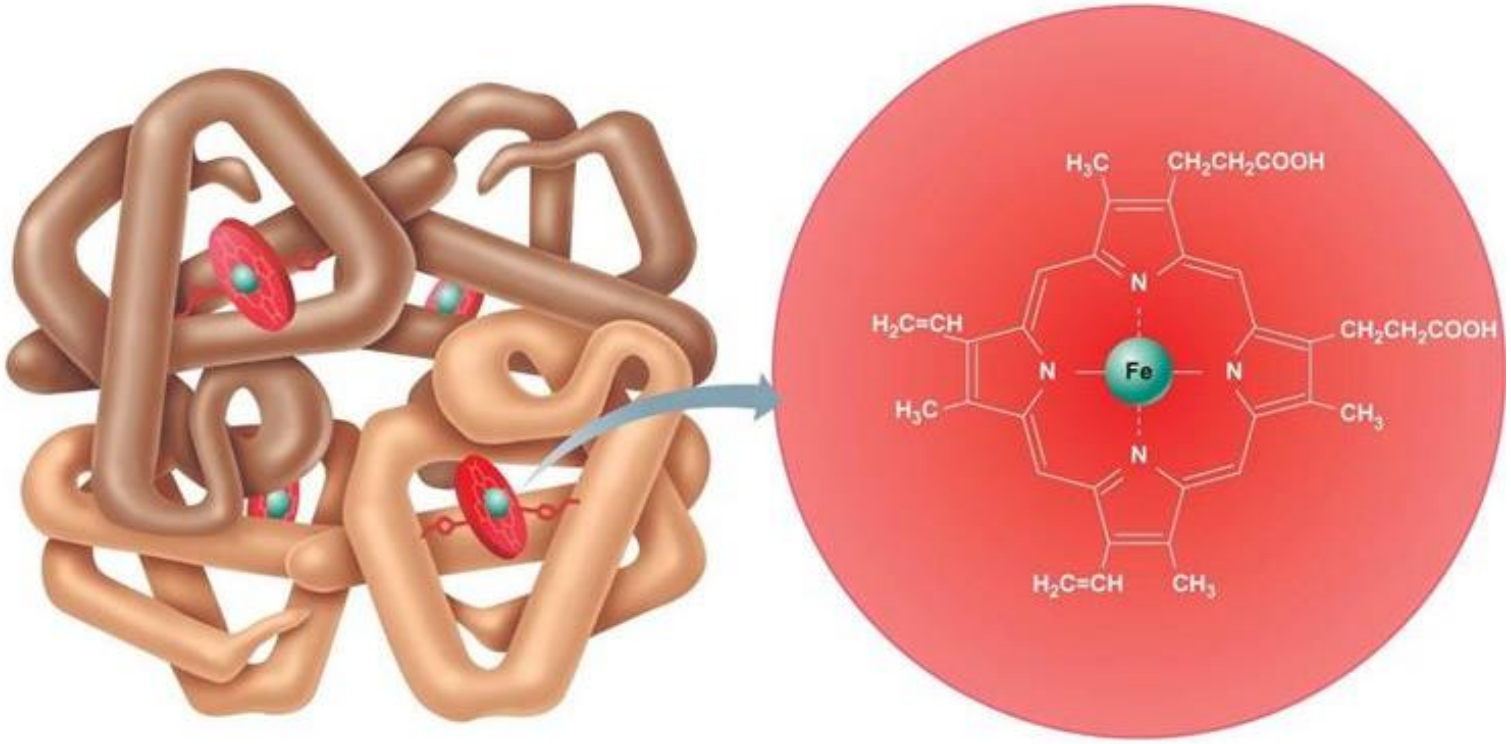
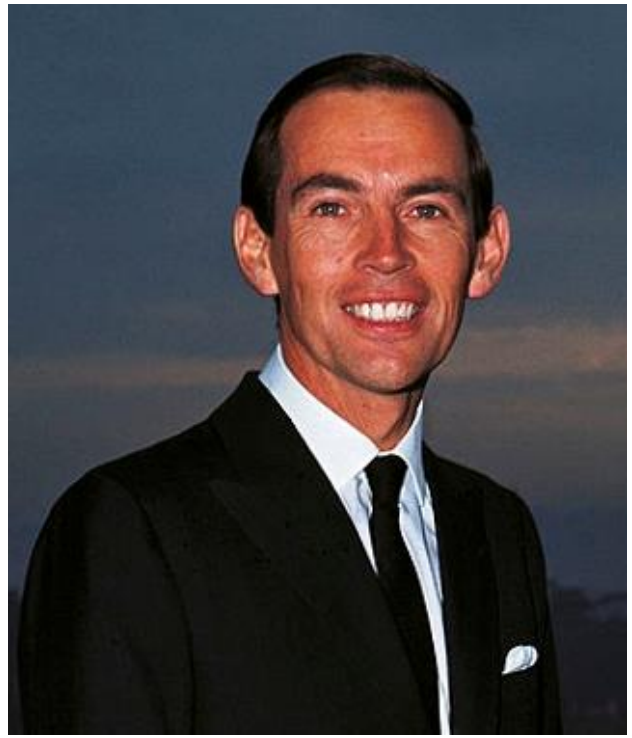


L'**emoglobina** (Hb) è una proteina globulare la cui struttura consta di quattro subunità. È solubile, di colore rosso ed è presente nei globuli rossi del sangue dei vertebrati, esclusi alcuni pesci antartici. È responsabile del trasporto dell'ossigeno molecolare da un compartimento ad alta concentrazione di O_2 (polmoni) ai tessuti che ne hanno bisogno. Ognuna delle sue 4 catene polipeptidiche è legata covalentemente al gruppo prostetico **eme,** costituito da una molecola di proto porfirina che coordina uno ione ferro Fe^{2+}, che sporge dal piano della molecola.



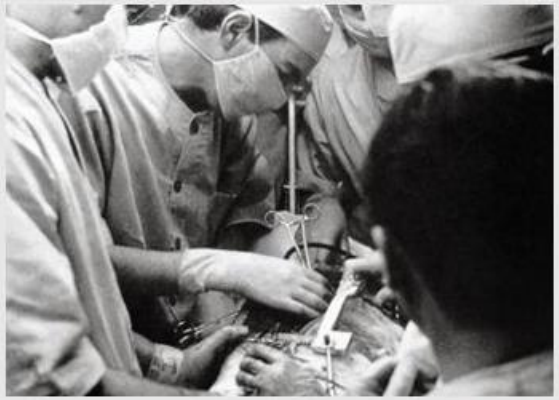
Il primo trapianto di cuore

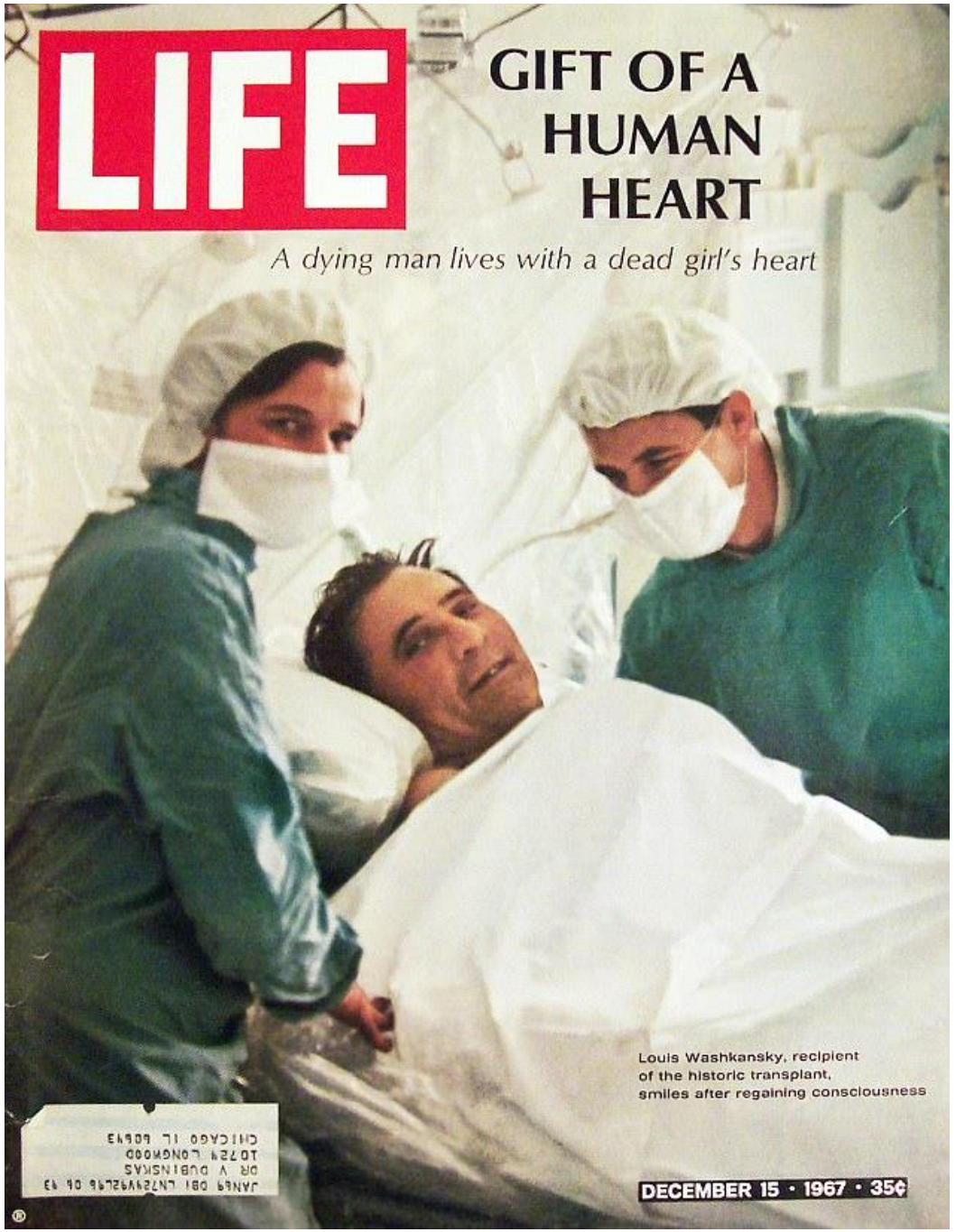


Il 3 dicembre 1967 muore a Città del Capo, in un incidente d'auto, Mrs. Myrtle Ann Darvall; la figlia Denise, 25 anni, è in morte cerebrale. All'Ospedale Groote Schuur era allorain cura uno sportivo lituano di 54 anni**, Louis Washkansky**, sofferente di diabete e di un inguaribile male cardiaco. Il padre di Denise acconsente al trapianto, il primo di cuore umano al mondo, effettuato lo stesso giorno da **Christiaan Barnard (1922-2001)** assistito da una trentina di collaboratori. Dopo 9 ore in sala operatoria il cuore di Denise è impiantato nel corpo di Washkansky e funziona regolarmente.
Dopo una settimana di buone condizioni, il rigetto. il 9 dicembre i globuli bianchi del paziente iniziano a diminuire, a causa di una polmonite bilaterale indotta dai **farmaci immunosoppressivi**. Le condizioni peggiorano, e la notte del 21 dicembre Washkansky muore, 18 giorni dopo il trapianto.

Nonostante il primo paziente con il cuore di un altro essere umano sia sopravvissuto solo poco più di due settimane, l'operazione di Barnard è una pietra miliare per la chirurgia.

- Inizi del XX secolo: primi interventi pionieristici nel campo dei trapianti di organi, con i tentativi di trapianti di cuore e di reni effettuati su animali.
- Prima metà del XX secolo: insuccesso dei tentativi di impiantare nuovi organi negli esseri umani.
- **1954**: primo trapianto di rene negli Stati Uniti.
- **1963**: primi trapianti di fegato e polmoni negli Stati Uniti.
- **1967**: primo trapianto di cuore eseguito dal chirurgo Christiaan Barnard in Sudafrica (nell'immagine a fianco).





NIGUARDA - *PRIMO TRAPIANTO CARDIACO EFFETTUATO A MILANO*

Fabio Gervasoni, 21 anni, il donatore del primo cuore trapiantato ieri mattina all'ospedale di Niguarda a Milano. A destra Luigi Savaris, 47 anni, il ricevente.

Interventi su donatore e ricevente per la prima volta contemporaneamente nello stesso centro

Il cuore e poi i reni

Riuscita l'operazione (4 ore) diretta dal professor Pellegrini - Gli organi renali destinati a due ammalati diversi, uno al Policlinico e l'altro ancora a Niguarda

[illegible]

Un primo prelievo non era stato concesso

di LUISELLA SEVESO

[illegible]

Ha battuto nel petto di un alpinista

di ALFONSO [illegible]

[illegible]

Il professor Alessandro Pellegrini che ha eseguito il trapianto di cuore (a destra)

FINALMENTE ANCHE A MILANO

Un cervello elettronico per vincere la sordità

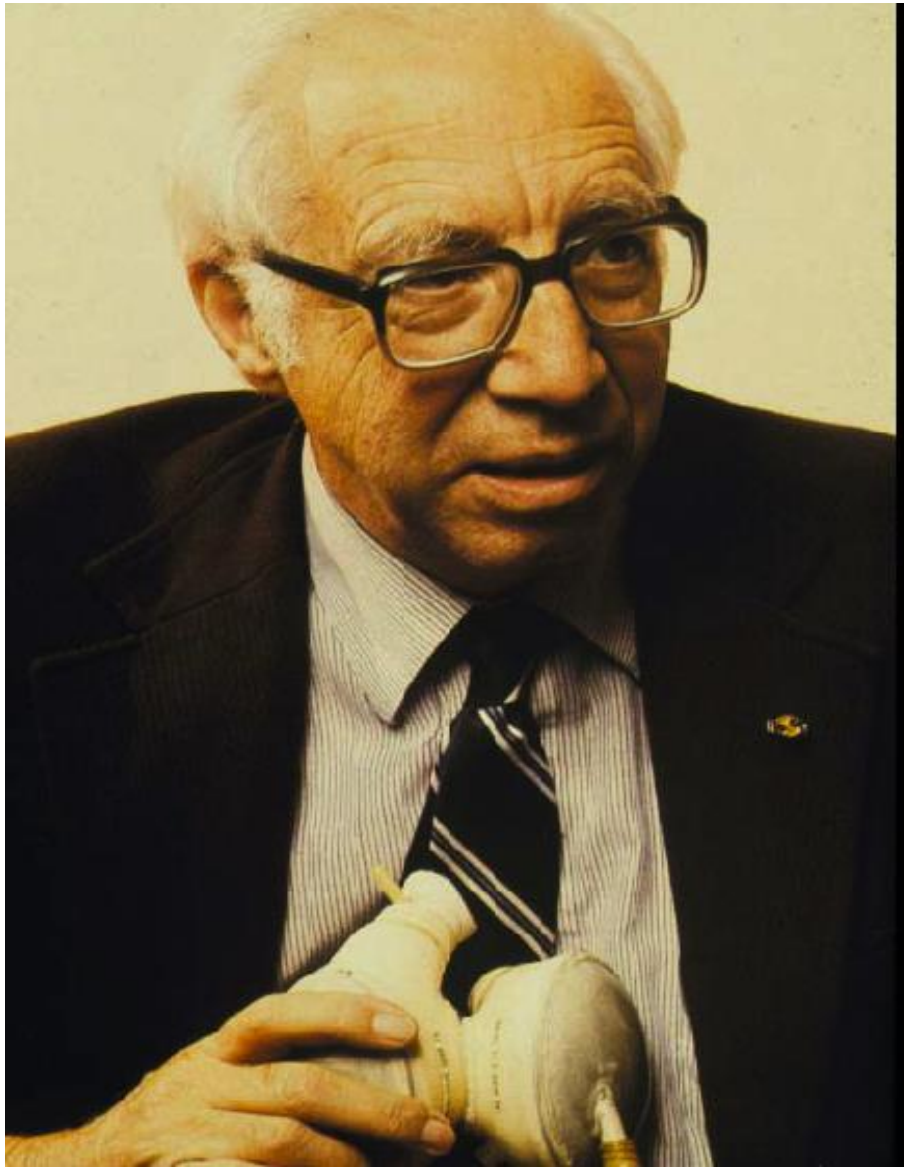
The Artificial Heart

An artificial heart is a device that replaces the heart. Artificial hearts are typically used to bridge the time to heart transplantation, or to permanently replace the heart in the case that a heart transplant is impossible.

Willem Kolff was also a pioneer in the development of the artificial heart. He implanted the first artificial heart in the Western hemisphere in a dog in 1957. the dog survived 90 minutes. The first artificial heart, indeed, was implanted in a dog in 1937 in URSS by Vladimir Demichov. The Kolff artificial heart was made of a thermosetting poly(vinyl chloride), **PVC**, cast inside hollow molds to prevent seams.

Although the heart is conceptually a pump, it embodies subtleties that defy straightforward emulation with synthetic materials and power supplies. Consequences include **severe foreign-body reaction** and **external batteries** that limit mobility. These complications limited the lifespan of early human recipients for hours to days.

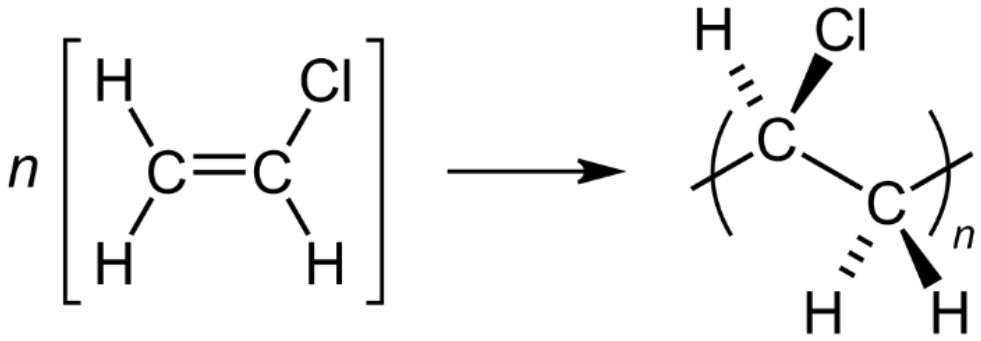
In 1953, the **heart-lung machine** was invented by John Gibbon, but this was useful only for acute treatment, such as during open heart surgery.



Willem “Pim” Kolff

Inventor of the artificial kidney and a pioneer in development of the artificial heart

Il **cloruro di polivinile**, o **polivinilcloruro (PVC)**, è il polimero del cloruro di vinile, con formula $-(CH_2CHCl)_n-$ e peso molecolare compreso tra 60.000 e 150.000 u.m.a. È una delle materie plastiche più usate al mondo. Puro è rigido,



deve la sua versatilità applicativa alla possibilità di essere miscelato anche in proporzioni elevate a composti inorganici e a plastificanti, come per esempio gli ftalati, che lo rendono flessibile e modellabile.

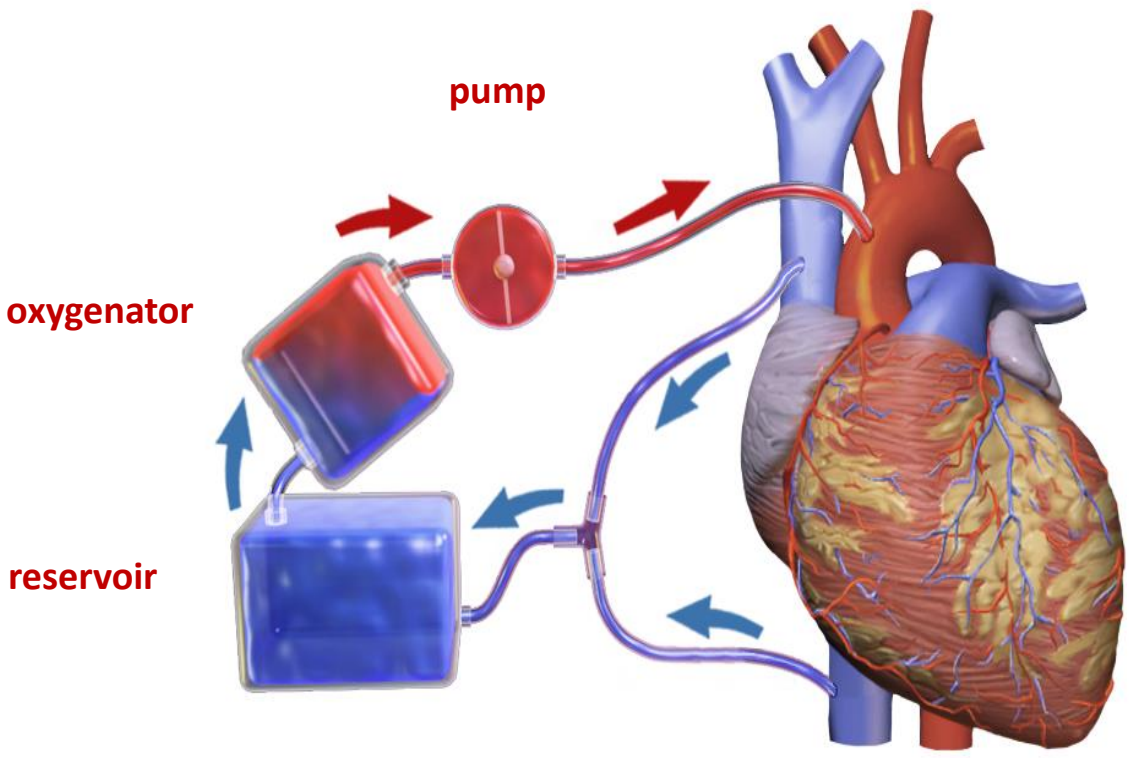
E' stabile e sicuro nelle applicazioni tecnologiche a temperatura ambiente, ma pericoloso se bruciato o scaldato a elevate temperature e in impianti inidonei al trattamento, per via della presenza di cloro che può liberarsi come acido cloridrico, secondo la reazione:

$$2\,C_2H_3Cl + 5\,O_2 \longrightarrow 4\,CO_2 + 2\,H_2O + 2\,HCl$$

Nelle stesse condizioni può inoltre avvenire il rilascio di **diossina** o di cloruro di vinile monomero.

