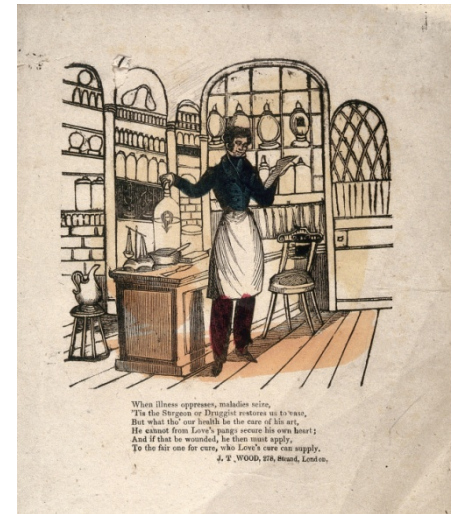
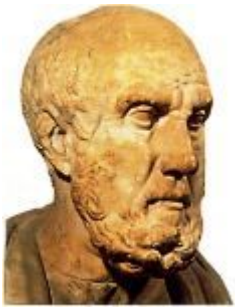
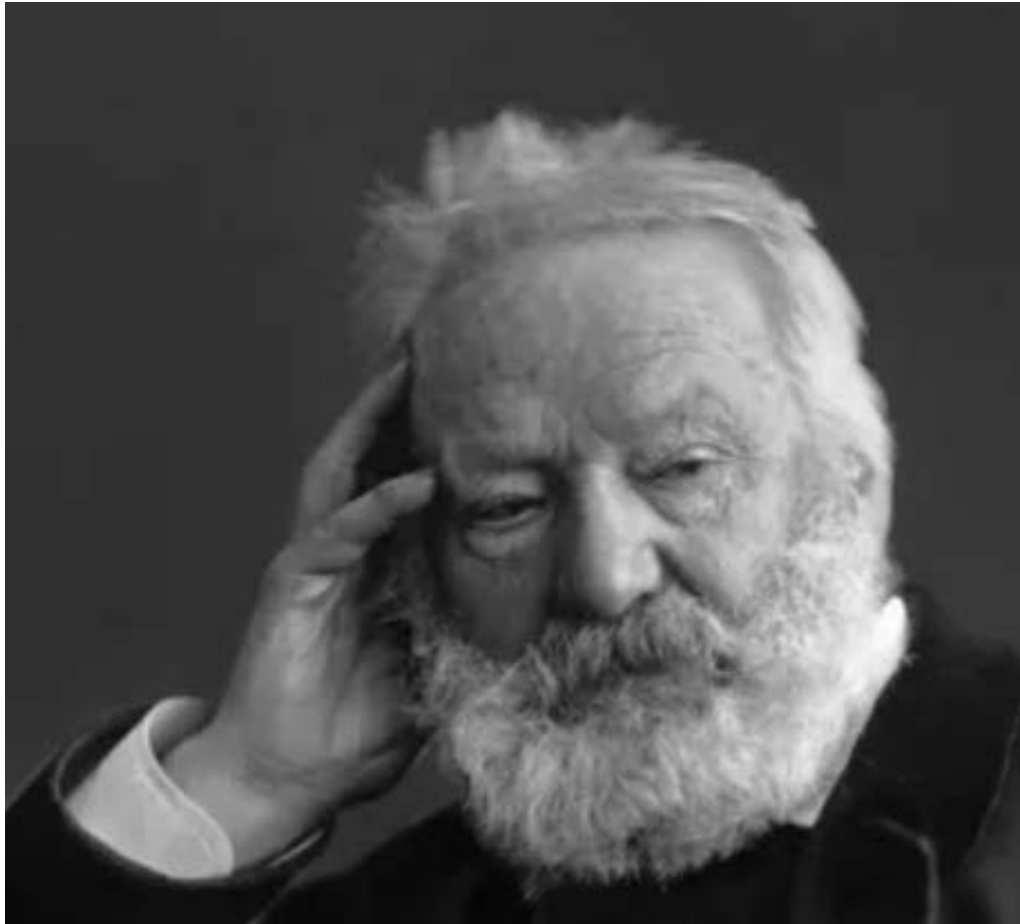




Historical overview of antithrombotic therapy



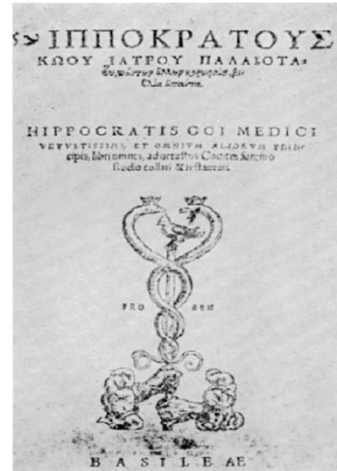
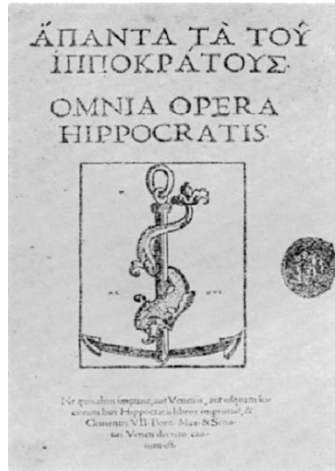
***E. Merkouri
Athens Medical Group
Medical School-University of Athens***



What is history?

“An echo of the past in the future, a reflex from the future on the past.”

Victor Hugo

A marble bust of the philosopher Plato, showing him with a balding head and a full, curly beard and hair. He is looking slightly to the right with a serious expression.

Hippocrates (450-350 BC)
Compression bandages to
treat leg ulcers



Avicenna (Ibn Sina) (980-1037)
“particle migration” in cases of vein surgery
consistent with embolization of DVT

Did Jesus Christ die of pulmonary embolism?

B. BRENNER

Director, Thrombosis and Hemostasis Unit, Rambam Medical Center, and Prof. of Hematology, Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel

To cite this article: Brenner B. Did Jesus Christ die of pulmonary embolism? *J Thromb Haemost* 2005; 3: 2130–1.

The life and teachings of Jesus Christ have attracted enormous attention throughout the past 2 millennia. His agony and death was the subject for numerous religious scholar and artistic creations. While the common views describe the death of Jesus on the cross as a result of bleeding, the following thesis will present another, yet unreported cause for his death.

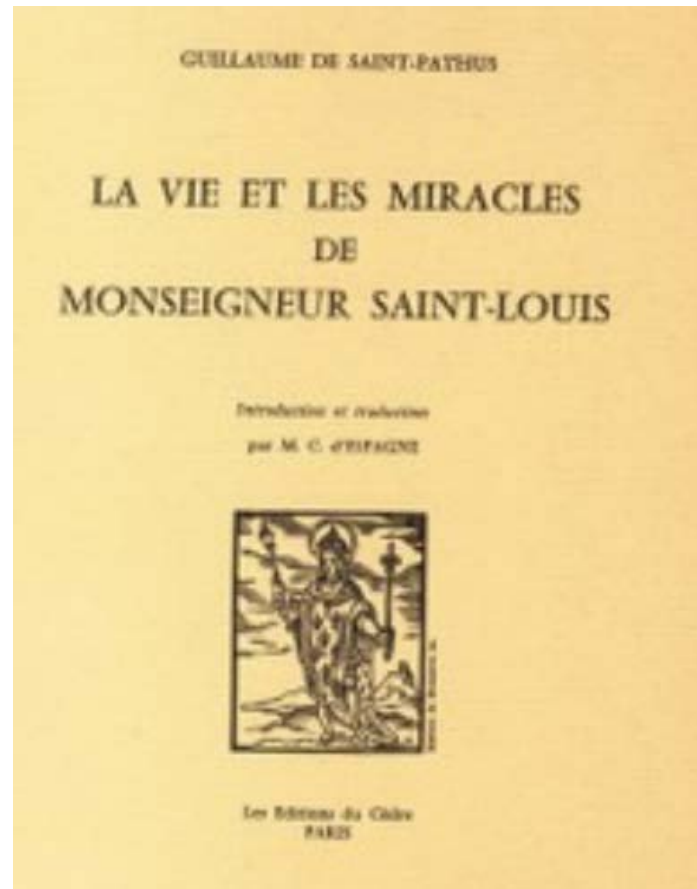
with significant activation of the coagulation system, mainly by tissue factor [7,8].