Heart – Lung machine

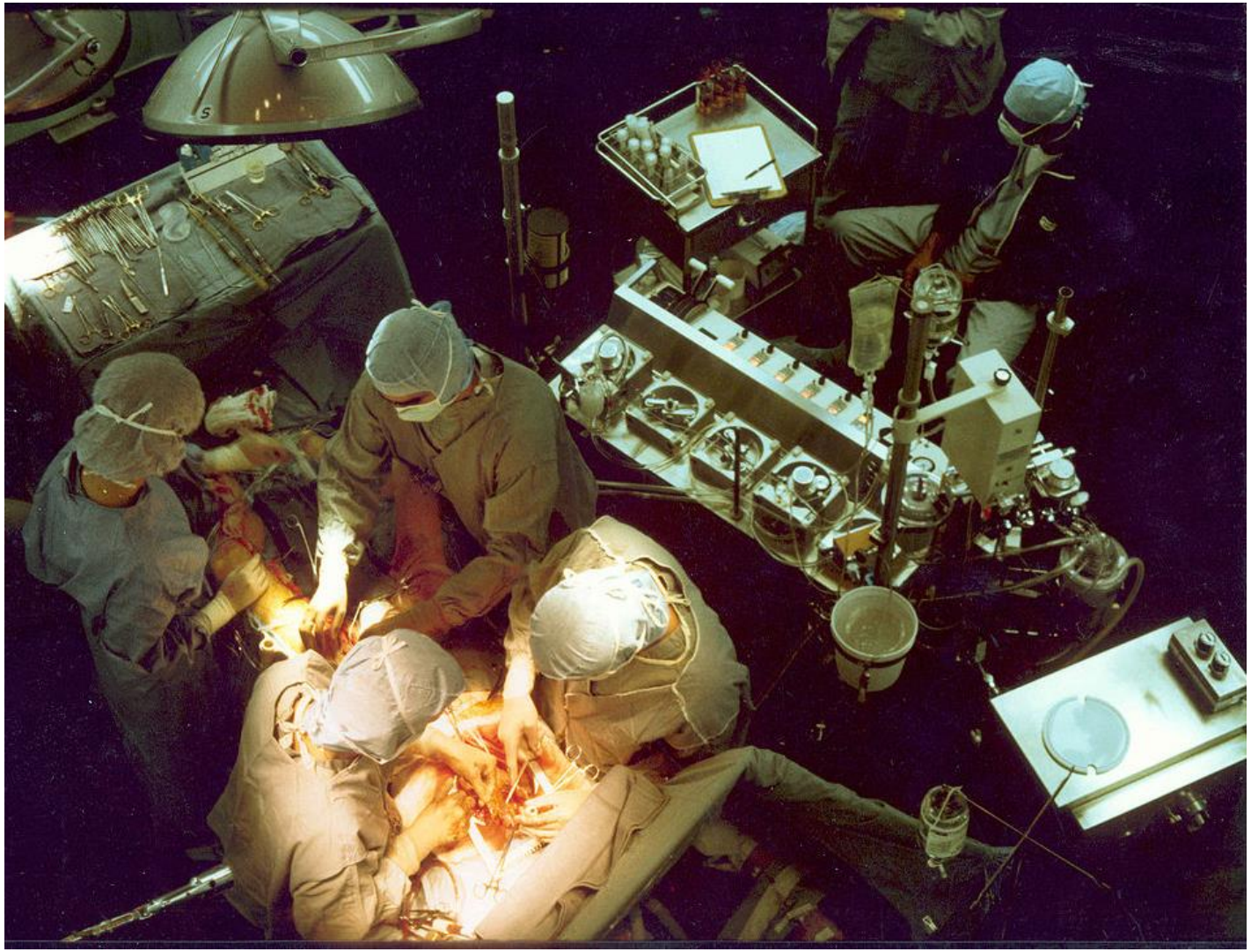
In the framework of developing materials and devices for the artificial heart, such as vascular grafts and cardiac valves, in 1953, the **heart-lung machine (Cardio Pulmunary Bypass, CPB)** was invented by John Gibbon. This device, though, this was useful only for acute treatment, such as during open heart surgery.



Extra Corporeal Membrane Oxygenation (ECMO), a simplified version of the heart-lung machine that includes a centrifugal pump and an oxygenator, is generally used for longer-term treatments. Most oxygenators can only be used for 6-10 hours, to grant they do not clot off and stop working. For longer periods ECMO is used, which can be operated for up to 31 days, e.g., as after the patient received a heart transplant.

Membrane oxygenators have supplanted bubble oxygenators since the 1980s, because they generate many fewer micro-bubbles, (gaseous microemboli) and reduce damage to blood cells. More recently, the use of **hollow-fiber oxygenators** has become more widespread.

A HEART–LUNG MACHINE (upper right) in a coronary artery bypass surgery



In 1964, the National Heart and Lung Institute of the National Health Institute (NIH) set a goal of a total artificial heart by 1970. In 1967 Kolff left Cleveland Clinic to start the Division of Artificial Organs at the University of Utah and pursue his work on the artificial heart.

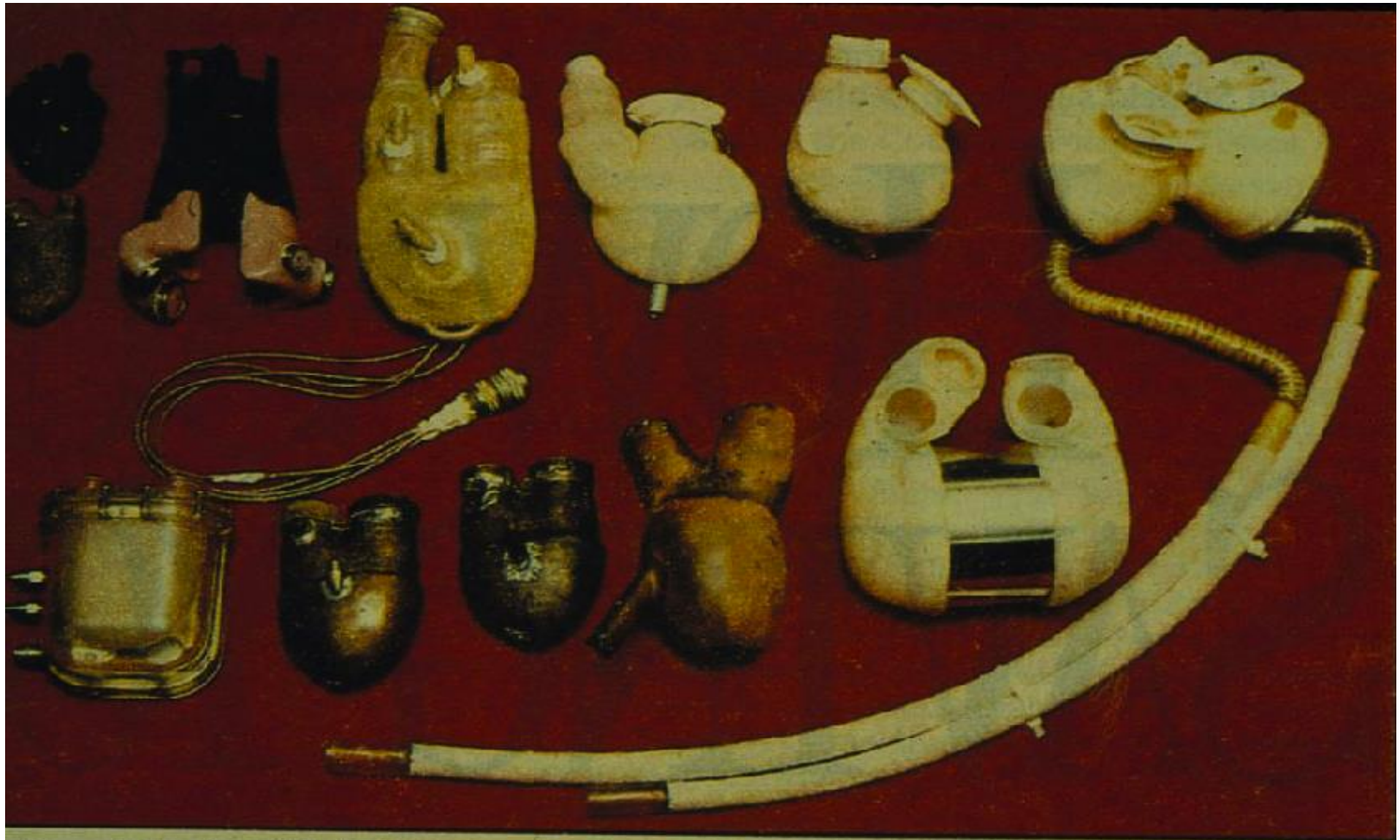
1973, a calf named Tony survived for 30 days on an early Kolff heart.

1975, a bull named Burk survived 90 days on the artificial heart.

1976, a calf named Abebe lived for 184 days on the Jarvik 5 artificial heart.

1981, a calf named Alfred Lord Tennyson lived for 268 days on the Jarvik 5.

More than 200 physicians, engineers, students and faculty developed, tested and improved Kolff's artificial heart. To help manage, Kolff assigned project managers, and each project was named after its manager. Grad. student Robert Jarvik was the project manager for the artificial heart which was named **Jarvik 7**.



st models of artificial hearts: Doctors are seeking cheaper, simpler ones.

Evolution of the Total Artificial Heart

Kolff 1958	Kolff 1965	Liotta 1969	Jarvik 1982	Abiomed 2001
				
PVC	Silicone Rubber		Lycra Spandex	Purified TPU

Courtesy of Bob Ward

LIFE

Can Women Cut I

in the Military?

September 1981/$2.00

THE ARTIFICIAL HEART IS HERE

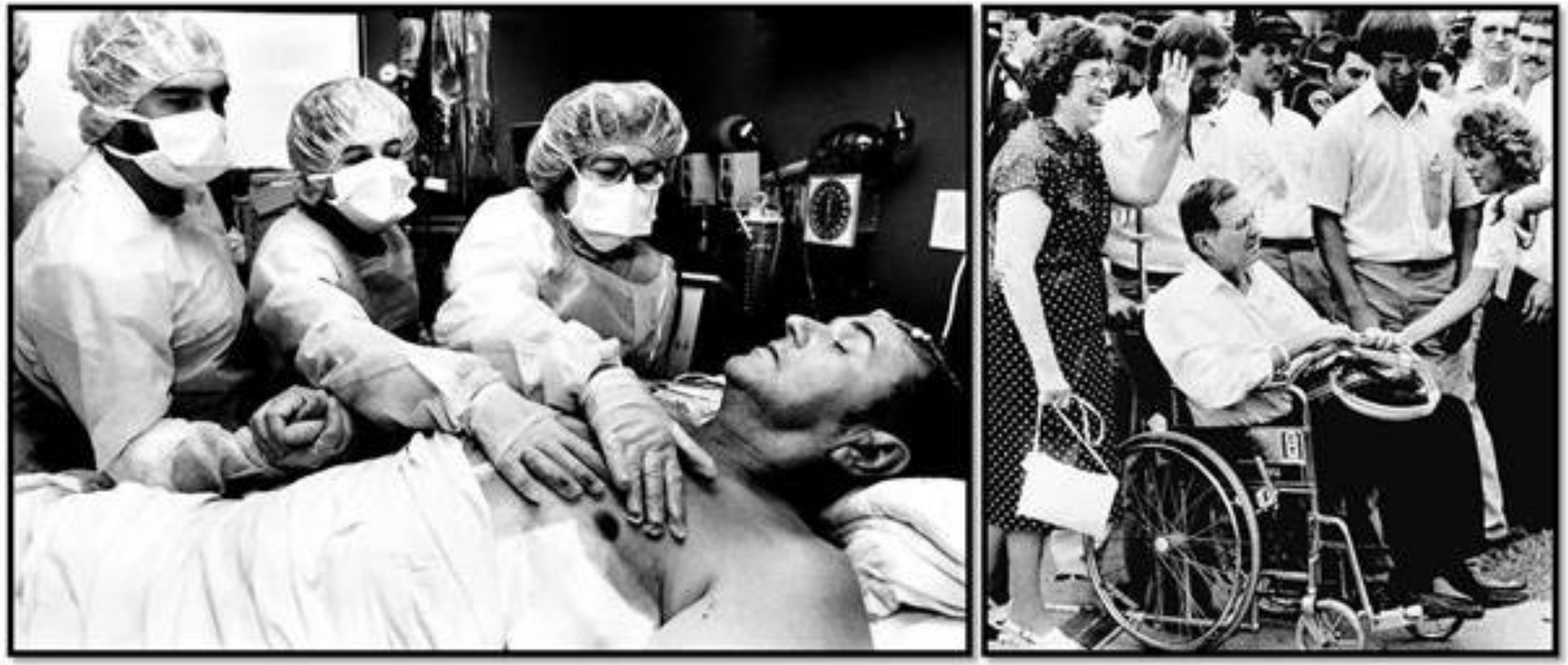
EXCLUSIVE PICTURES OF DR. COOLEY'S HISTORIC HEART SURGERY

In 1981, William DeVries asked FDA permission to implant the **Jarvik 7** into a human being.

On 2 December 1982, Kolff implanted the Jarvik 7 artificial heart into **Barney Clark**, a dentist from Seattle with severe congestive heart failure. Clark lived for 112 days tethered to an external compressor weighing some 400 pounds (180 kg).

During that time he suffered long periods of confusion and many instances of bleeding, and asked several times to be allowed to die.

Utah Total Artificial Heart (or Jarvik-7 Heart)

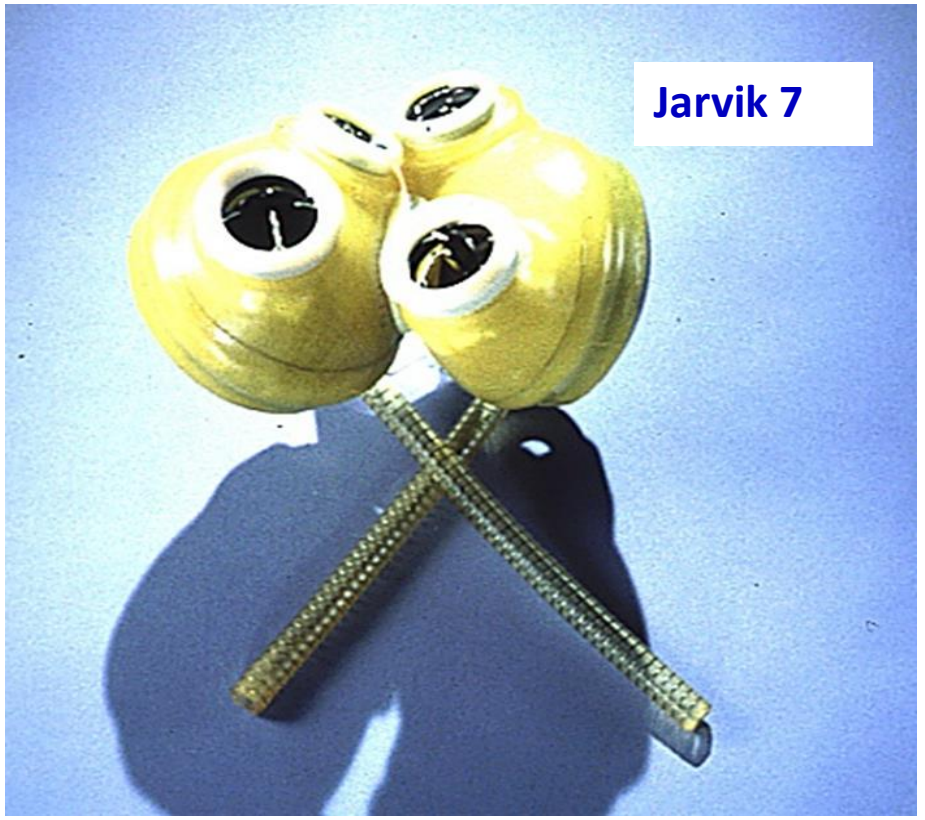


William (Bill) Schroeder (1932-1986) lived 620 days with his artificial heart

In the period 1982–1985, Dr. William De Vries implanted a number of Jarvik hearts based upon designs originated by Drs. Clifford Kwan-Gett and Donald Lyman.
Bill Schroeder, the second recipient of the Jarvik 7 artificial heart lived for a record 620 days.

Contrary to popular belief and erroneous articles in several periodicals, the Jarvik heart was not banned for permanent use.

Today, the modern version of the Jarvik 7 is known as the SynCardia **temporary Total Artificial Heart (TAH)**.



The Jarvik 7 consists of two ventricles (the heart lower chambers) with air chambers and six valves. It attaches to the patient's natural auricles (the heart upper chambers).

the SynCardia (CardioWest) temporary Total Artificial Heart

SynCardia is based in Tucson, Arizona; they had two separate models available, in a 70cc and 50cc size. The 70cc model is used for biventricular heart failure in adult men, while the 50cc is for children and women.

As good results with the TAH as a bridge to heart transplant, a trial of the **CardioWest TAH** (developed from Jarvik 7 and now marketed as Syncardia TAH) was initiated in 1993 and completed in 2002.

The SynCardia was approved for use in 2004 by the FDA. 79% patients survived during the clinical trials (New England Journal of Medicine 2004; 351: 859-867), the highest rate for TAHs.

It has been implanted in more than 1,350 people as a bridge to transplantation. In 2016, Syncardia filed for bankruptcy protection and was later acquired by the private equity firm Versa Capital Management.

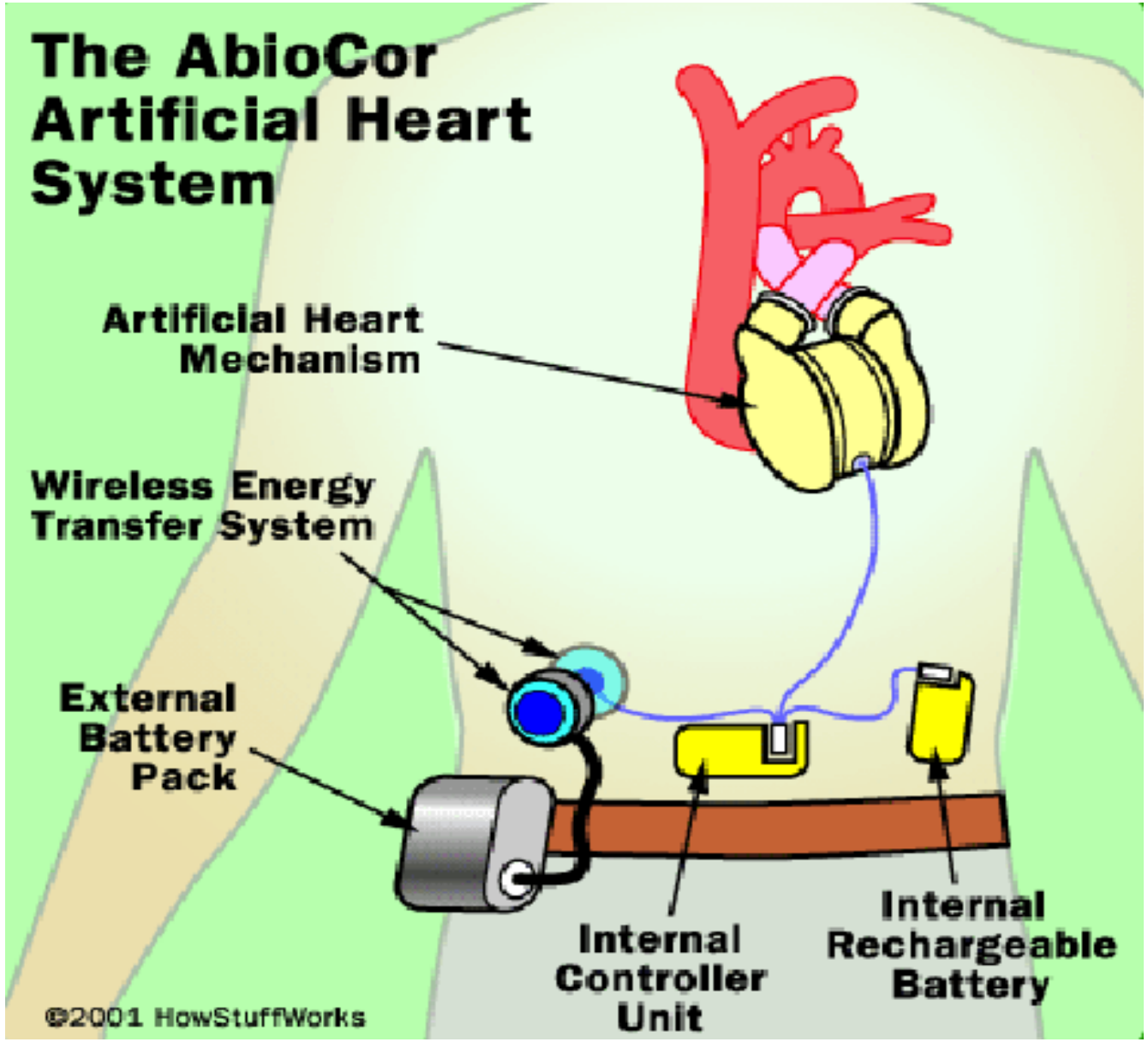
Cuore sostitutivo AbioCor

Diversamente dal CardioWest TAH, Il cuore sostitutivo **AbioCor** della Abiomed, è completamente impiantabile nel torace, progettato per non necessitare di cavi o tubi passanti attraverso la pelle, per diminuire il rischio di infezioni.

AbioCor fu approvato per pazienti all'ultimo stadio di malattie cardiache a entrambi i ventricoli. Ad oggi, 15 pazienti hanno ricevuto un impianto AbioCor, con uno di loro che ha vissuto per 512 giorni dopo l'impianto. Abiocor ha ricevuto l'approvazione FDA nel 2006.

Il primo impianto di AbioCor fu eseguito il 24 luglio 2009 al Robert Wood Johnson University Hospital, New Jersey (USA). Il 30 settembre 2010 è stato innestato in un ragazzo di 15 anni affetto da distrofia muscolare di Duchenne, una patologia che non permette il trapianto di cuore. **E' il primo caso al mondo in cui un dispositivo viene innestato con l'intento di mantenerlo fino al termine naturale della vita del paziente**.

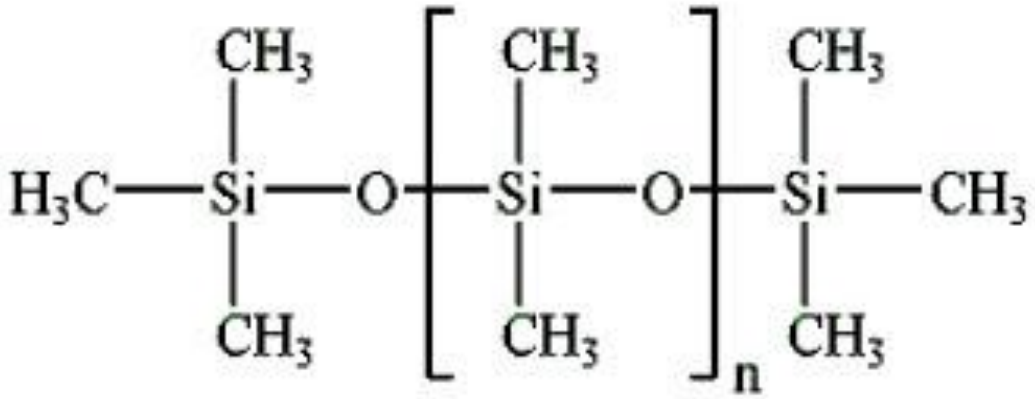
Nel 2015, però, Abiomed ha abbandonato lo sviluppo del Total Artificial Heart. Dal 2019 offre solo heart pumps "intended to help pump blood in patients who need short-term support (up to 6 days), which are not total artificial hearts".


The AbioCor Artificial Heart System
Artificial Heart Mechanism
Wireless Energy Transfer System
External Battery Pack
Internal Controller Unit
Internal Rechargeable Battery
©2001 HowStuffWorks

Siliconi

I **siliconi** (o polisilossani) sono polimeri basati su una catena **silicio-ossigeno** e gruppi funzionali organici (R) legati agli atomi di silicio. Il termine inizialmente indicava i composti aventi formula generica $R_2Si=O$, in analogia ai chetoni. Si riteneva infatti, che potessero essere isolati come composti monomerici, ma anche dopo la scoperta della vera struttura il nome è stato usato ancora, e lo è tuttora, per indicare gli organopolisilossani.

Il silicone fu sintetizzato nel 1907 da Frederick Kipping. Il polimero siliconico più comune è il **polidimetilsilossano (PDMS).**



Soft Artificial Heart

In 2017, Nicholas Cohrs and colleagues presented a new concept of a soft TAH, developed in the Functionals Materials Lab, ETH, Zurich. The **Soft Artificial Heart (SAH)** was created in a silicone monoblock with 3D printing technology. It weighs 390 g, has a volume of 679 cm^3, about the same size as the patient heart, to imitate the human heart as close as possible. It is operated through pressurized air.

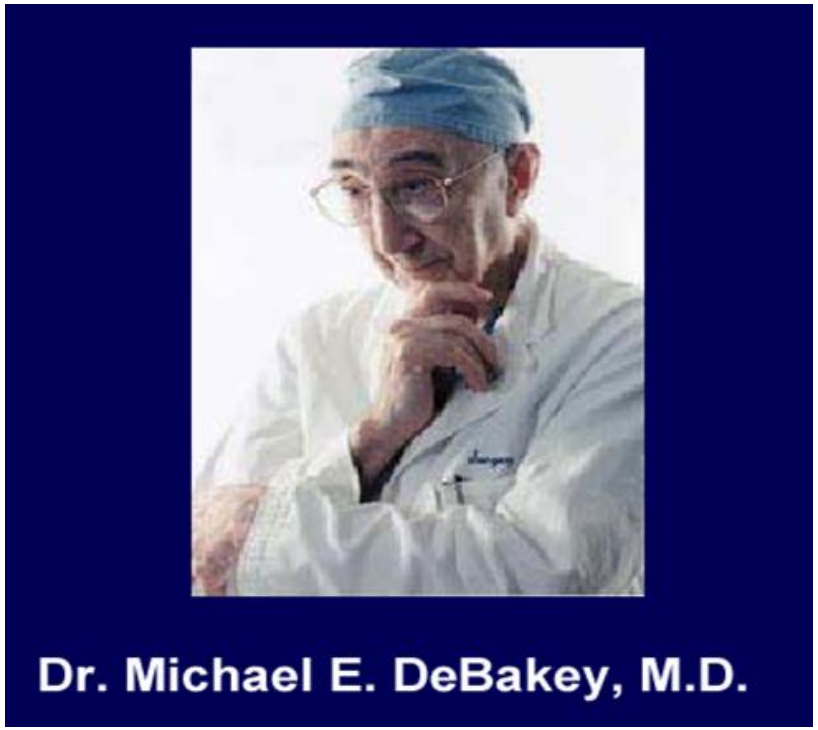
The first SAH only beated for 3000 beats (about 30-50 min for an average individual heart) in a hybrid mock circulation machine, after which the silicone membrane (2.3 mm thick) between the Left Ventricle and the Air Expansion Chamber ruptured.

Soft Total Artificial Heart, ETH Zürich
work in progress, 2019

The working life of a more recent prototype (with various polymers) was still limited in early 2018, with a useful life of 1 million heartbeats, roughly 10 days in a human. The team is experimenting with CAD software and 3D printing, to develop a model that would last up to 15 years.

Ventricular Assist Device (VAD)

is an electromechanical device for assisting cardiac circulation, which is used either to partially or to completely replace the function of a failing heart. The function of a VAD differs from that of an **artificial cardiac pacemaker** in that a VAD pumps blood, whereas a pacemaker delivers electrical impulses to the heart muscle. Some VADs are for short-term use, typically for patients recovering from **heart attack or** from **cardiac surgery**; some are for long-term use (months to years to ever), typically for patients suffering from advanced **heart failure**.



VADs are designed to assist either the **right ventricle (RVAD)** or the **left ventricle (LVAD)**, or to assist **both (BiVAD)**. The type of VAD implanted depends on the type of heart disease, and on the pulmonary arterial resistance, which determines the workload of the right ventricle. The LVAD is the most common device applied to a defective heart, in waiting for a transplant.

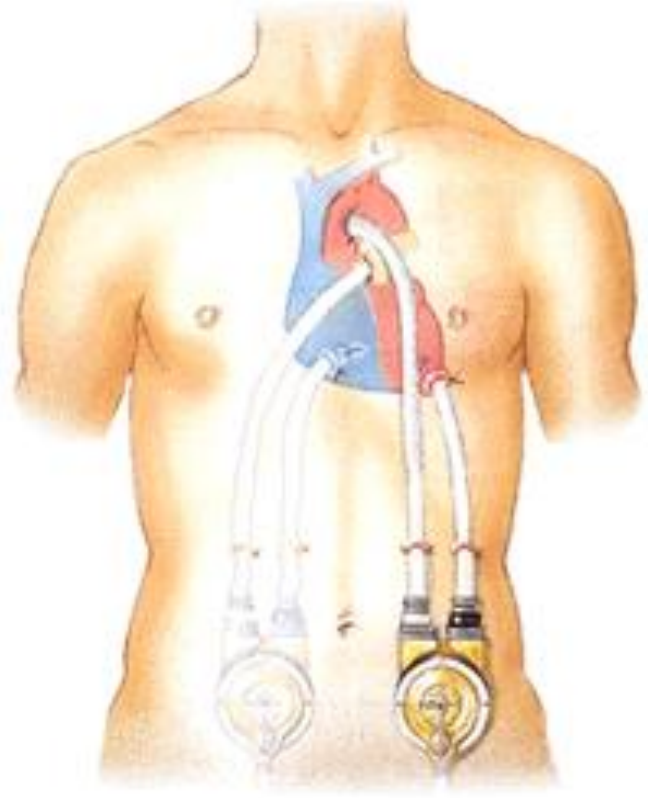
Dr. Michael De Bakey implanted a **left ventricular assistance device (LVAD)** in a human in 1966.

Left Ventricular Assist Devices (2000):

Heartmate (Thermo Cardio Systems)

Novacor (Baxter) Assist Pump

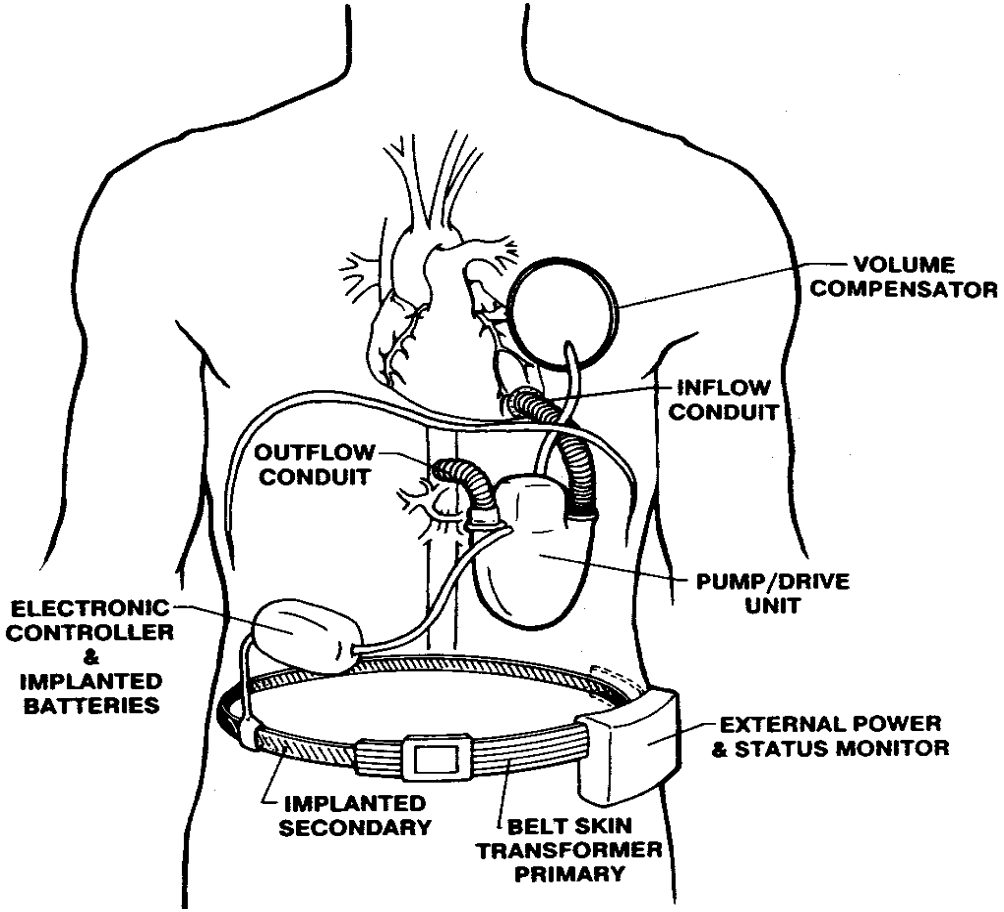
Thoratec Assist Pump

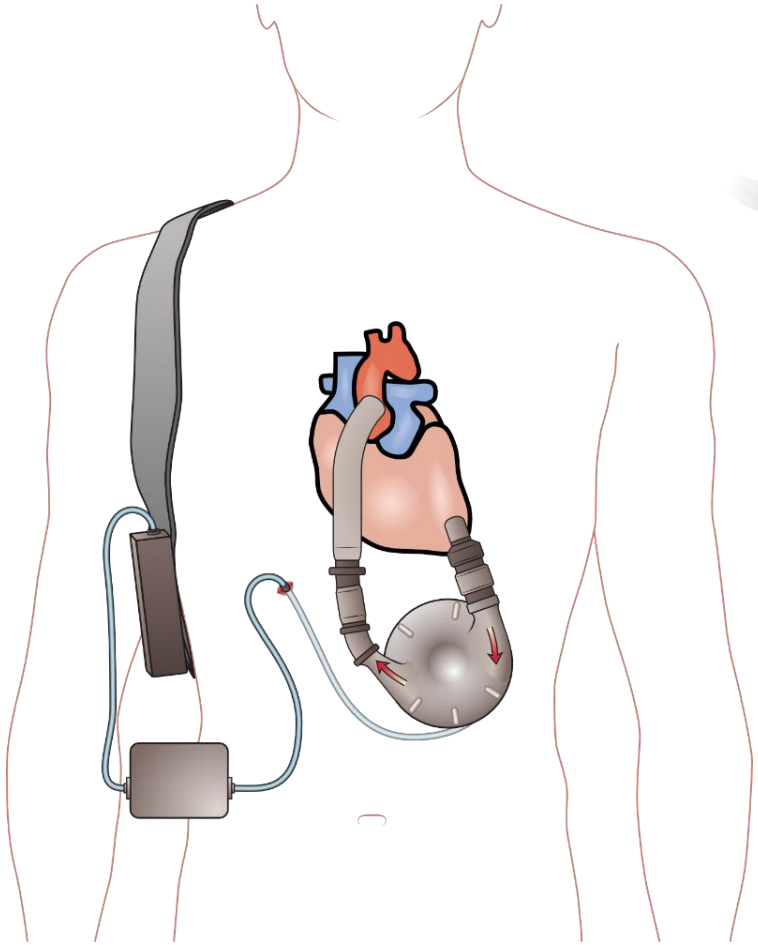


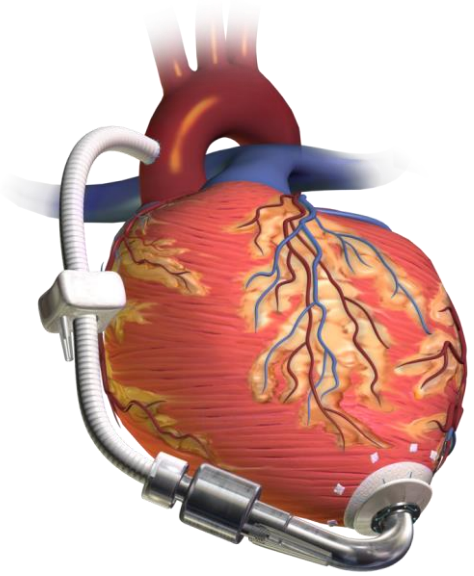
Thoratec VAD

Thoratec power unit

A **left ventricular assist device (LVAD)** pumping blood from the left ventricle to the aorta, connected to an externally worn control unit and battery pack. VADs differ from artificial hearts, which are designed to assume cardiac function, and generally require the removal of the patient's heart.



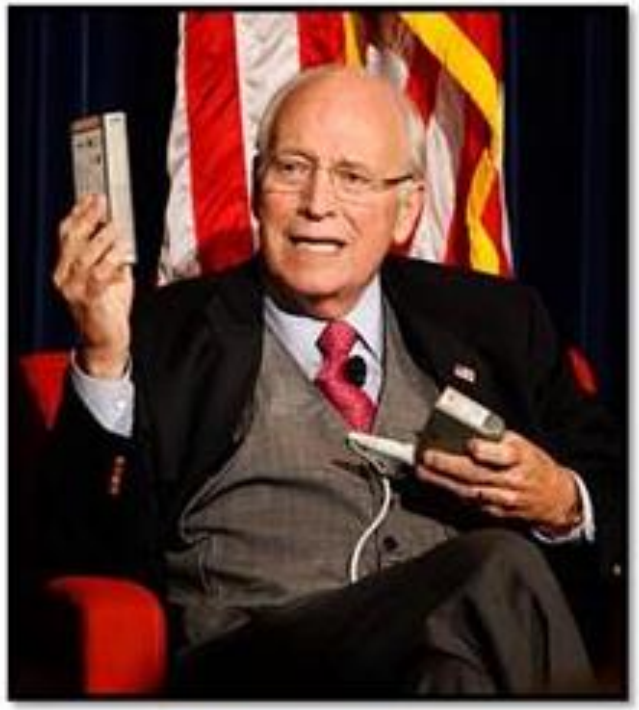




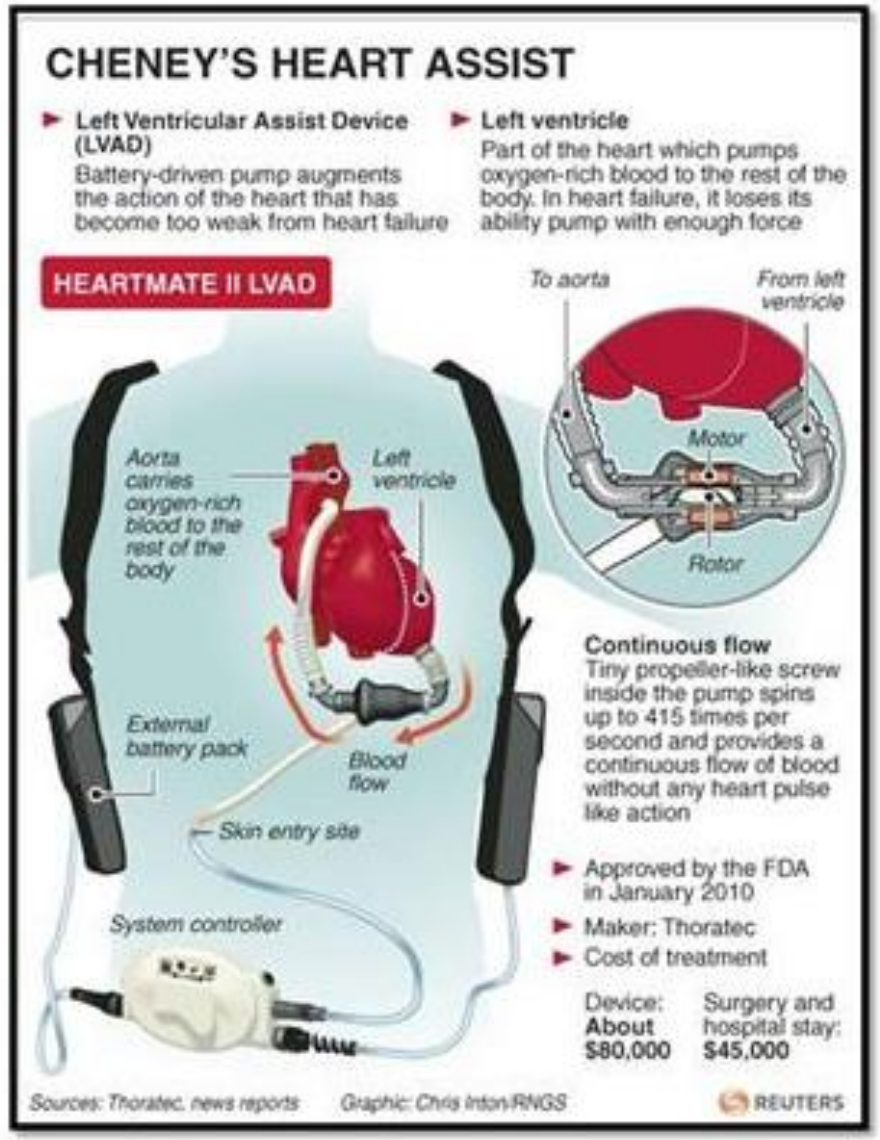
July 2010 – Former Vice President Dick Cheney implanted with a HeartMate II LVAD

Suffering from end-stage heart failure, **former Vice President Dick Cheney** had a VAD implanted at INOVA Fairfax Hospital, in Fairfax Virginia in July 2010.

In 2012, he received a heart transplant at age 71 after 20 months on a waiting list.



he HeartMate II Left Ventricular Assist Device (LVAD)



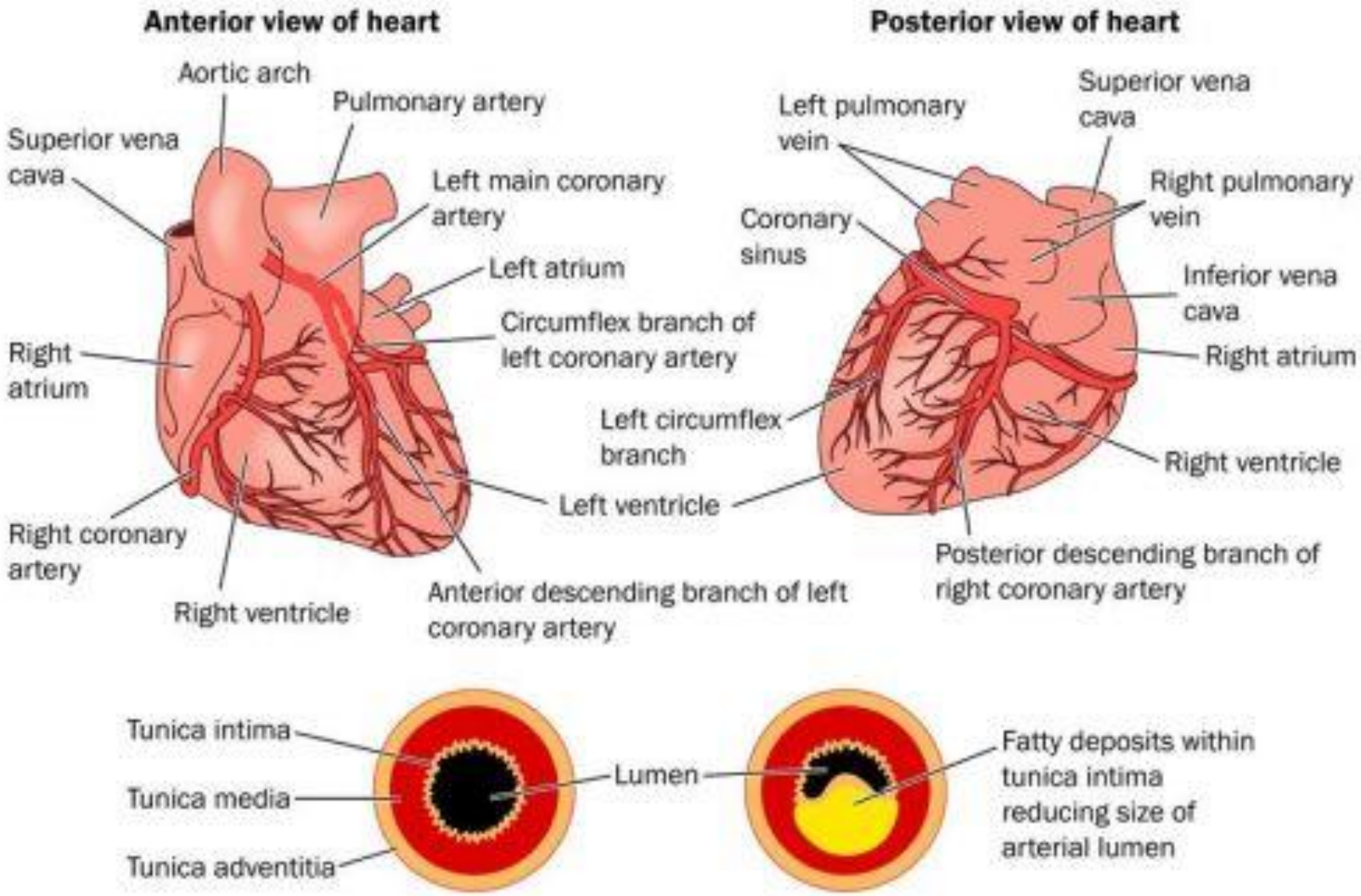
Vascular Grafts

Surgeons have long needed methods to repair damaged and diseased blood vessels. Early in the 20th century, Dr. **Alexis Carrel** developed methods to **anastomose** (suture) blood vessels, that awarded him the Nobel Prize in medicine in 1912.