After scourging, Jesus was forced to carry on his shoulders the patibulum of the cross, which weighted 34–57 kg for 600 m to the site of crucifixion [6]. This led to further dehydration and exhaustion.

At crucifixion, nailing of the wrists and ankles to the cross led



The first case report of DVT (1271)



- The patient “Raoul”, 20 years old, Normal cobbler, presented unilateral pain and swelling of the right calf
- Referred to the “surgical department”
- Doctor Henri de Perche advised “wait and see”
- Development of leg ulcer
- The patient was referred to St Eloi’s shrink
- No improvement



- The patient was transferred to the tomb of the King Saint Louis
- 1st line treatment: Praying
- No improvement
- 2nd line treatment: Application of dust from the tomb directly to the ulcer
- Healing

Fig 1. The illustrated manuscript depicting the first case of venous thrombosis. Cliché Bibliothèque National de France, Paris.

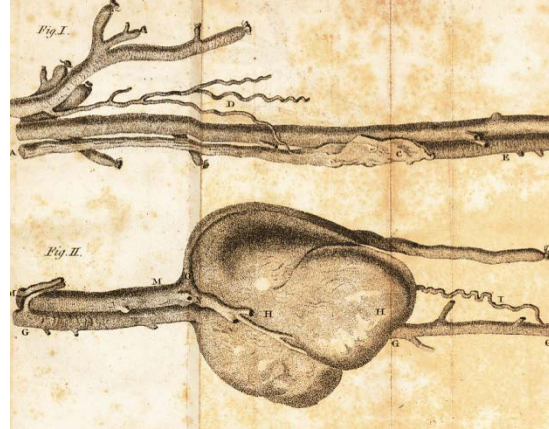
Renaissance

- Pregnancy-related DVT
- First attributed to “evil humors”
- Retention of unconsumed milk (Milk leg)
- Breast-feeding strongly encouraged
- Bloodletting

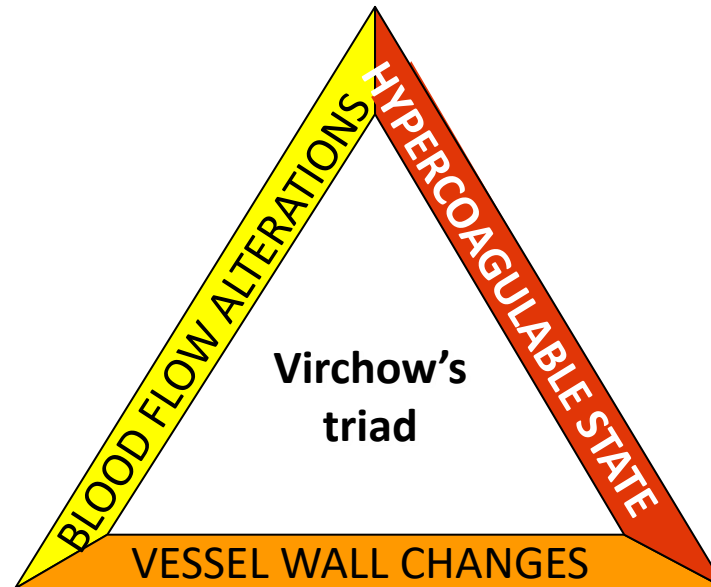


***Le malade imaginaire*
(1673)**

1793



1856



19th Century

- “Inflammation of the vessel wall”
- Anti-inflammatory medication
 - Cold baths
 - Application of leeches
 - Antiseptic agents (ZnCl_2)
 - Drugs targeting specific diseases
 - *Cinchona officinalis* (quinine) for malaria-related DVT
 - Mercury for syphilis-related DVT
 - Autumn crocus (*Colchicum autumnale*, colchicine) for gout-related DVT

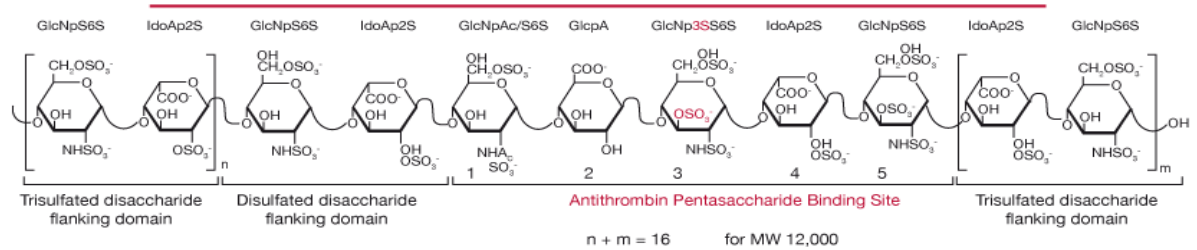


Hirudin



- Haycraft (1884)
- Production by genetic engineering (1984)





- Discovered by Jay McLean, a medical student in William Howell's lab in **1916**
- Mc Lean's experiments concerned tissue extractions from brain, liver and heart seeking for procoagulant molecules
- Some of these extracts named "heparphosphatide" became anticoagulant agents after long term exposure to air
- **1918:** Howell renamed Heparphosphatide to "Heparin"
- **1922:** Howell discovered the water soluble heparin extracted from dog liver

Heparin

- Charles and Scott produced crystalline heparin in 1933
- Heparin used in humans in 1935
- Bauer's comparative historical series
 - Mortality from PE
 - 1929-1938 (18%)
 - 1940-1949 (0.4%)