In 1942 Blackmore used Vitallium tubes to bridge arterial defects in wounded soldiers. Columbia University surgical intern **Arthur Voorhees** (1922–92), during a postmortem in 1947 noticed that tissue had grown around a **silk** suture left inside a lab animal. This event stimulated the idea that a cloth tube might also heal by being colonized by the body tissues. Perhaps such a healing reaction could be used to replace an artery with a tube. His first experimental vascular grafts were sewn from a **silk handkerchief** and then **parachute fabric** (**Vinyon N**), using his wife's sewing machine.

The first human implant of a vascular graft was in **1952**. The patient lived years after this procedure, inspiring many surgeons. By 1954 the clear benefit of a **porous (fabric) tube** over a solid polyethylene tube was established. In 1958, the following technique was described in a textbook on vascular surgery: "The **Terylene**, **Orlon** or **Nylon** cloth is bought from a draper's shop and cut with pinking shears to the required shape. It is then sewn with thread of similar material into a tube and sterilized by **autoclaving** before use".

arterie coronarie

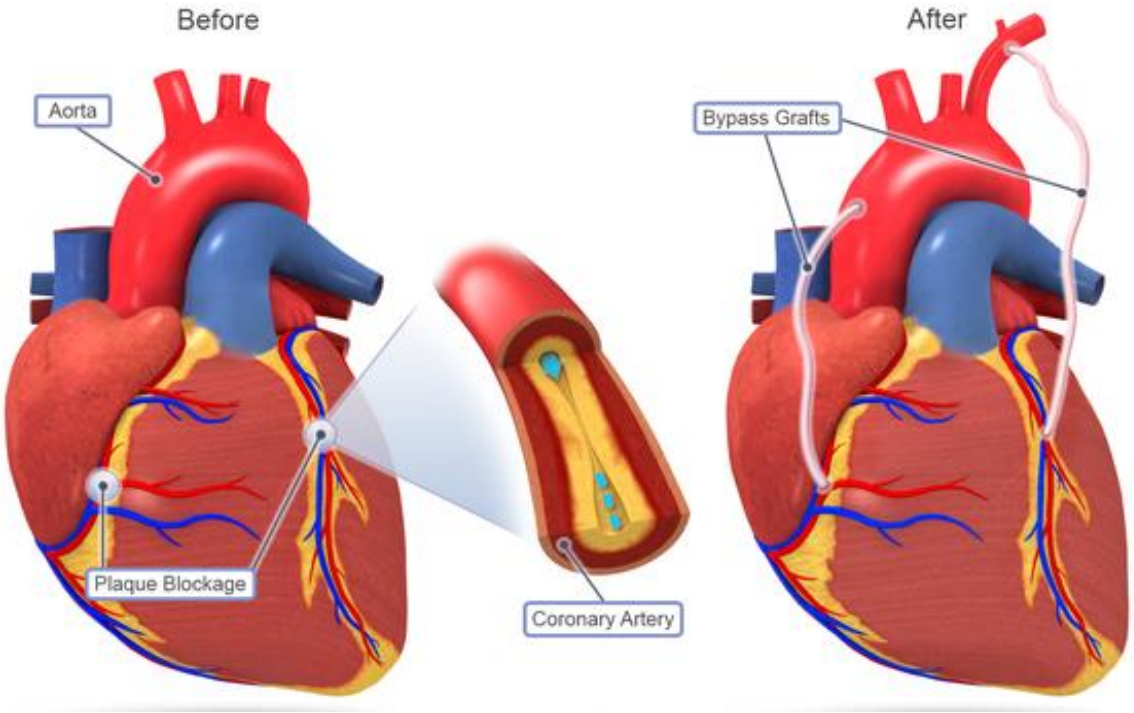


vascular bypass

is a surgical procedure performed to redirect blood flow from one area to another by reconnecting blood vessels. Often, this is done to bypass around a diseased artery, from an area of normal blood flow to another relatively normal area. It is commonly performed due to **inadequate blood flow (ischemia)** caused by atherosclerosis, as a part of organ transplantation, or for vascular access in hemodialysis.

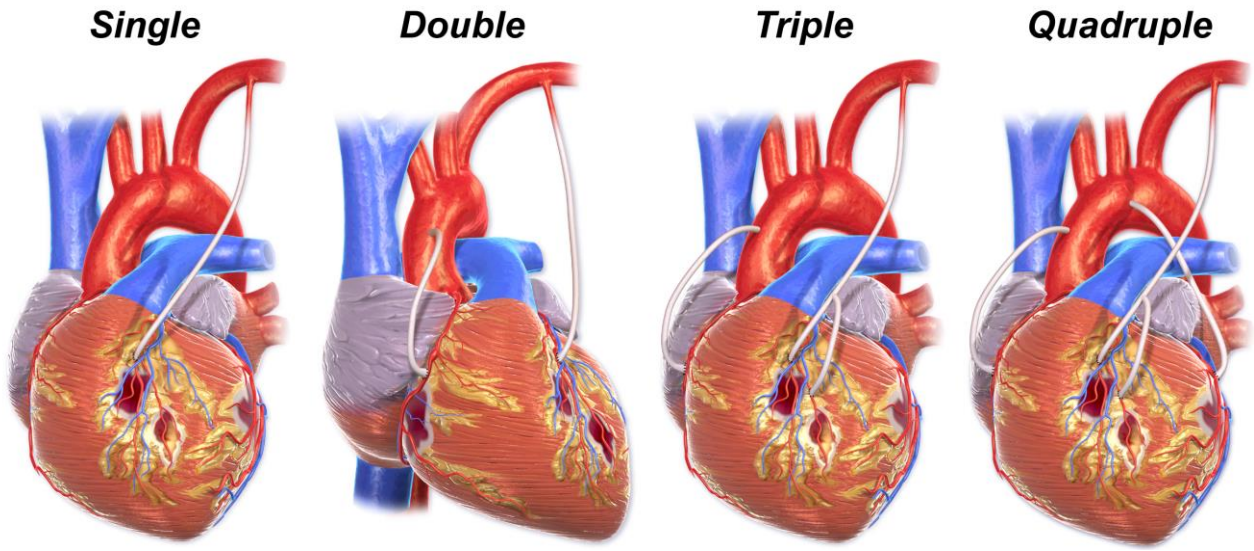
In general, **someone's own vein (autograft)** is the preferred graft material (or conduit) for a vascular bypass, but other types of grafts such as **polytetrafluoroethylene (Teflon), polyethylene terephthalate (Dacron), or a different person's vein (allograft)** are also used. Arteries can also serve as vascular grafts. A surgeon sews the graft to the source and target vessels by hand using surgical suture, creating **a surgical anastomosis**.

Common bypass sites include **the heart (coronary artery bypass surgery)** to treat coronary artery disease, and the legs, where lower extremity bypass surgery is used to treat peripheral vascular disease.



Coronary Arthery Bypass Graft (CABG)

Autologous veins are used to by pass clotted coronary artheries



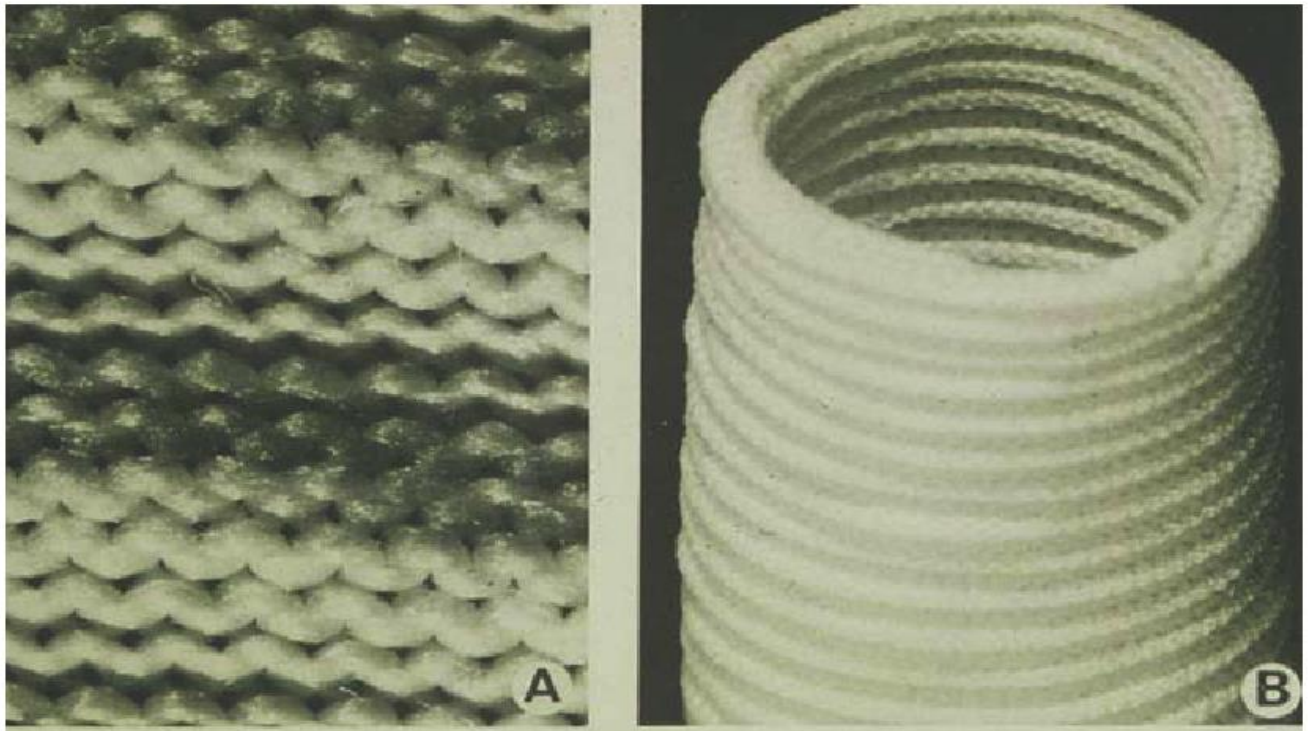


FIG. 3A. Appearance of knitted Dacron graft material ×85. B, Crimped tube graft.

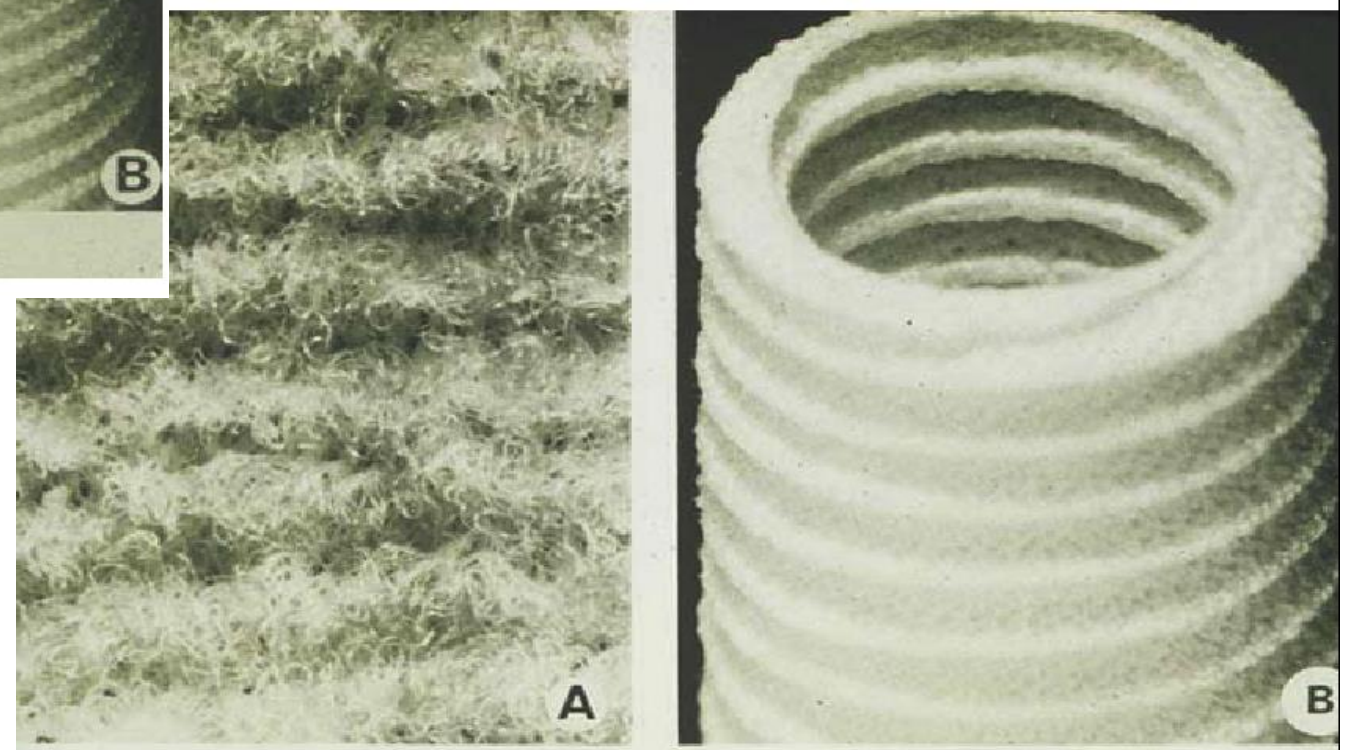
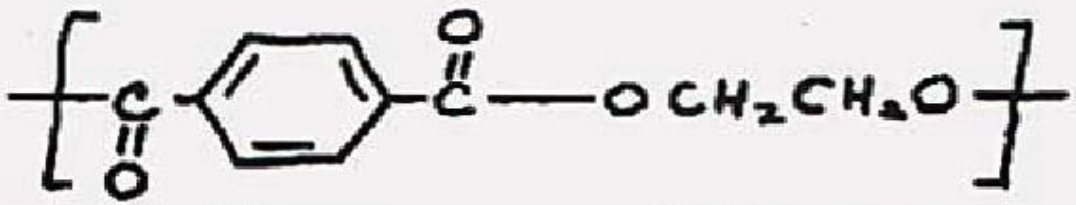


FIG. 4A. Appearance of Dacron velour graft material ×85. B, Crimped tube graft.

The PET Molecule



stiff group (dominates)

flexible group

Uses
Vascular grafts,
Implant fixation
(e.g., sewing rings)
Ingrowth felts

- Stiff groups along main chain:
- Low polarity
  (electrons above and below stiff group)
- Regular, "streamlined" shape along chain

All these lead to a crystalline, high melting, lowwater sorption polymer, useful as a fiber.

$$--(-CF_2-CF_2-)_x--$$

Poly(tetrafluoroethylene)
Teflon®

A highly symmetrical chain, but very stiff, so it is both crystalline and high melting (327°C)

In the early days, *woven* Teflon® was used as a vascular graft. It was not strong enough and often burst under the blood pressure. Later, *expanded* Teflon® or e-PTFE has been successfully used as a vascular graft. It is widely known as Gore-Tex®.

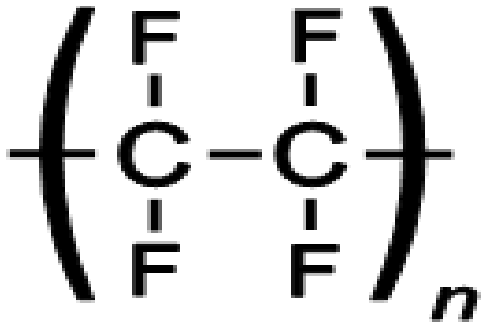
Polytetrafluoroethylene (PTFE)

is a synthetic fluoropolymer of tetrafluoroethylene with many applications. The best-known brand name of PTFE-based formulas is **Teflon®** by Chemours, a spin-off of DuPont, which originally discovered the compound in 1938.

PTFE is a fluorocarbon solid, as it is a high molecular weight compound consisting of carbon and fluorine. PTFE is hydrophobic: neither water nor water-containing substances can wet PTFE, due to the high electronegativity of fluorine.

PTFE has one of the lowest **coefficients of friction**. It is used as a non-stick coating for pans and other cookware. It is nonreactive, partly because of the strength of the C-F bonds, and so it is often used in containers and pipework for reactive and corrosive chemicals. When used as lubricant, PTFE reduces friction, wear, and energy consumption of machinery.

Commonly used as a graft material in surgical interventions, it is Also frequently used as coating on catheters; this limits the ability of bacteria and other infectious agents to adhere to catheters and cause hospital-acquired infections.



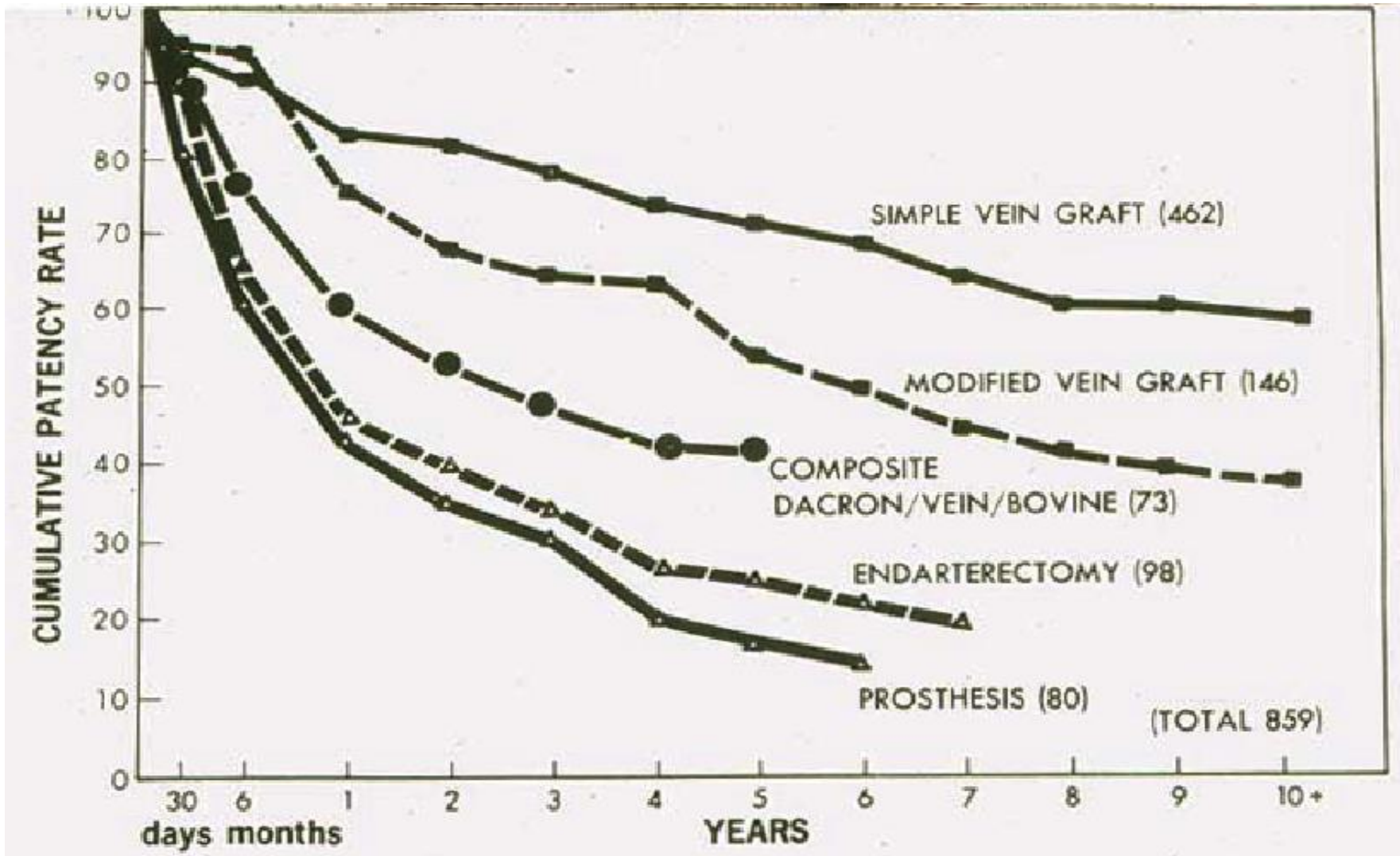


FIG. 3. Patency rates of 859 femoropopliteal grafts, as determined by life table method (1960–1974).