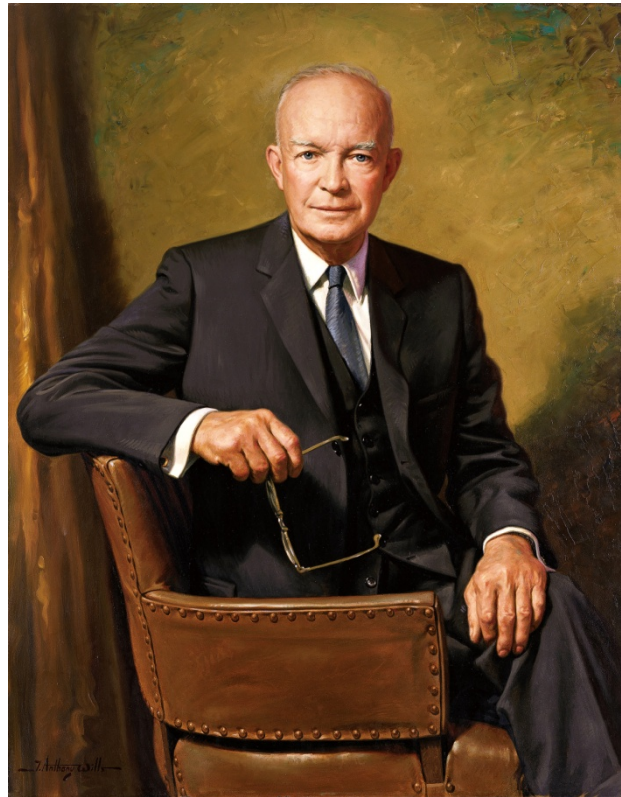




Karl Link in his laboratory



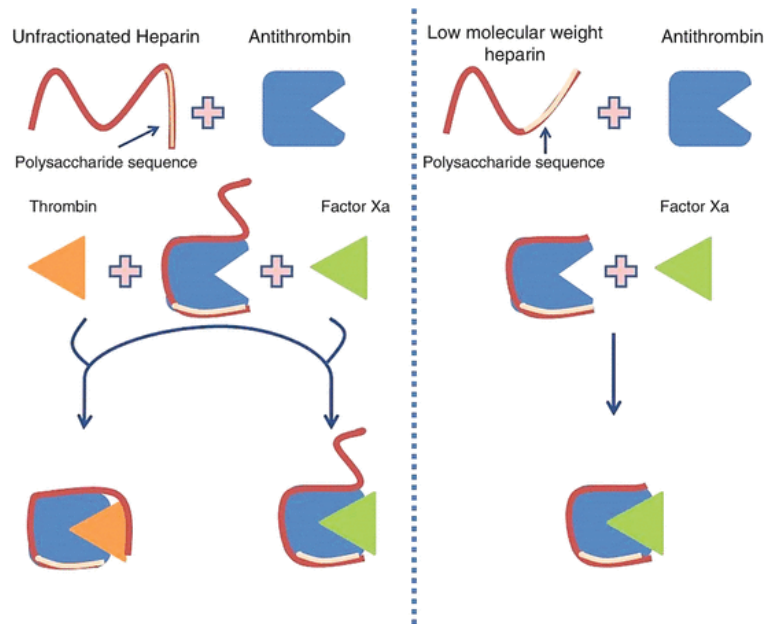
- A mysterious bleeding disease devastated the cattle herds
- **1921**: Schoefield showed that this disease was caused by spoiled sweet clover
- **1939**: Link demonstrated that coumarin was oxidised to dicoumarol in spoiled clover. Bleeding effects could be reversed with VitK
- **1945**: Dicoumarol was used for the control of rodents (WARFARIN)



In 1955, Warfarin was given to President Dwight Eisenhower following a myocardial infarction. As Duxbury and Poller point out; ‘What was good for a war hero and the President of the United States must be good for all, despite being a rat poison!’ (Duxbury & Poller, 2001).

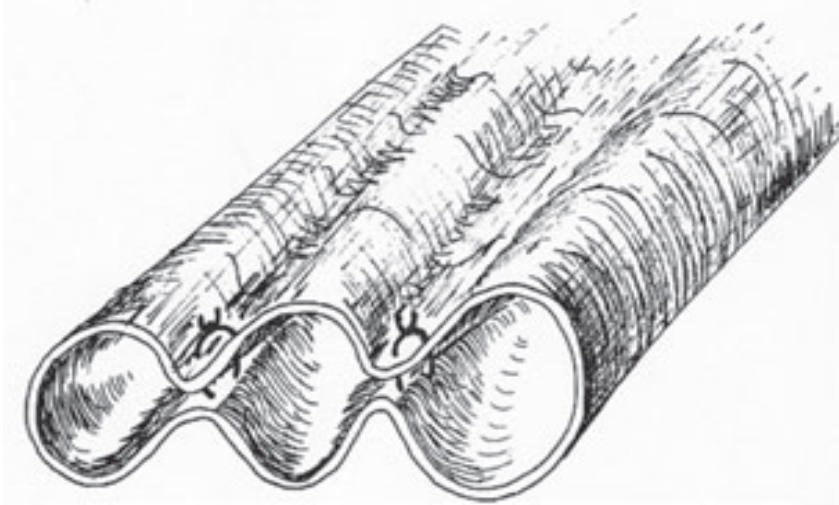
Low Molecular Weight Heparins

A new era

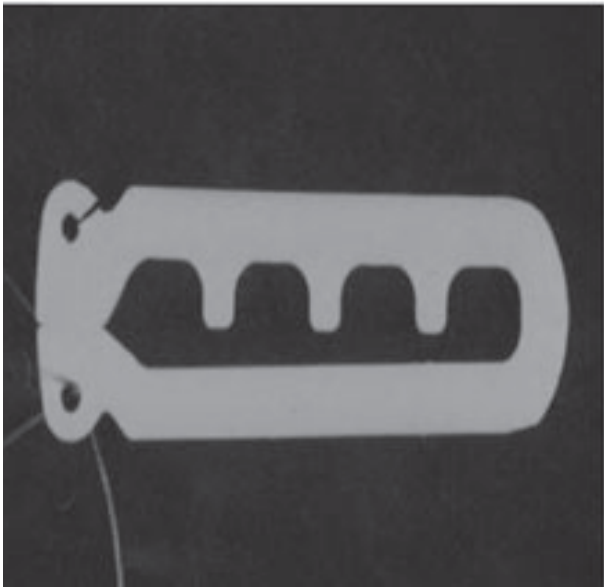
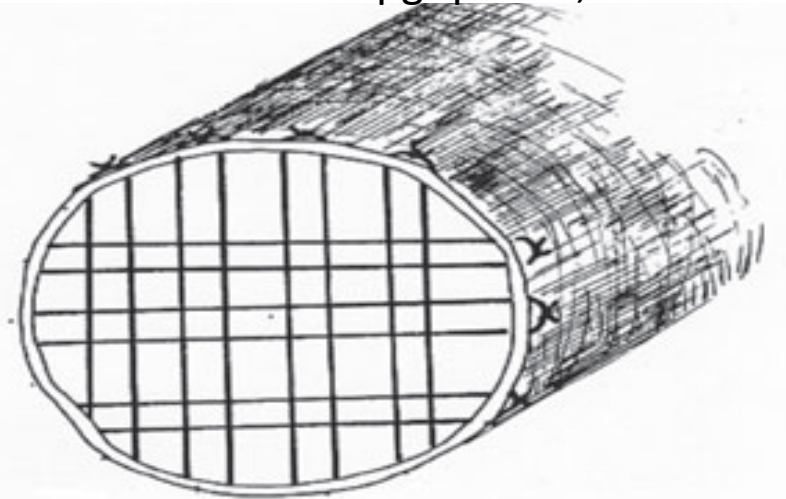


- Ambulatory patient
- Short hospitalizations
- Lab monitoring not necessary in most of the cases
- Development of guidelines and reversal protocols

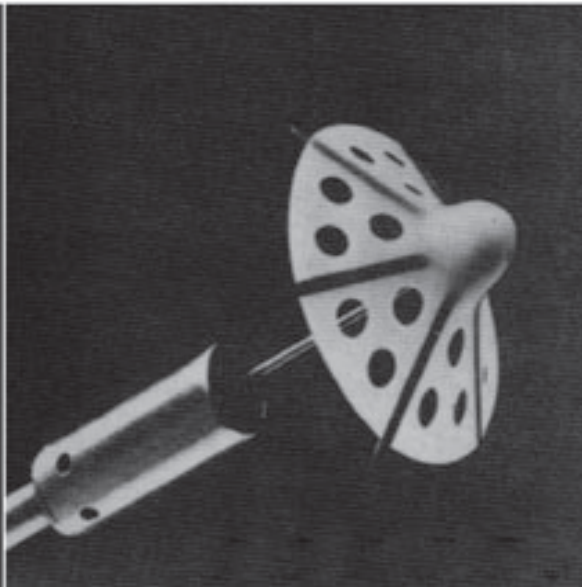
Plication of the vena cava, Spencer 1960