Thrombosed small diameter Dacron vascular grafts

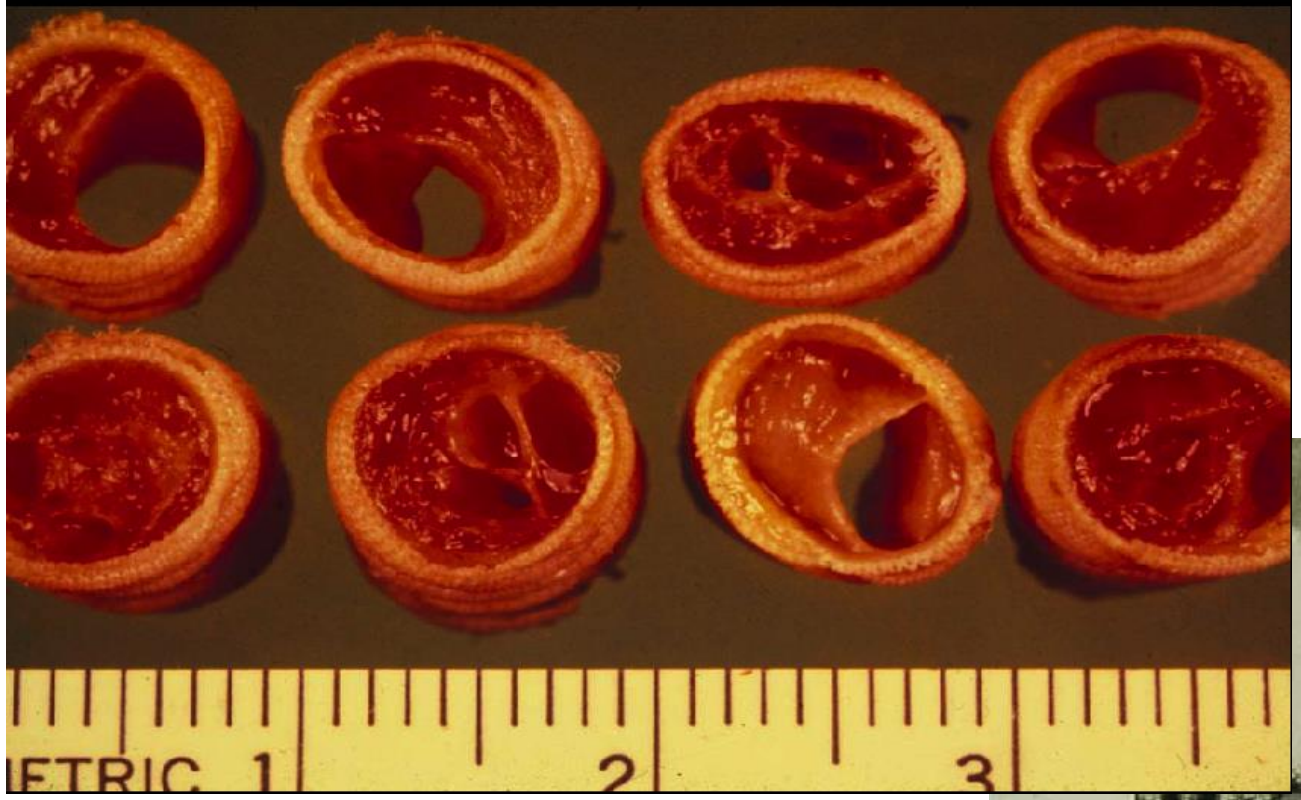
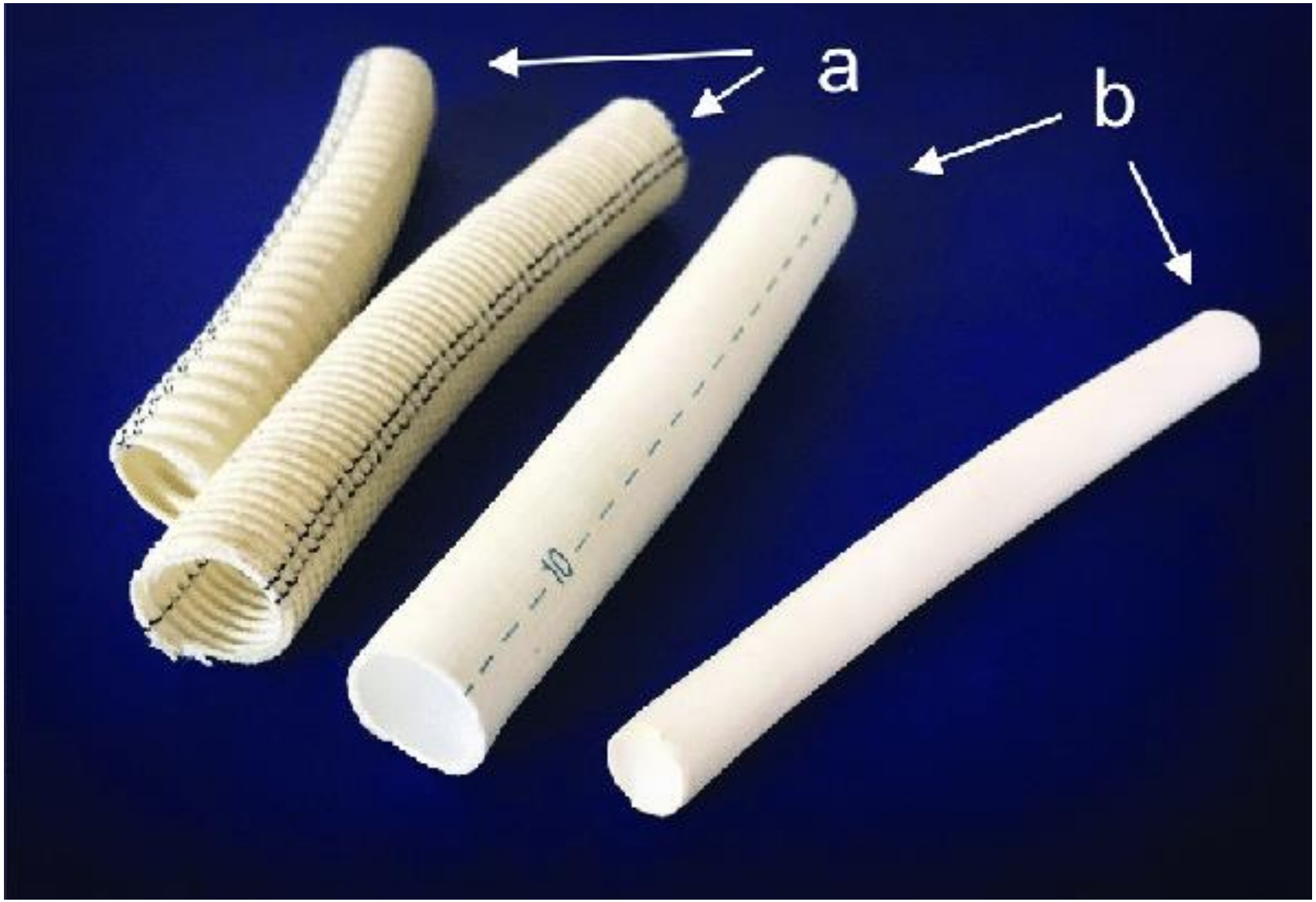
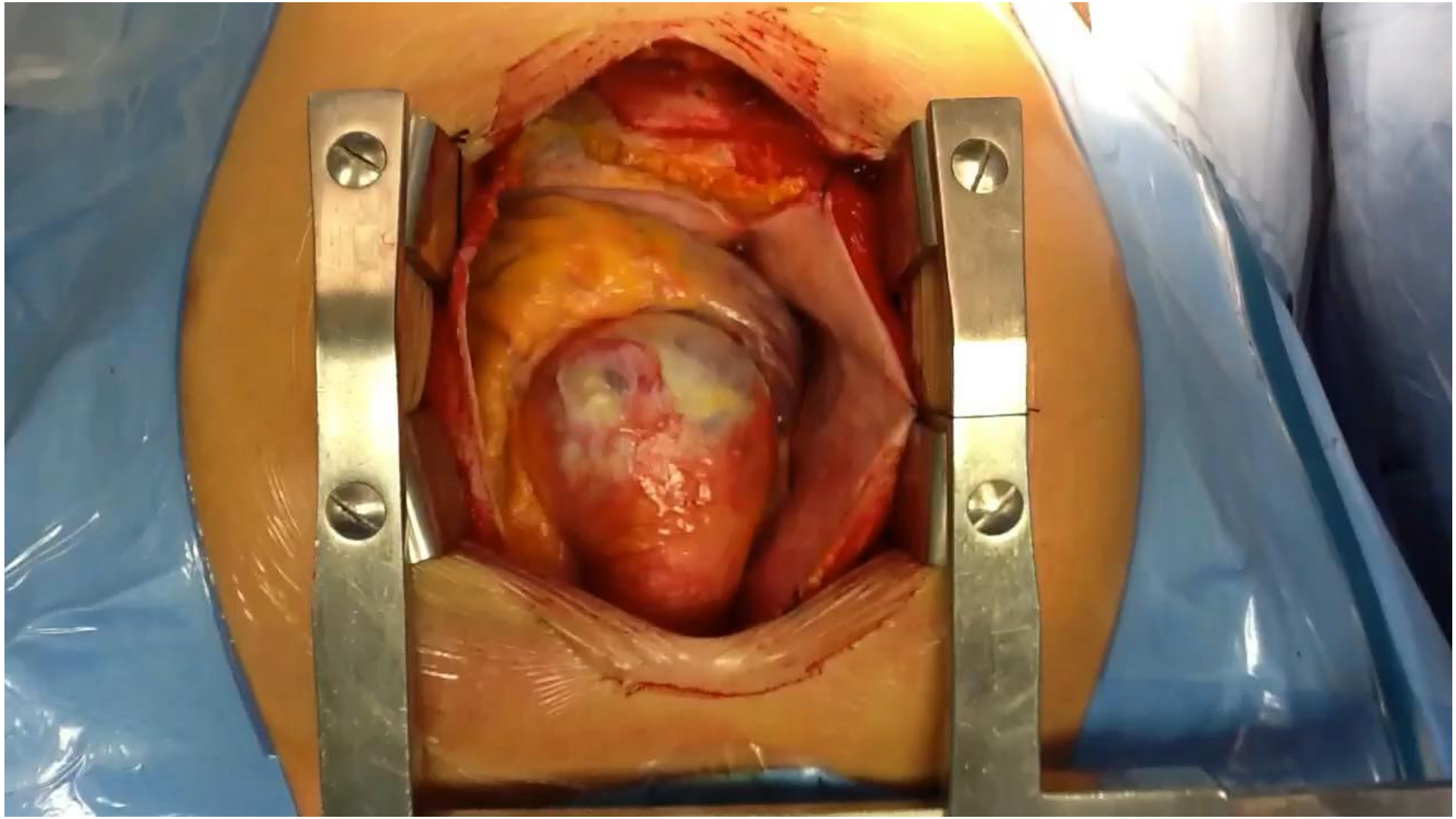


FIG. 1. Photographs of operative specimens showing two causes of delayed false aneurysm following arterial prosthetic implantation. [redacted]. B. Blow-out of a woven Edward's Teflon graft 8 years after implantation. Photograph kindly supplied by R.H. Hayward, M.D., Scott and White Clinic, Temple, Texas.[1] This aneurysm is the obvious result of deterioration of the Teflon yarn which has been widely advertised as indestructible in the body.

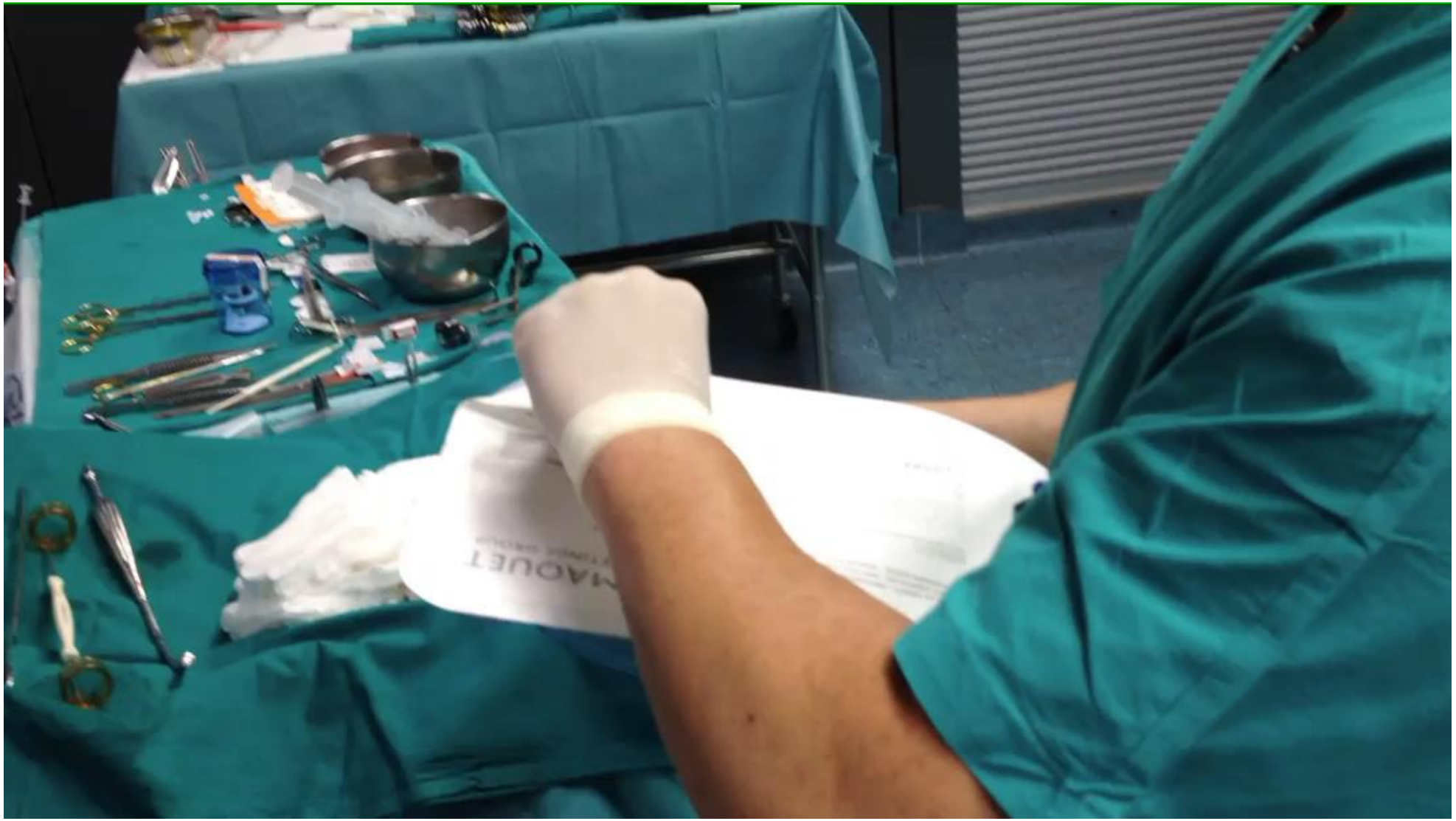


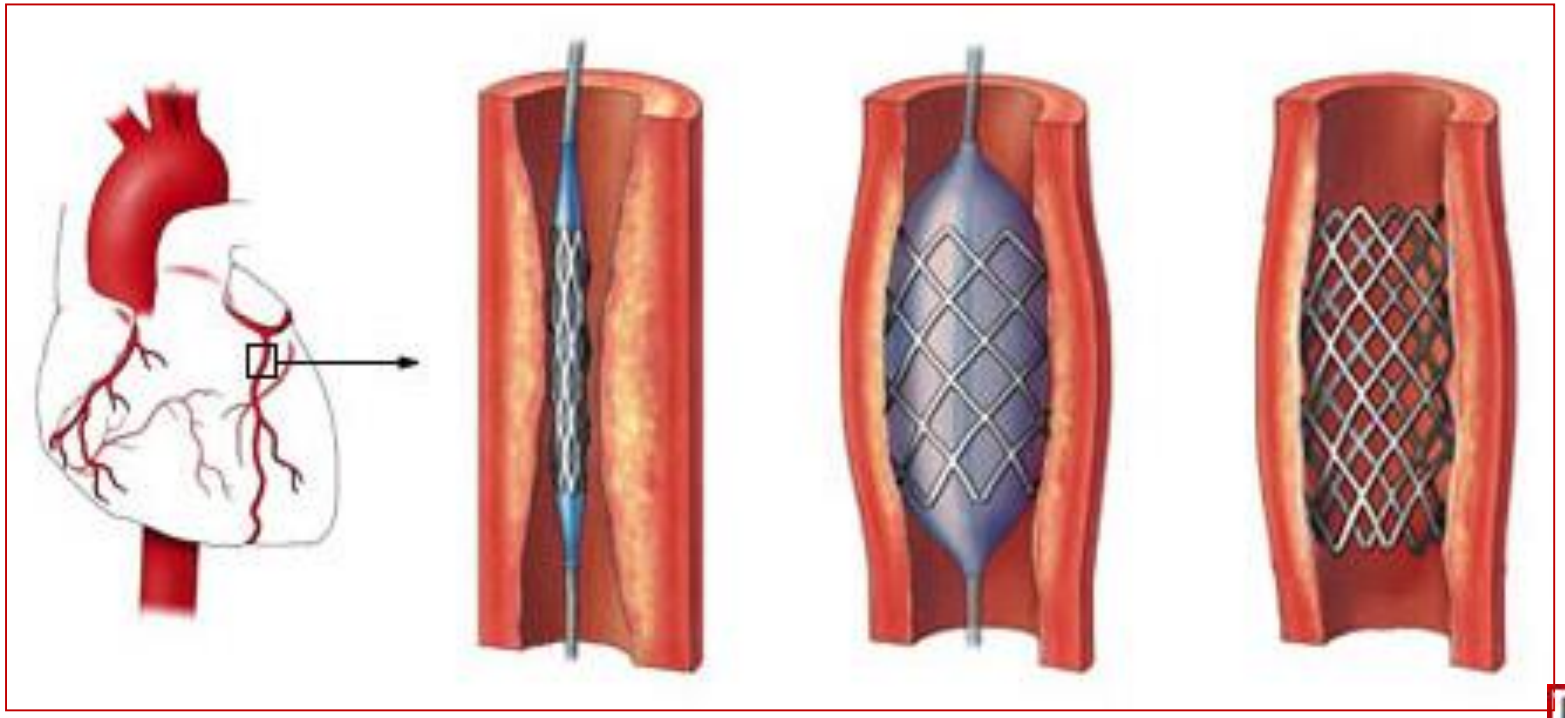
vascular grafts made from polyethylene terephthalate, PET (left, a) and expanded polytetrafluoroethylene, e-PTFE, Gore-Tex (right, b).

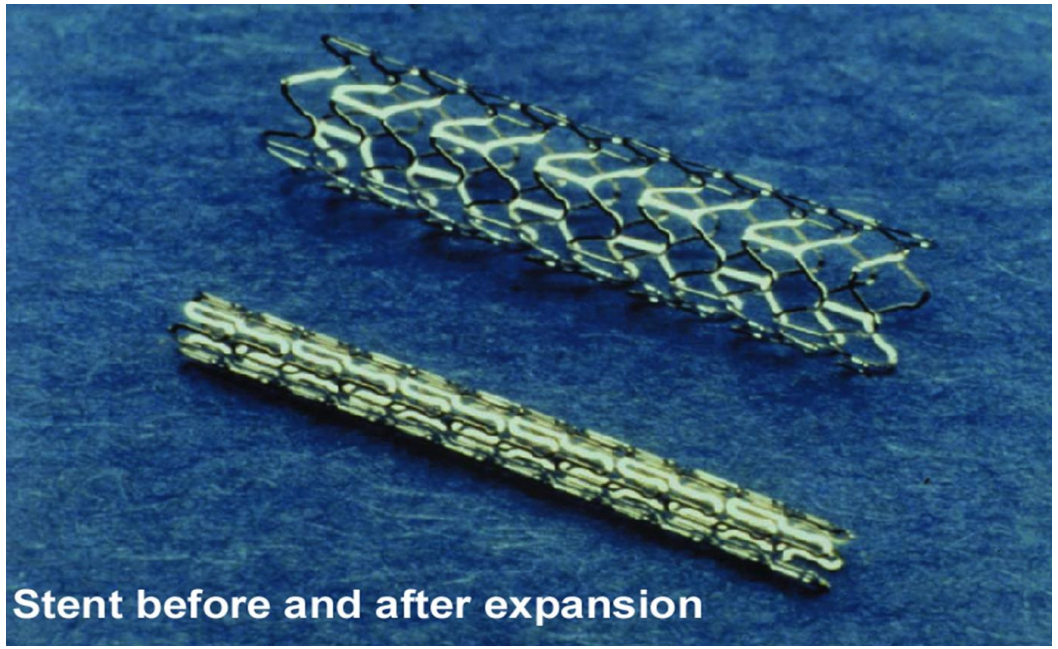
video
ANEURISMA
e VG AORTA 1

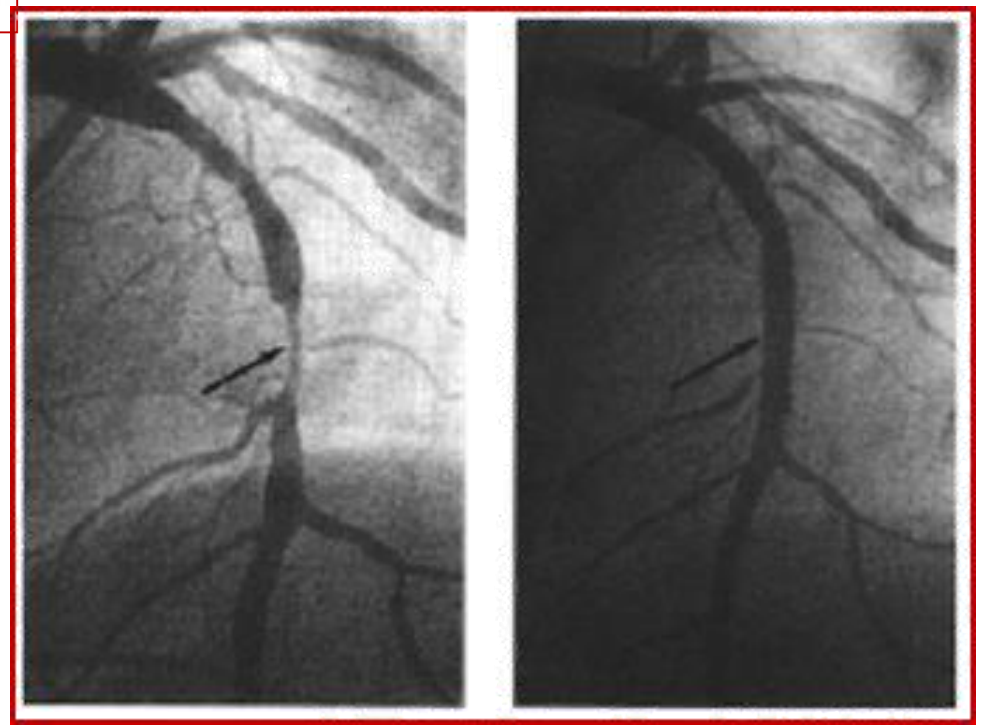


video
ANEURISMA
e VG AORTA 2






Stent before and after expansion



Cardiovascular stents

Partially occluded coronary arteries lead to angina, diminished heart functionality, and eventually, when the artery occludes (i.e., myocardial infarction), to the death of a localized portion of the heart muscle. Bypass take a section of a vein from another part of the body and replace the occluded coronary artery with a clean conduit. This is major and expensive surgery, hard on the patient.

However, in many cases the coronary artery can spasm and close for the trauma of the procedure. Synthetic vascular grafts in the 3 mm diameter size, appropriate to the human coronary artery anatomy, will thrombose, thus cannot be used.

Another option is **Percutaneous Transluminal Coronary Angioplasty (PTCA).** A balloon is threaded on a catheter into the coronary artery and then inflated to open the lumen of the occluding vessel.