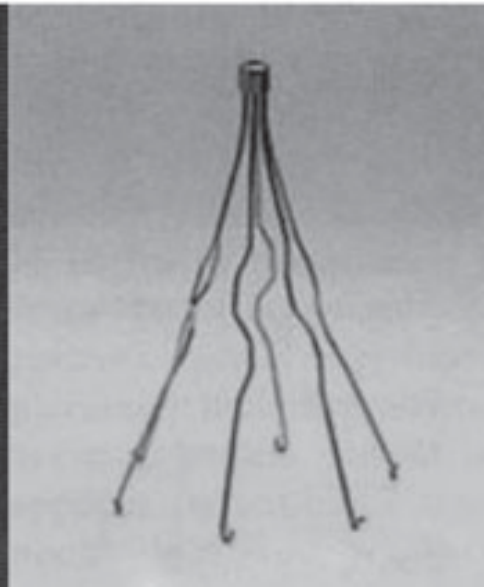
DeWeese harpgrip filter, 1958



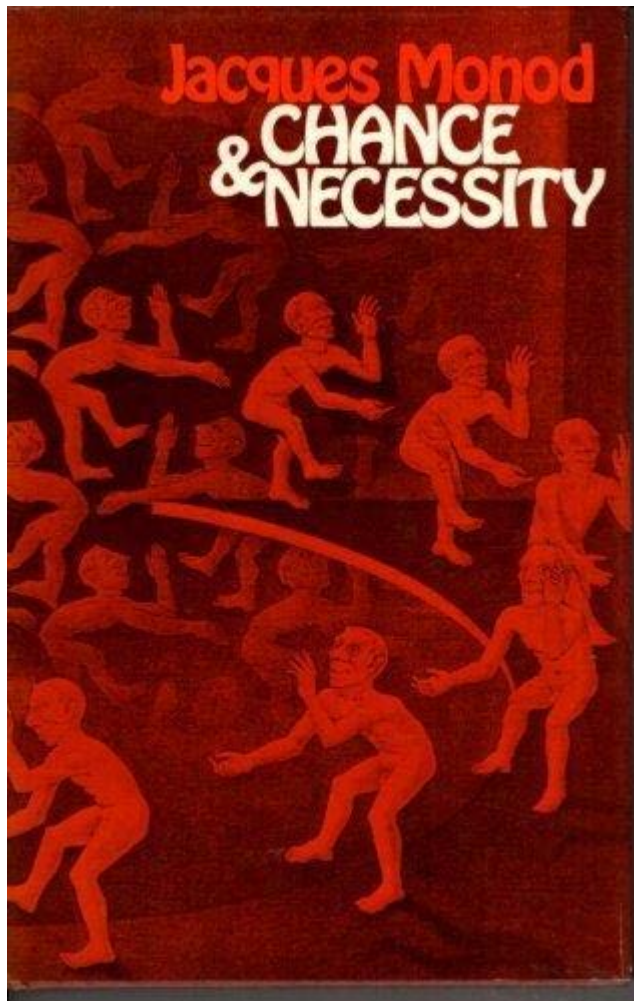
Adams-DeWesse clip 1966

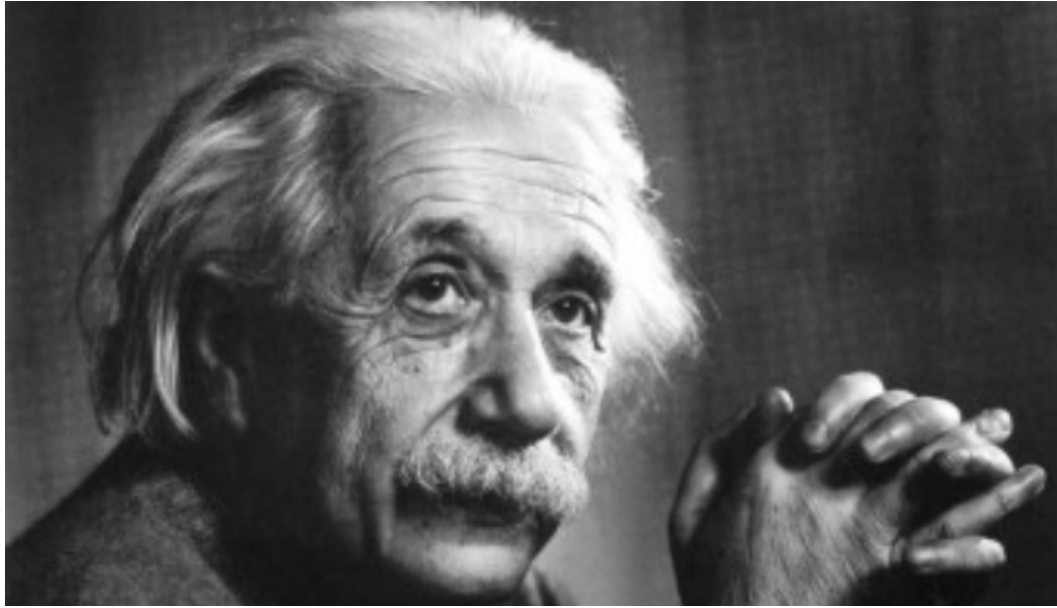


Mobbin-Uddin endovascular
Filter, 1967



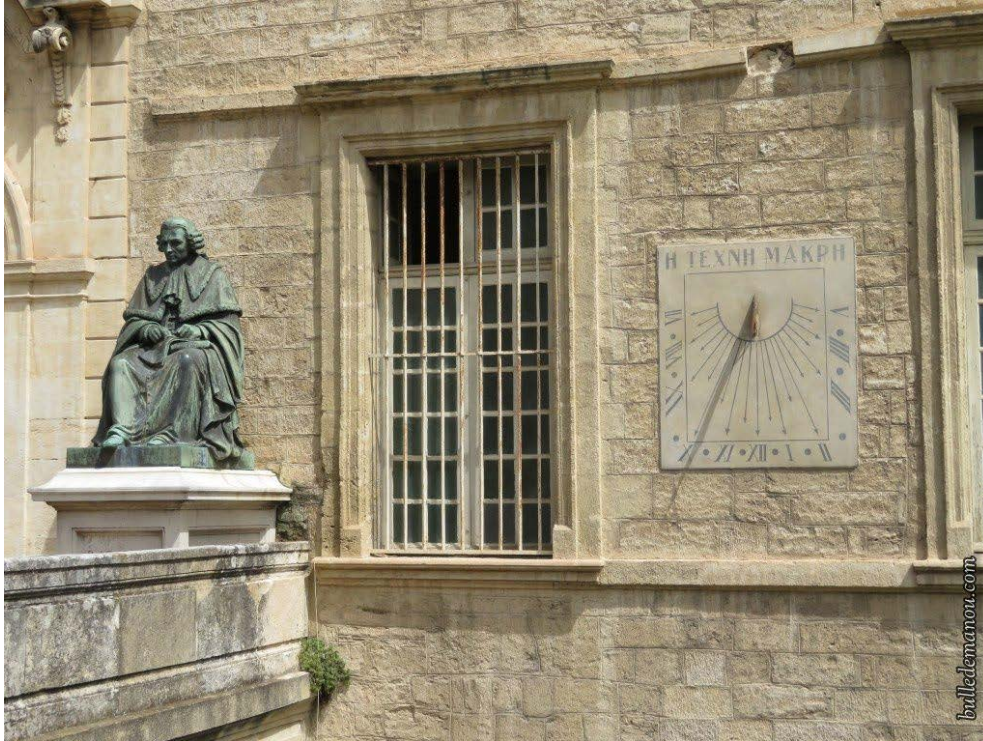
Greefield filter without
venotomy, 1981





*Student: Dr. Einstein,
Aren't these the same
questions as last year's
final exam?*

*Dr. Einstein: Yes; But this
year the answers are
different*



*“Ὁ βίος βραχύς,
ἡ δὲ τέχνη μακρὴ,
ἡ δὲ πεῖρα σφαλερὴ,
ἡ δὲ κρίσις χαλεπὴ”*

Hippocrates (450-350 BC)