The invention in 1978, by Dr. **Julio Palmaz**, of the **coronary artery stent**, an **expandable mesh structure** that holds the lumen open after PTCA, was revolutionary in the treatment of coronary occlusive disease. Coronary artery stenting is now performed in well over 1.5 million procedures per year.

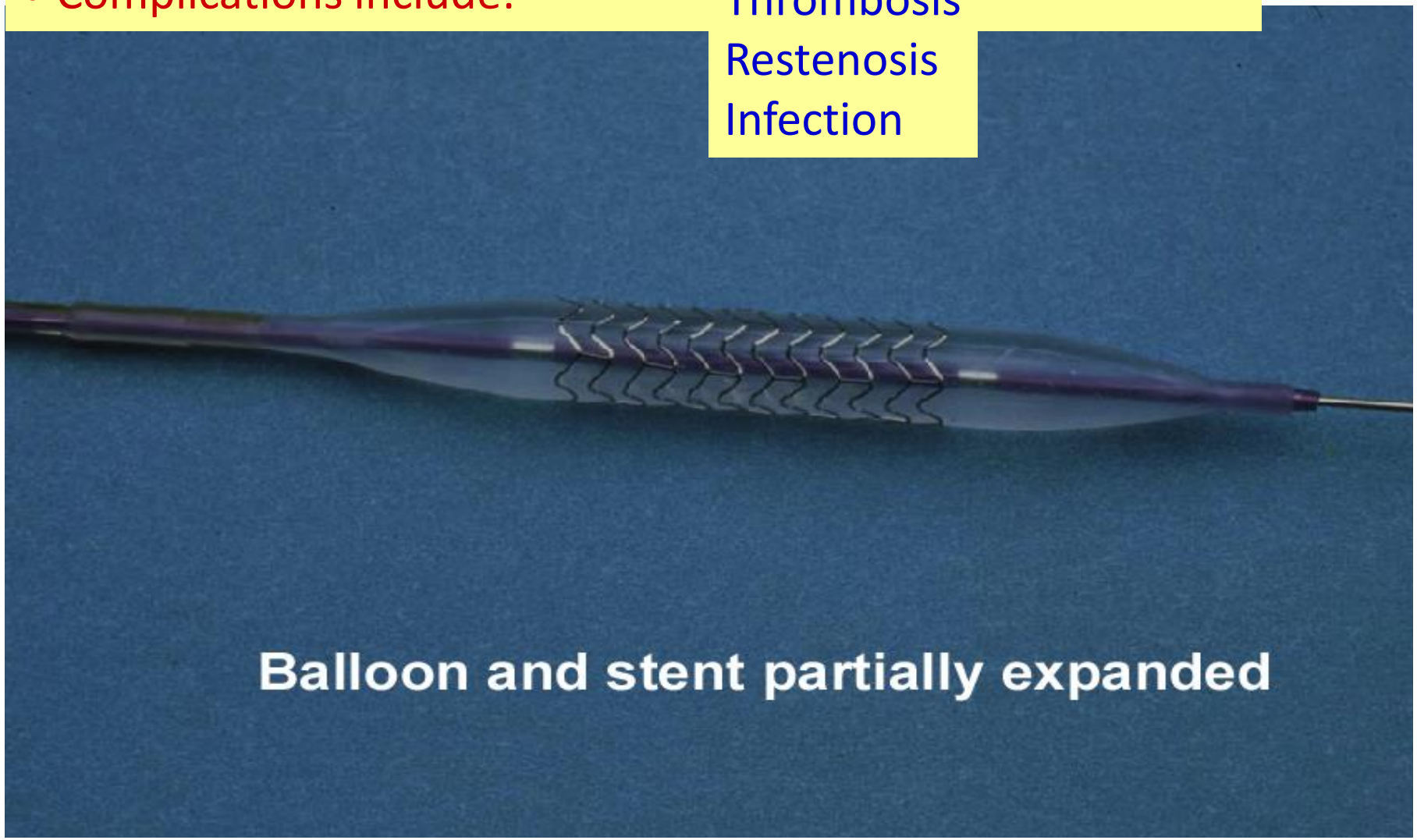
Dr. Julio Palmaz, inventor of the coronary artery stent.

In 1978 the main therapy of coronary heart disease was surgical bypass. Dr. Gruntzig showed his promising new technique to open up coronary atherosclerotic blockages without the need for open chest surgery, using his own plastic balloon catheters. …. he made it clear that in a third of the cases, the treated vessel closed back after initial opening with the angioplasty balloon because of elastic recoil or delamination of the vessel wall layers. This required standby surgery facilities and personnel, in case acute closure after balloon angioplasty, prompted emergency coronary bypass.

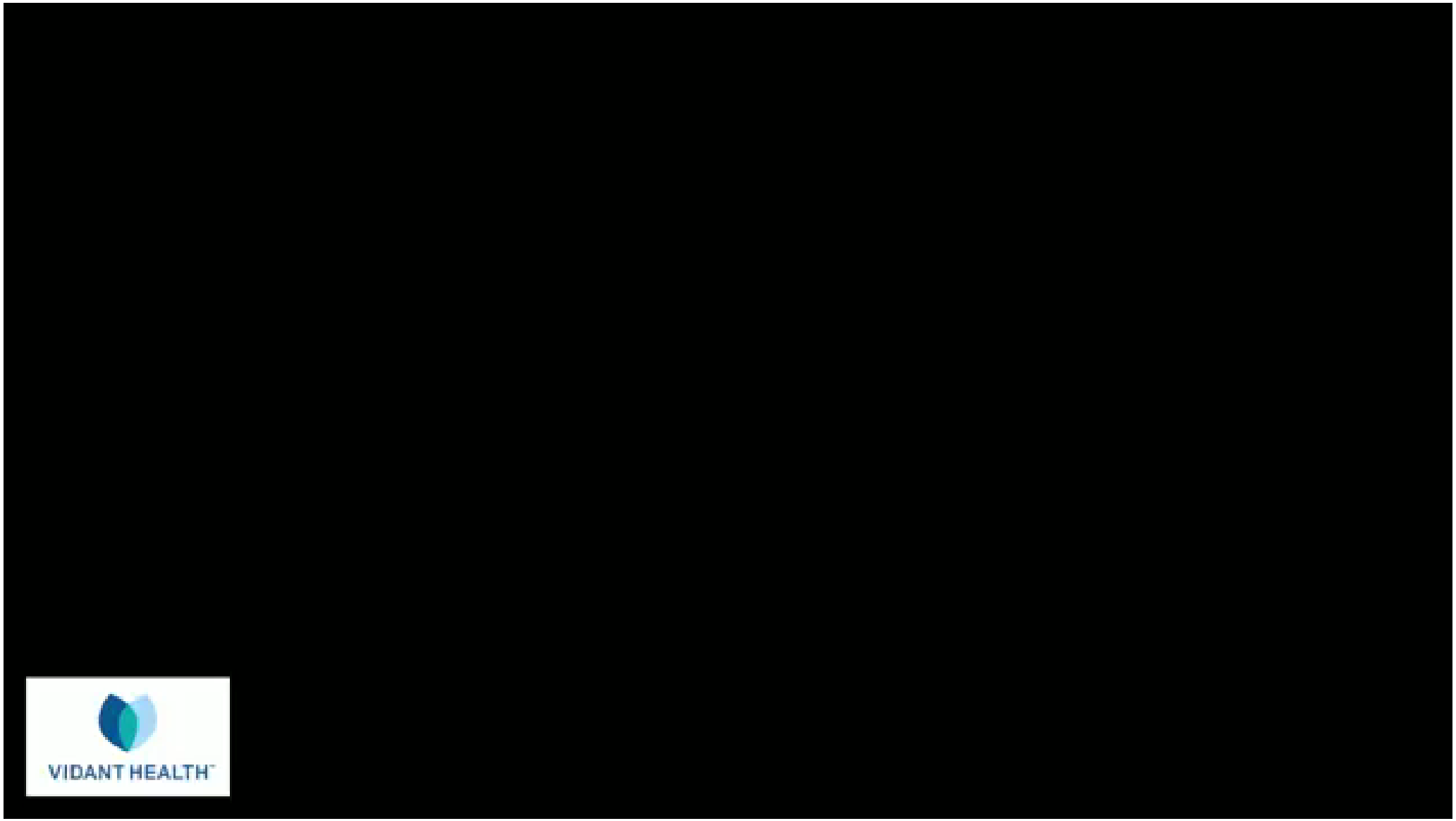
Gruntzig description of the vessel reclosure elicited in my mind the idea of using some sort of support, such as used in mine tunnels or in oil well drilling. Since the coronary balloon goes in small (folded like an umbrella) and is inflated to about 3–4 times its initial diameter, my ideal support device needed to go in small and expand at the site of blockage with the balloon. I thought one way to solve this was a malleable, tubular, crisscross mesh.

I went back home in the Bay Area and started making crude prototypes with copper wire and lead solder, which I first tested in rubber tubes mimicking arteries. I called the device a BEIS or balloon expandable intravascular graft. However, the reviewers of my first submitted paper wanted to call it a stent. When looked the word up, I found out that it derives from Charles Stent, a British dentist who died at the turn of the century. Stent invented a wax material to make dental molds for dentures. This material was later used by plastic surgeons to keep tissues in place, while healing after surgery. The word "stent" was then generically used for any device intended to keep tissues in place while healing.

- Typically stainless steel, but polymers have been explored.
- Prevents collapse of recently cleaned artery.
- Complications include:
  - Thrombosis
  - Restenosis
  - Infection



video
STENT
INSERTION



Pacemakers

In London, 1788, Charles Kite wrote “An Essay Upon the Recovery of the Apparently Dead,” where he discussed electrical discharges to the chest for heart resuscitation. In the time 1820–80 it was already known that electric shocks could modulate the heartbeat (read *Frankenstein* from that era).

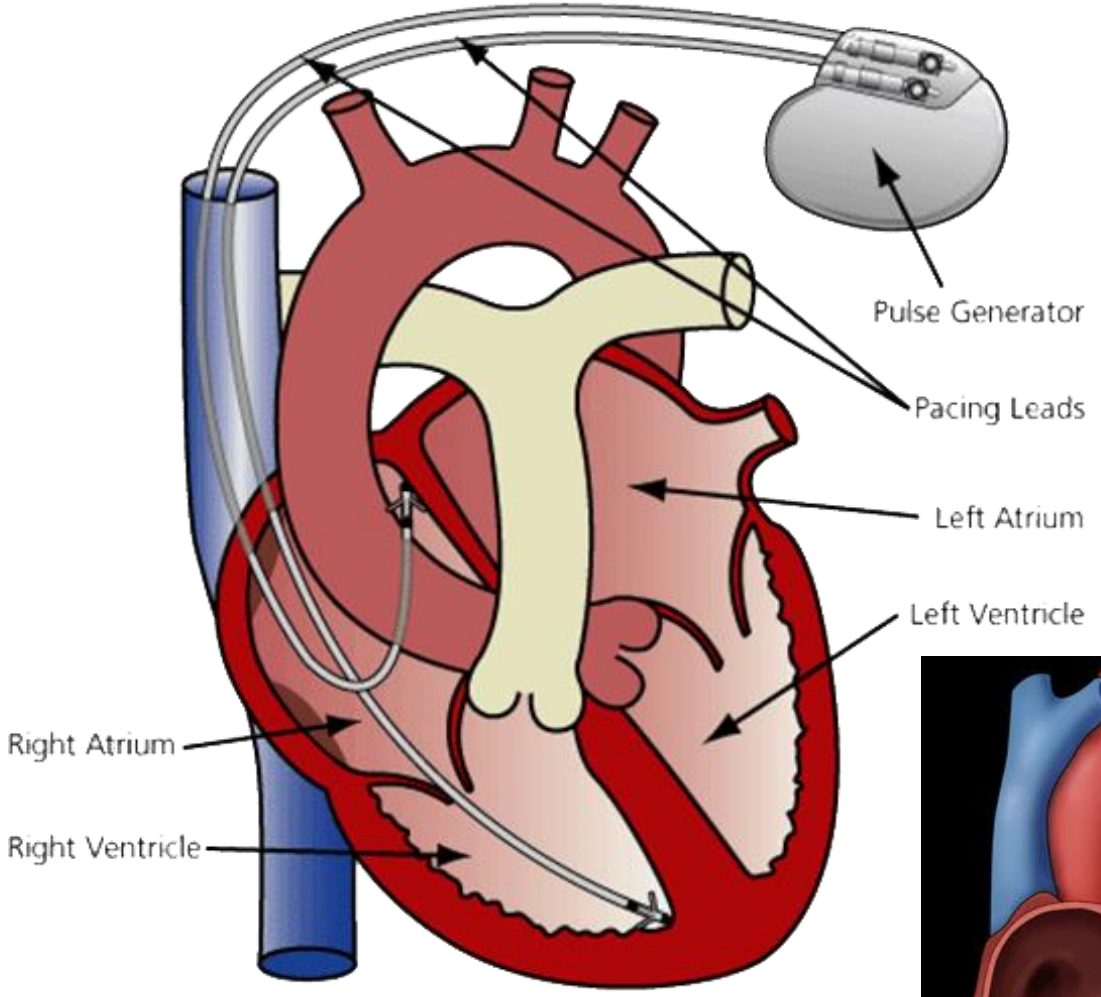
The invention of the portable pacemaker, hardly portable then, may have taken place almost simultaneously in two groups in 1930–31, Dr. A.S. Hyman in USA and Dr. M.C. Lidwill in Australia. Canadian electrical engineer, John Hopps, while conducting research on hypothermia, in 1949 invented an early pacemaker. Hopps’ discovery was that if a cooled heart stopped beating, it could be electrically restarted. This led to the invention of a **vacuum tube cardiac pacemaker** in 1950.

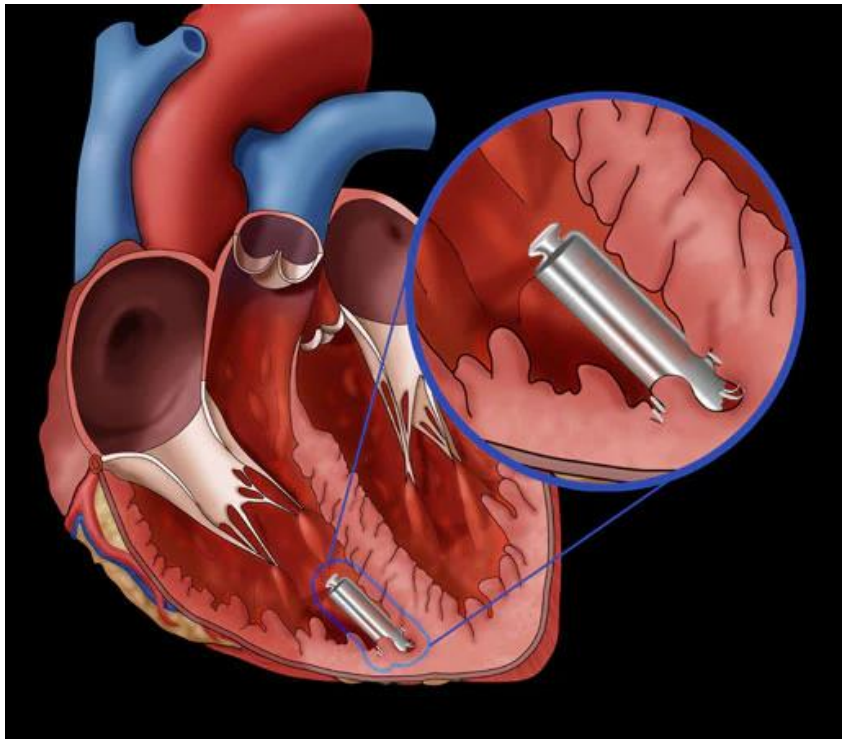
Paul M. Zoll developed a pacemaker jointly with the Electrodyne Company in 1952. About the size of a small microwave oven, powered with external current, it stimulated the heart through electrodes on the chest. This caused pain and burns, although it could pace the heart.

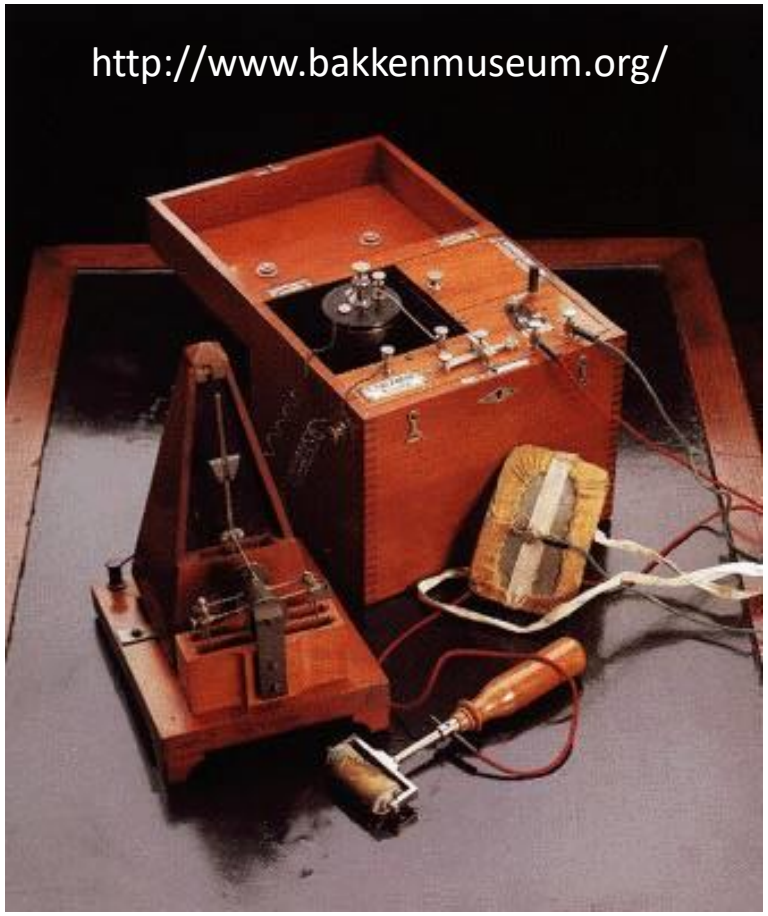
In 1957–58, **Earl E. Bakken, founder of Medtronics, Inc**., developed the first wearable transistorized (external) pacemaker for heart surgeon Dr. C. Walton Lillehei. Bakken quickly produced a prototype that Lillehei used on children with post surgery heart block. Medtronic commercially produced this wearable, transistorized unit as **the 5800 pacemaker**.

In 1959 the first fully implantable pacemaker was developed by engineer W. Greatbatch and cardiologist W.M. Chardack. He used two Texas Instruments transistors, a technical innovation that permitted small size and low power drain. The pacemaker was encased in epoxy to inhibit body fluids from inactivating it.

The Albert Hyman Model II portable pacemaker 1932–33

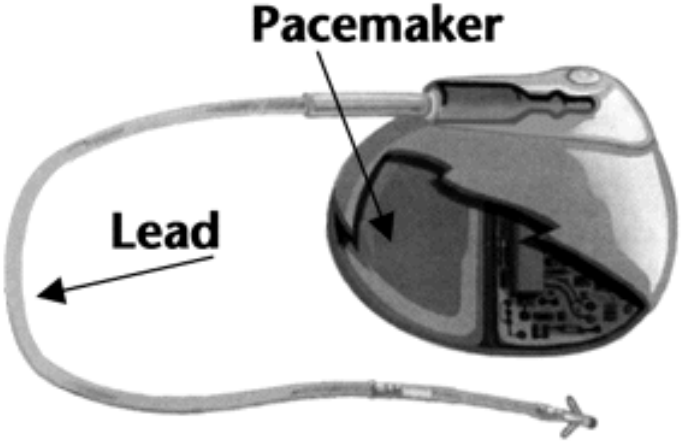






Late 19th century pacemaker
based on a metronome

1958 first transistor
implantable pacemaker

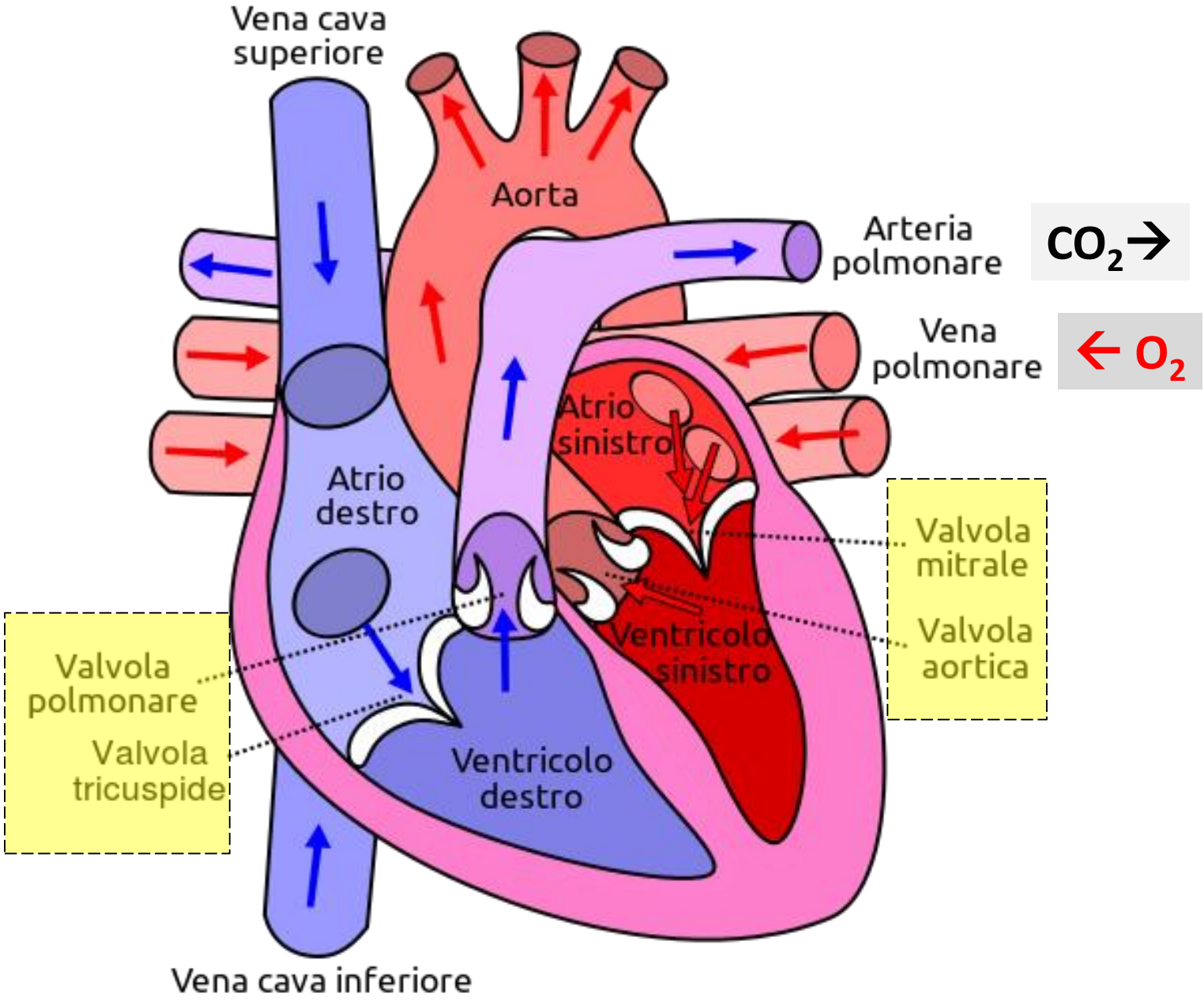


modern pacemaker

pacemakers are remarkably successful, but complications do occur

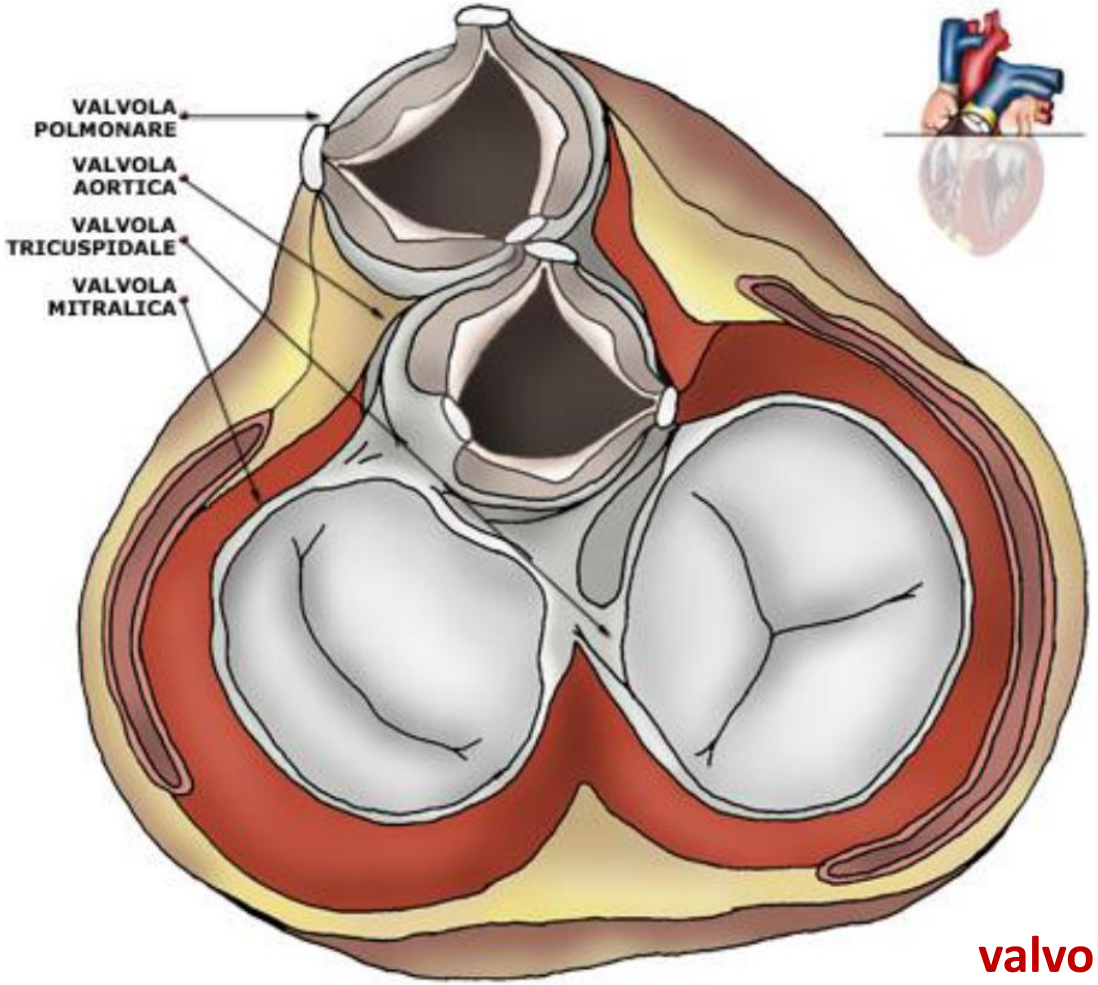
- ***Infection***
- ***Thrombosis***
- ***Scar formation***
- ***Loosening of electrodes***
- ***Removal of electrodes***

Il cuore


Vena cava superiore
Aorta
Arteria polmonare
CO_2→
Vena polmonare
← O_2
Atrio sinistro
Atrio destro
Valvola mitrale
Valvola aortica
Ventricolo sinistro
Valvola polmonare
Valvola tricuspide
Ventricolo destro
Vena cava inferiore

valvole cardiache artificiali

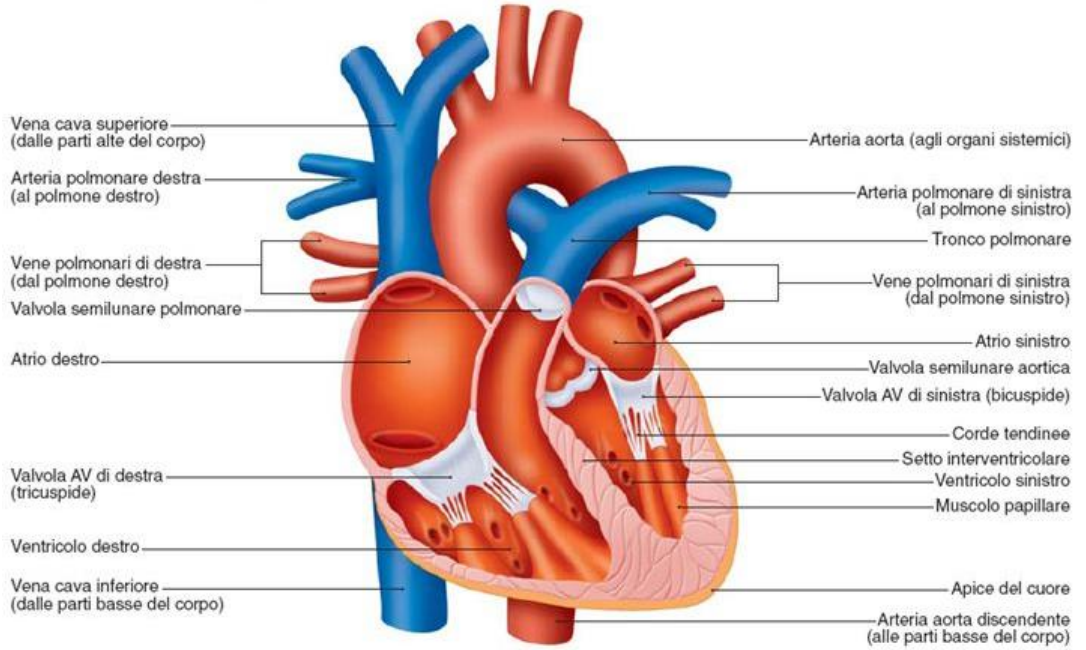
valvole semilunari



valvole atrioventricolari

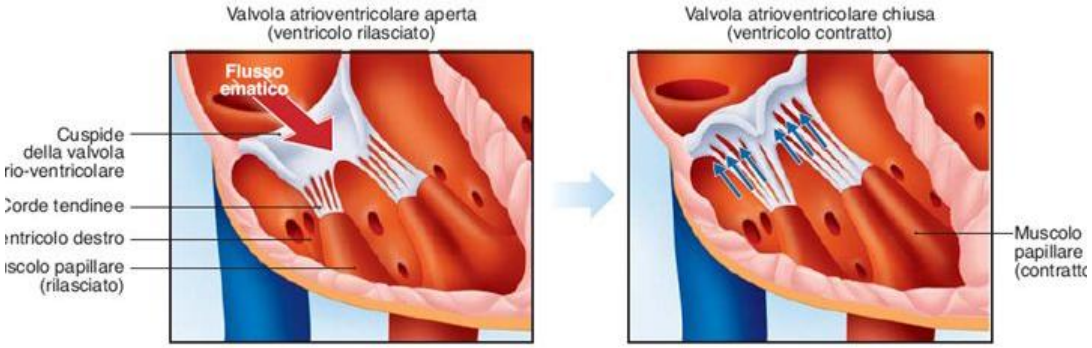
Le camere e le valvole cardiache

- Il sangue fluisce da una regione all'altra per gradiente di pressione
- Le valvole permettono che ciò avvenga unidirezionalmente



Le valvole atrioventricolari

- ***tricuspide*** (destra) e ***bicuspide (mitrale)*** (sinistra)
- si aprono quando Patriale > Pventric (diastole)
- si chiudono quando Pventric > Patriale (sistole)

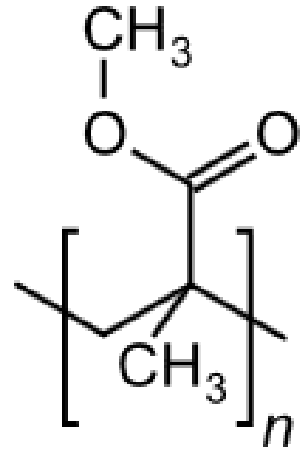


Heart Valves

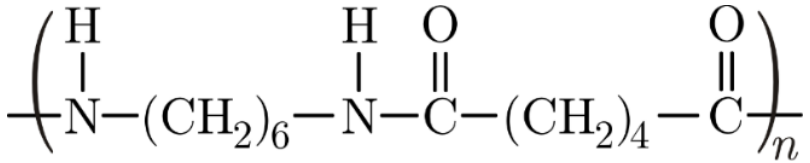
The development of the prosthetic heart valve paralleled developments in cardiac surgery. Until the heart could be stopped and blood flow diverted, the replacement of a valve would be challenging. Charles Hufnagel, in 1952, implanted a valve consisting of a **PMMA tube and nylon ball** in a beating heart. This was a heroic operation and basically unsuccessful, but an operation that inspired cardiac surgeons to consider that valve prostheses might be possible. The 1953 development of the heart-lung machine by Gibbon allowed the next stage in the evolution of the prosthetic heart valve to take place.

The Hufnagel heart valve, consisting of a PMMA tube and nylon ball

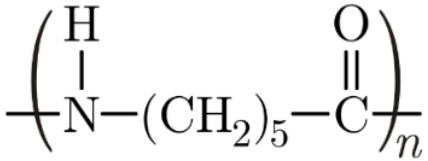
Il polimetilmetacrilato, **PMMA**, è una materia plastica formata da polimeri del **metacrilato di metile**, estere metilico dell'acido metacrilico. Nel linguaggio comune il termine metacrilato si riferisce generalmente a questi polimeri. È noto anche con i nomi commerciali di Plexiglas, Perspex, Lucite, Trespex, Vitroflex, Acrivill, Perclax, Limacryl, Crylux, Oroglas, Setacryl, Altuglas.



Il **Nylon** è una famiglia di poliammidi sintetiche. Il termine nylon indica le poliammidi alifatiche, ma talvolta si usa per indicare anche la classe delle poliaramidi (es Kevlar e Nomex), che sono invece poliammidi aromatiche. I nylon sono usati soprattutto come fibra tessile e per produrre piccoli manufatti.
Il primo a sintetizzare le poliammidi fu Wallace Carothers, che sintetizzò la poli-esametilen-adipamide (**nylon 6,6**) in un laboratorio della DuPont nel 1935.
Il **nylon 6** fu prodotto per la prima volta da Paul Schlack nei laboratori IG Farben nel 1938, a partire dal caprolattame.



Nylon 66



Nylon 6

In 1960, a **mitral valve replacement** was performed in a human by surgeon **Albert Starr**, using a valve design consisting of a **silicone ball and PMMA cage** (later replaced by a **stainless steel** cage). The valve was invented by engineer **Lowell Edwards**. The heart valve was based on a design for a bottle stopper invented in 1858. Starr was quoted as saying: "Let's make a valve that works and not worry about its looks," referring to its design that was radically different from the leaflet valve that nature evolved in mammals.

Before the Starr–Edwards valve, no human had lived with a prosthetic heart valve longer than 3 months.

The Starr–Edwards valve was found to permit good patient survival.

The major issues in valve development Then were **thrombosis** and **durability**.

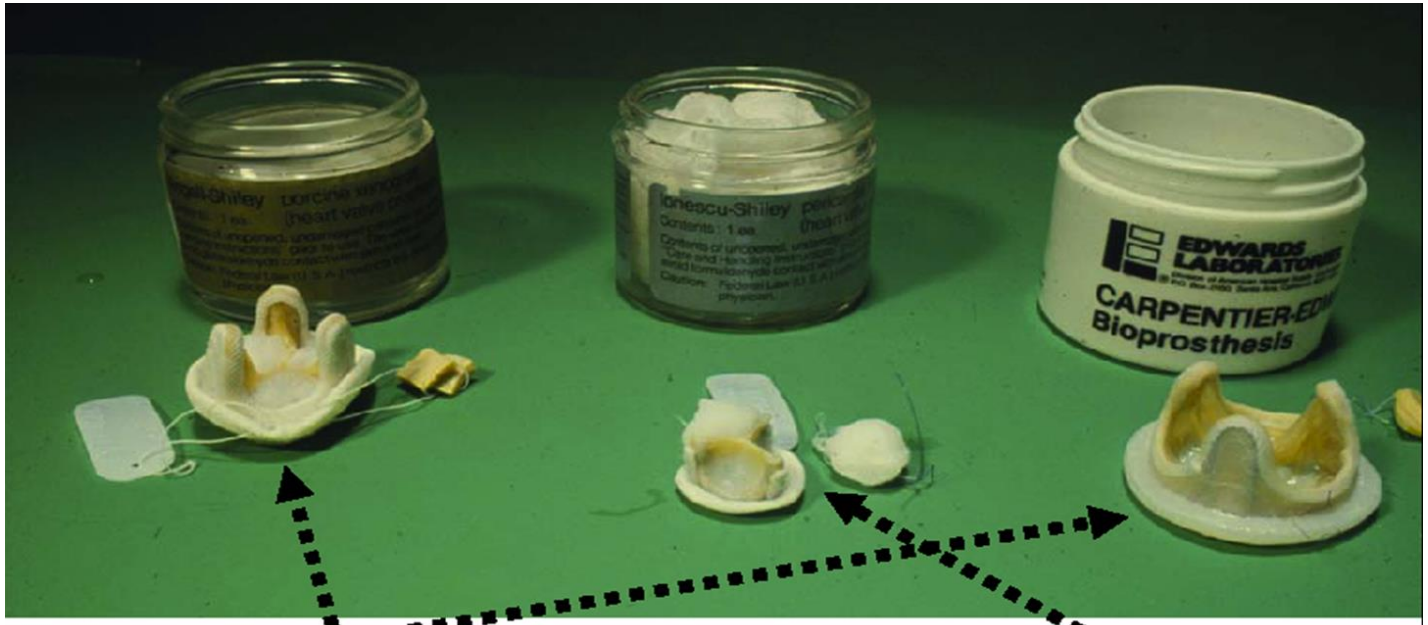
Glenn Baker was just 32 years old when he underwent a relatively new surgical procedure in 1966 to replace a heart valve. In 2016, the 82-year-old and his family celebrated 50 years of living with the original valve — a feat not many patients can claim. Baker began to experience heart problems when he was about 15 years old. One day, his heart began beating very fast and wouldn't slow down. At the hospital, he learned he had premature heartbeats, which are extra, abnormal heartbeats. "They were taking the sickest people and hoping for the best," said Carol Baker, Glenn's wife. "When I stop and think about it today, I'm overwhelmed that he survived," she added.

Baker was among the early patients to receive a **Starr-Edwards heart valve**, which was created by young surgeon, Dr. Albert Starr, and a semi-retired engineer, Lowell Edwards. The first Starr-Edwards valve successfully placed in a human — tests were done first on dogs — occurred in 1960 at the University of Oregon Medical School, now Oregon Health & Science University. Prior to the Starr-Edwards valve, there were no published reports of patients living more than 3 months with a prosthetic valve in the mitral position.

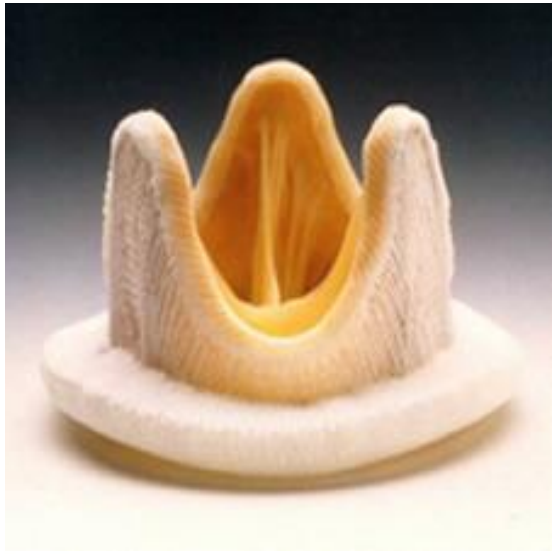
Vancouver man marks 50 years since getting Starr-Edwards heart valve

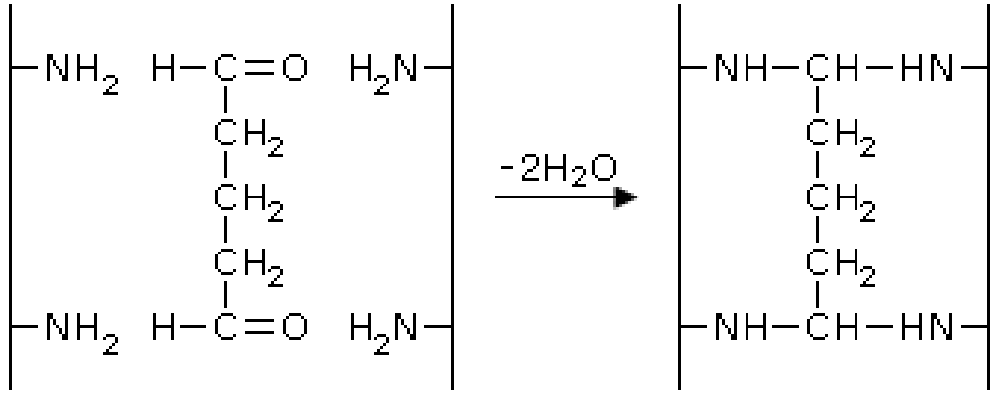
Carol Baker created posters about Dr. Albert Starr and the Starr-Edwards valve, a type of valve placed in her husband's heart in 1966. Carol and Glenn Baker celebrated the 50th anniversary of the procedure with a party where the posters were displayed.

In 1969, Warren Hancock started the development of the first leaflet tissue heart valve based upon **glutaraldehyde-treated pig valves**, and his company and valve were acquired by Johnson & Johnson in 1979.

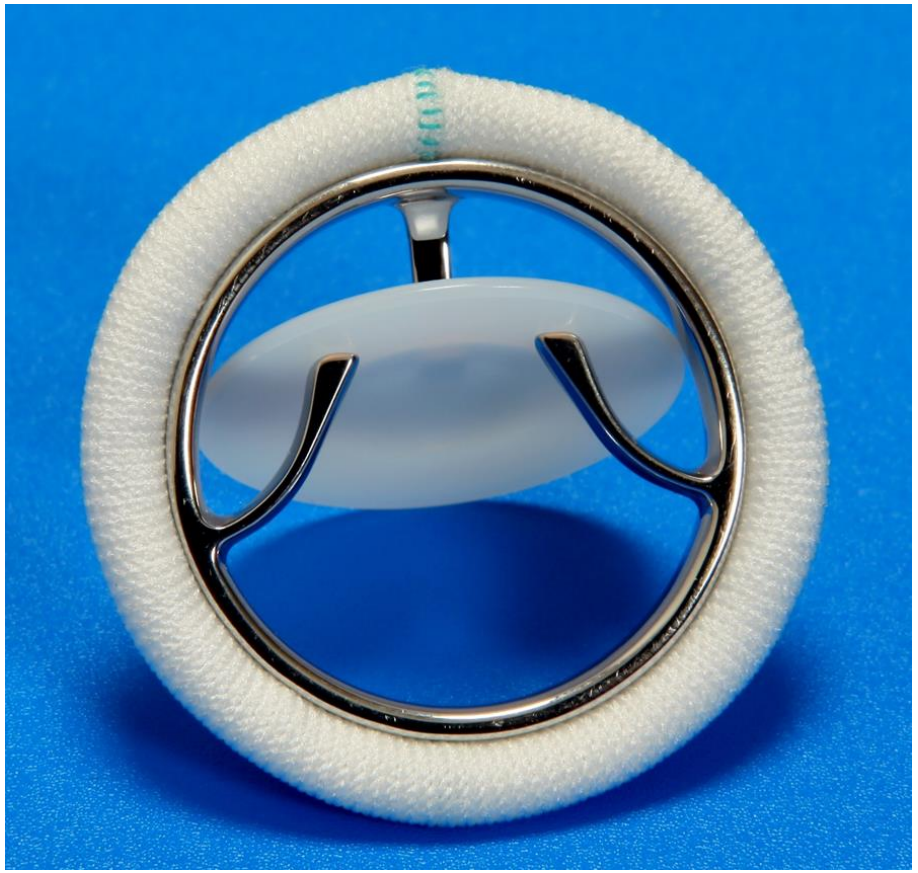


Natural pig valves and pericardial tissue valv

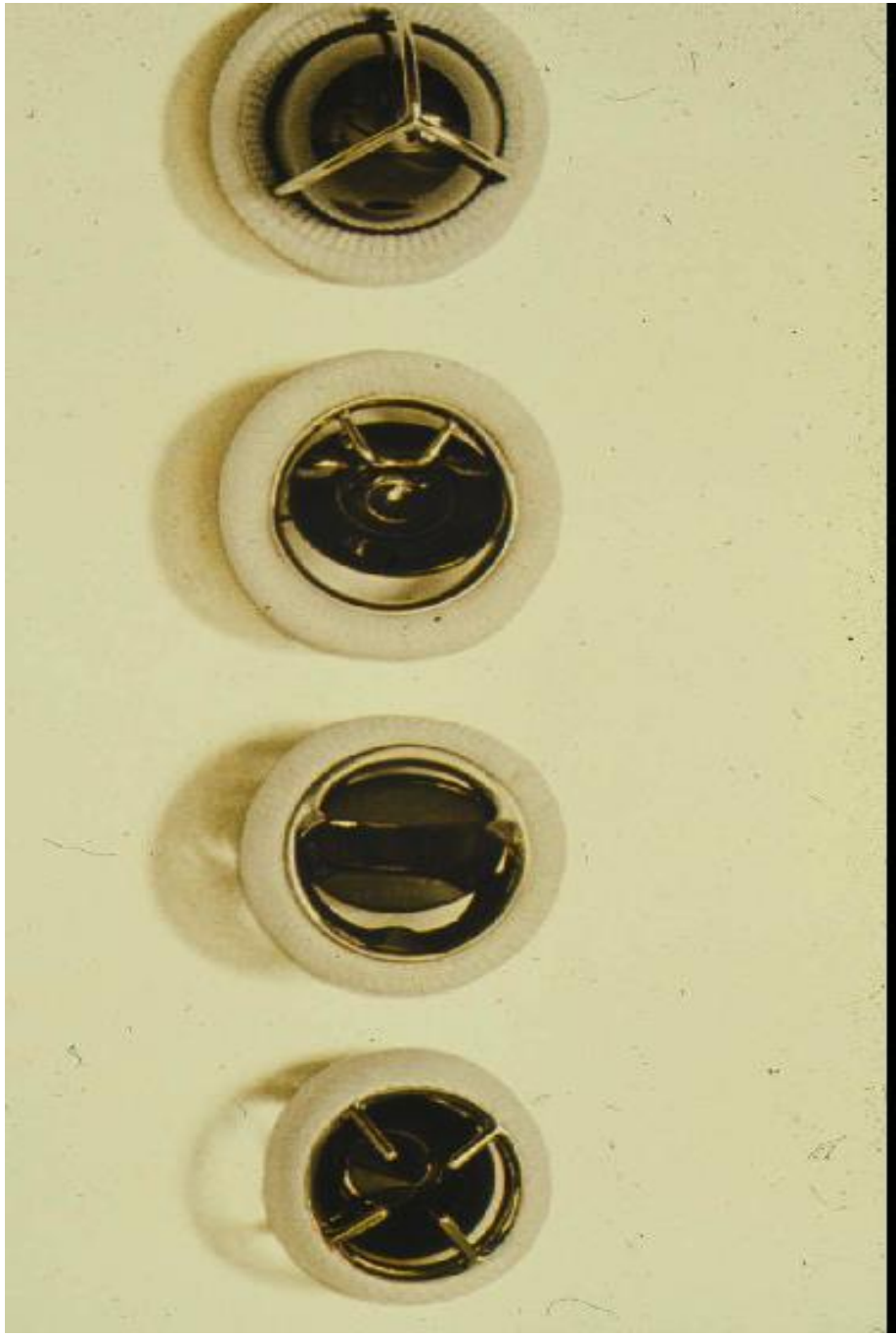




Tilting-disc valves came soon after. The first clinically available tilting disk valve was the Bjork-Shiley valve, with many significant design changes since its introduction in 1969. Tilting disk valves have a single circular occluder controlled by a metal strut. They are made of a metal ring covered by an **ePTFE fabric**, into which the suture threads are stitched for holding the valve in place. The metal ring holds, by means of two metal supports, a disc which opens and closes as the heart pumps blood through the valve. The disc is usually made of an **extremely hard carbon material (pyrolytic carbon),** in order to allow the valve to function for years.



The **Medtronic-Hall** model is the most common design in US. In some models of mechanical valves, the disc is divided into two parts, which open and close as a door.



Pyrolytic Carbon®
heart valves:
(one ball-in-cage and
three tilting disc valves)

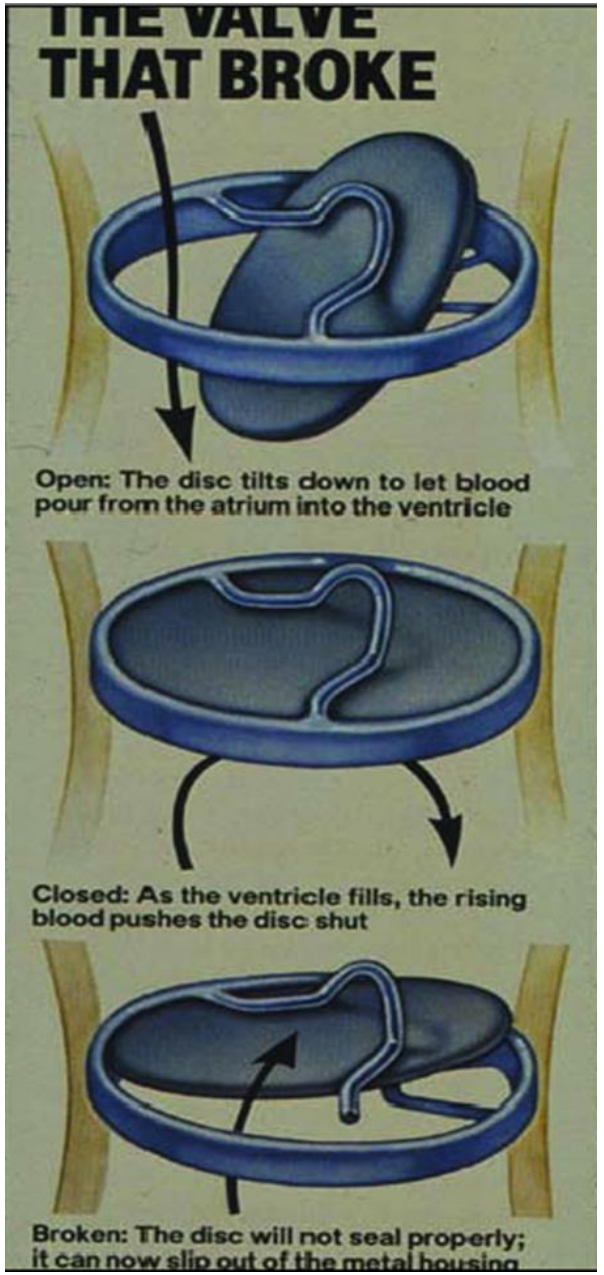
Il carbonio pirolitico è un materiale simile alla grafite, ma con qualche legame covalente tra gli strati di graphene, a causa di imperfezioni dovute al metodo (PVD) di deposizione.

Durability

Mechanical heart valves (MHV) are considered more durable in comparison to their bioprosthetic counterparts. Struts and occluders are made out of either **pyrolytic carbon** or **titanium** coated with pyrolytic carbon, and the sewing ring cuff is **Teflon (PTFE)**, **polyester** or **dacron**.

Whern structural failure does happen, it usually results from occluder impact on the components. Impact and friction wear dictate the loss of material in MHV. Impact wear usually occurs in the hinge regions of bileaflets, between the occluder and ring in tilting-discs, and between the ball and cage in caged-ball valves. Friction wear occurs between the occluder and strut in tilting-discs, and between the leaflet pivots and hinge cavities in bileaflets.

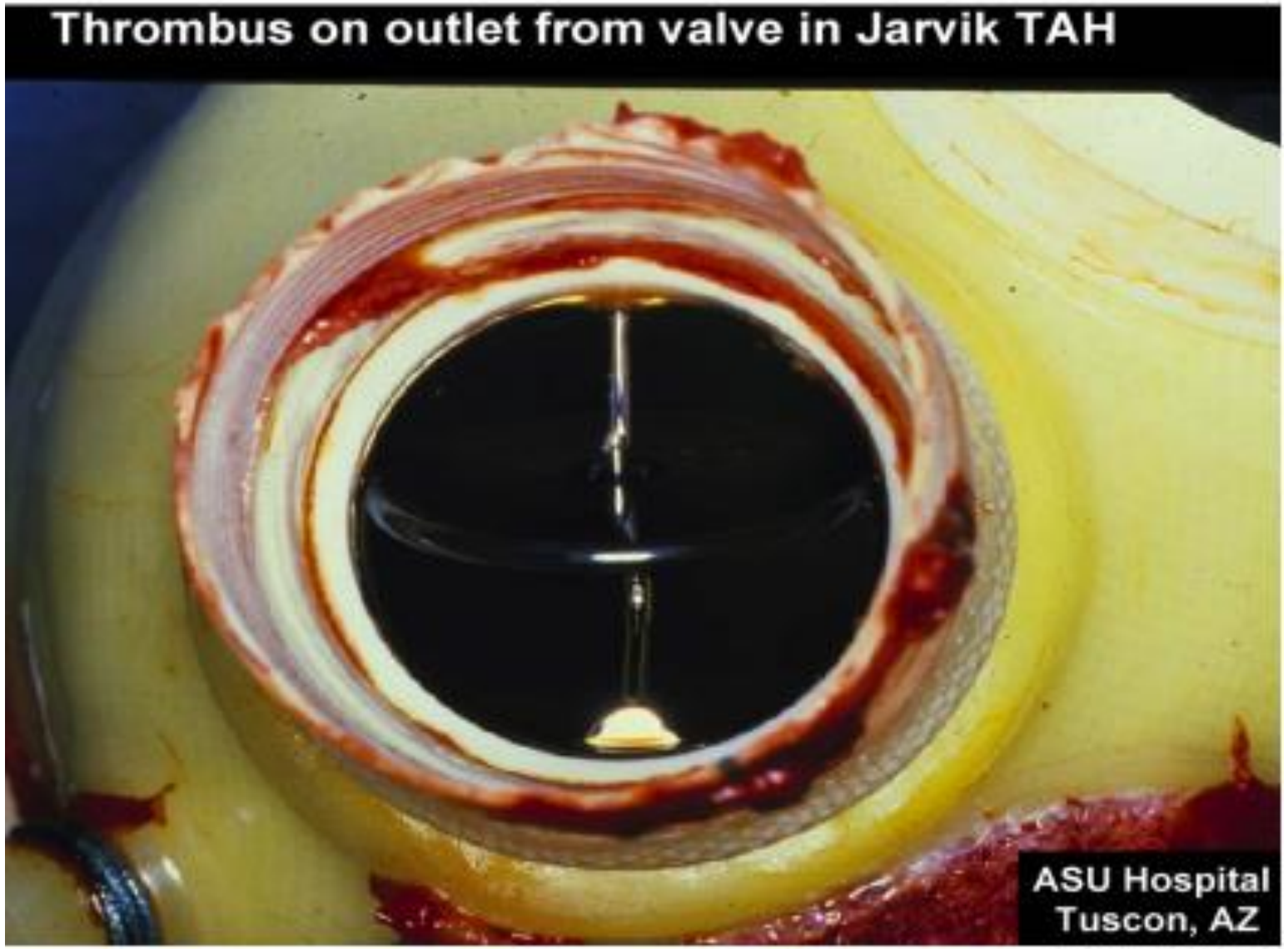
MHV made out of metal are also susceptible to fatigue failure due to the polycrystalline characteristic of metals, but this is not an issue with pyrolytic carbon MHV because this material is not crystalline.



Bileaflet heart valves consist of two semicircular leaflets that rotate about struts attached to the valve housing. This design was introduced in 1979. While they take care of some of the issues seen in the other models, bileaflets are vulnerable to backflow and so they cannot be considered as ideal. Bileaflet valves, however, provide much more natural blood flow than caged-ball or tilting-disc implants.

One of the main advantages of these valves is that they are well tolerated by the body. Only a small amount of blood thinner is needed by the patient each day in order to prevent clotting of the blood when flowing through the valve.

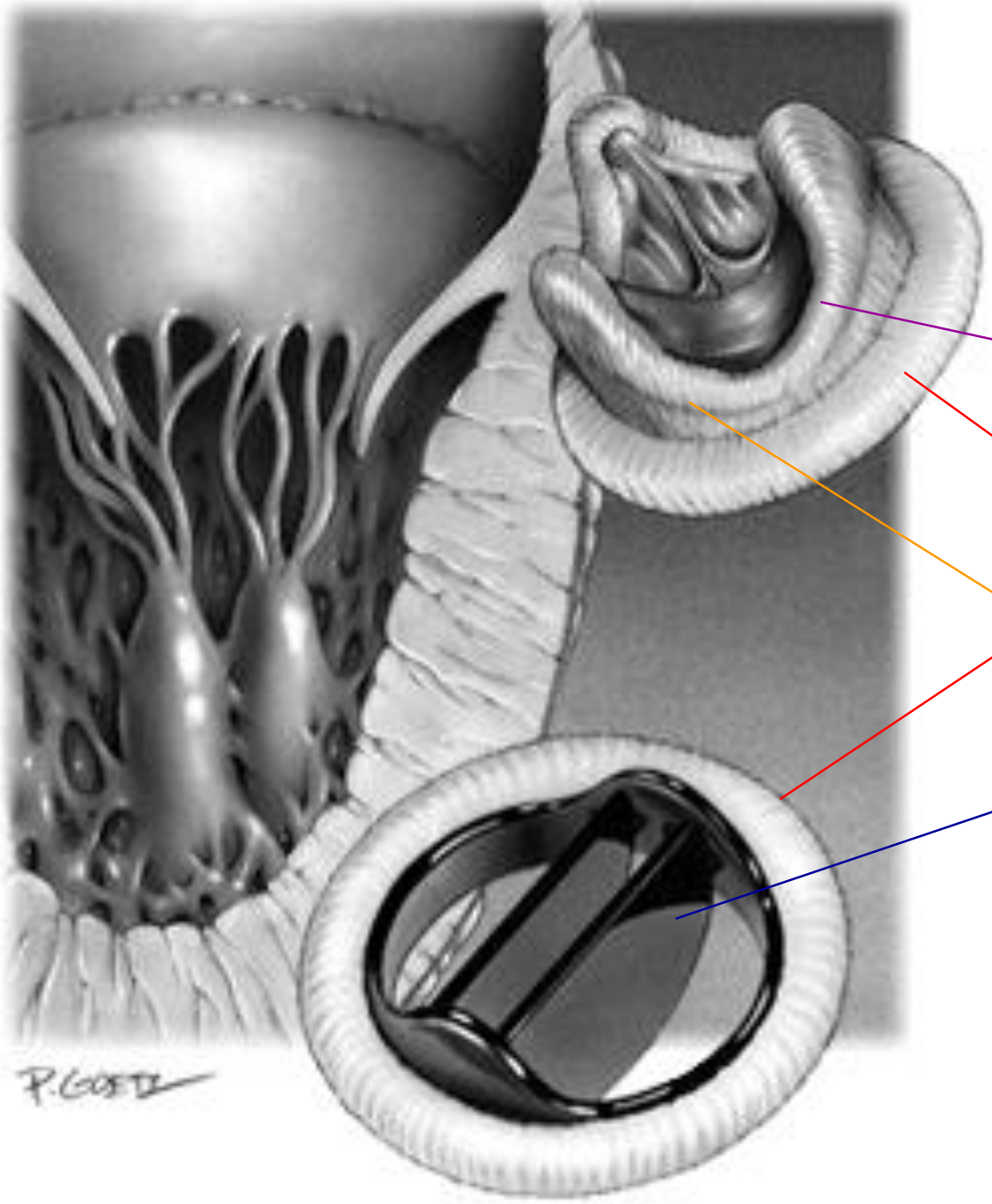
These bileaflet valves have a greater effective opening area, 2.4–3.2 cm^2 vs. 1.5–2.1 for the single-leaflet valves. Also, they are the least thrombogenic of the artificial valves. Mechanical heart valves are today very reliable and allow the patient to live a normal life. Most mechanical valves last for at least 20 to 30 years



Issues in Heart Valves

- Thrombosis
- Calcification
- Infection
- Mechanical failure
- Scarring at sewing ring

Materials in Heart Valves at the start of the 21st Century



Fixed tissue (“leather”)

Dacron or e-PTFE

Delrin or polypropylene or metal

carbon

stainless steel

titanium

Breast Implants

The breast implant evolved to address the poor results achieved with direct injection of substances into the breast for augmentation. In the 1960s, California and Utah classified use of silicone injections as a criminal offense. In the 1950s, poly(vinyl alcohol) sponges were implanted as breast prostheses, but results with these were also poor.

University of Texas plastic surgeons Thomas Cronin and Frank Gerow invented the first silicone breast implant in the early 1960s**, a silicone shell filled with silicone gel**. Many variations of this device have been tried over the years, including cladding the device with **polyurethane foam** (the Natural Y implant). This variant of the breast implant was fraught with problems. However, the basic silicone rubber–silicone gel breast implant was generally acceptable in performance.

video
BREAST IMPLANT

https://youtu.be/6gj59kbyyRE

implant selection

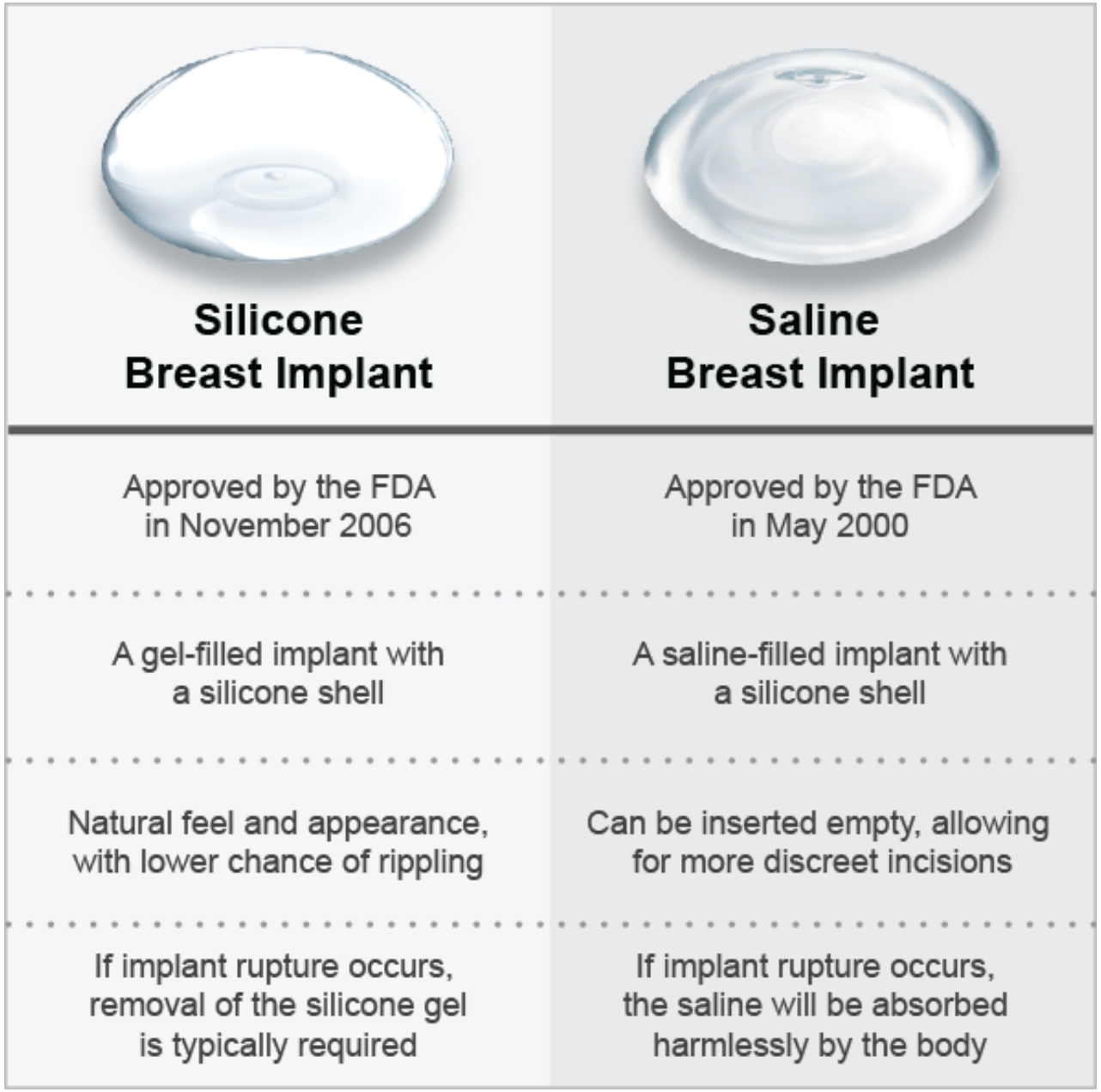
https://youtu.be/8g8qdtnrSp0

https://youtu.be/ZM0Ve-czFgY

protesi a gel di silicone

https://youtu.be/pSJX4gIILPc

breast implant surgery



Silicone Breast Implant	Saline Breast Implant
Approved by the FDA in November 2006	Approved by the FDA in May 2000
A gel-filled implant with a silicone shell	A saline-filled implant with a silicone shell
Natural feel and appearance, with lower chance of rippling	Can be inserted empty, allowing for more discreet incisions
If implant rupture occurs, removal of the silicone gel is typically required	If implant rupture occurs, the saline will be absorbed harmlessly by the body

Hydrogels

Hydrogels in nature exist since ever. Bacterial biofilms, hydrated extracellular matrix components, and plant structures are ubiquitous, water swollen motifs in nature. Gelatin and agar were also known for various applications. But the modern history of hydrogels as a class of materials for medical applications can be accurately traced.

In 1936, DuPont scientists published a paper on recently synthesized methacrylic polymers, where poly(2- hydroxyethyl methacrylate), **polyHEMA**, was mentioned. It was described as a hard, brittle, glassy polymer, and clearly not considered important. pHEMA was forgotten until 1960, when Wichterle & Lim, in a paper in *Nature* described the polymerization of HEMA and a cross-linking agent in presence of water and other solvents, to obtain a soft, water-swollen, elastic, clear gel. Wichterle then developed an apparatus, built originally from a children's construction set, for centrifugally casting the hydrogel into contact lenses of the proper refractive power. This innovation led to the **soft contact lens industry**, and to the modern field of biomedical hydrogels.

Important early applications of hydrogels included acrylamide gels for electrophoresis, **PVA** porous sponges (Ivalon) as implants, many hydrogel formulations as soft contact lenses, and alginate gels for cell encapsulation.


Otto Wichterle (1913–98) *and* he centrifugal casting apparatus he used to create the first soft, hydrogel contact lenses. (Photo by Jan Suchy, Wikipedia)