2017 MID-ATLANTIC
CONFERENCE

*7th ANNUAL* CURRENT CONCEPTS IN
VASCULAR THERAPIES

2017

**C SCOTT MCENROE**

**Medical Director**
**Vein Center of Virginia**
**Sentara Medical Group**

**April 21, 2017**

# The Transformation of Deep Venous Therapies

# The Transformation of Deep Venous Therapies

# *The Transformation of Deep Venous Therapies*

- **From the first case of DVT to the pre-anticoagulant era (1271-1920's)**
- **From the discovery to the development of anticoagulants (1920's-1950)**
- **The modern era: ambulatory management of DVT and the development of complementary treatments (since 1950)**

# From the first case of DVT to the pre-anticoagulant era (1271-1920's)

- 1st reported DVT 1271: Raoul, 20 yr old cobbler
- 1st Pulmonary Embolus? 33: Jesus Christ

# From the first case of DVT to the pre-anticoagulant era (1271-1920's)

- **Renaissance: increase in reported spontaneous leg swelling ( DVT )**
  - **1st pathologic hypotheses: pregnancy related**
    - **Caused by unconsumed milk in the legs: " MILK LEG "**
    - **1st line treatment: breast feeding**


# From the first case of DVT to the pre-anticoagulant era (1271-1920's)

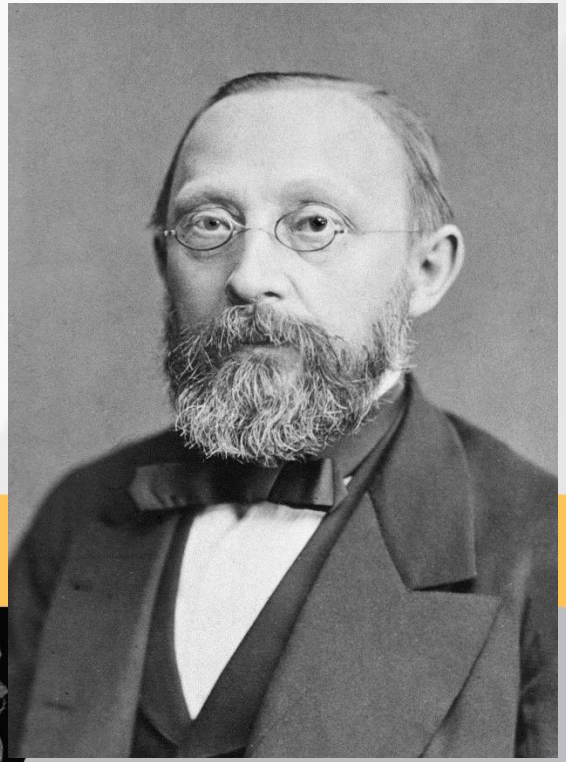
- **Renaissance: increase in reported DVT**
  - **Retention of " Evil Humors "**
    - **Blooding letting predominant treatment until the 1900's**


# *From the first case of DVT to the pre-anticoagulant era (1271-1920's)*

- **1784-early 1920's: Evidence based treatment of DVT**
  - **" Humoral Theory " gradually abandoned**
    - **Wiseman 1676: DVT consequence of alteration the blood**
    - **Hunter 1793: occlusion of vein by blood clots**
      - **1784: venous ligation decreased mortality from DVT**
        - **» Widely used until end of the 19th century**

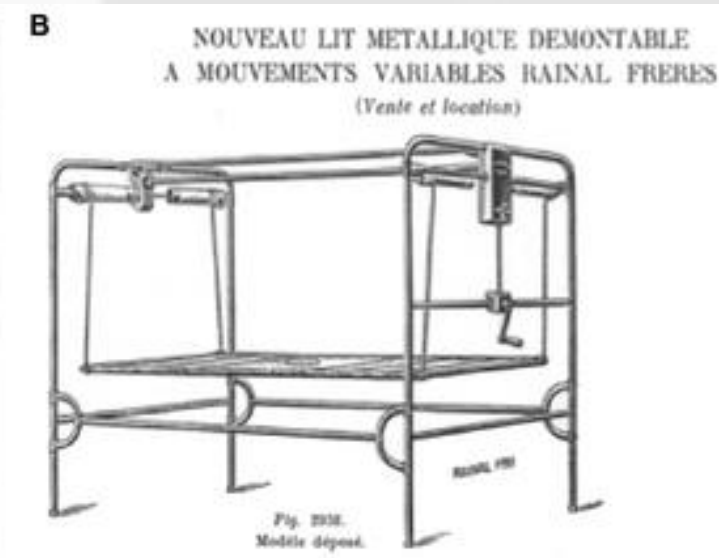
# From the first case of DVT to the pre-anticoagulant era (1271-1920's)

- **1784-early 1920's: Evidence based treatment of DVT**
  - **Rudolf Virchow 1856**
    - **Relationship between DVT and fatal pulmonary embolus**
    - **" Vichow's Triad "**
      - **Venous stasis**
      - **Vessel wall alteration**
      - **Hypercoagulability**



# From the first case of DVT to the pre-anticoagulant era (1271-1920's)

- **1784-early 1920's: Evidence based treatment of DVT**
  - **Treatment formulated to manage fatal thrombus migration, improve venous drainage, *not* DVT itself**
    - **Strict bedrest and immobilization**


# From the first case of DVT to the pre-anticoagulant era (1271-1920's)

- **1784-early 1920's: Evidence based treatment of DVT**
  - **DVT result of inflammation of vein wall provoked by infection( 1900$^{th}$ century )**
    - **Frequently associated with fever**
    - **Septic surgical procedures**
    - **Postpartum**
    - **During bedrest for infectious disease**

# From the first case of DVT to the pre-anticoagulant era (1271-1920's)

- **Cornerstone of treatment prior to anticoagulants**
  - **Anti-inflammatory medication**
  - **Bloodletting: leeches, cupping, purging**
  - **Bedrest, elevation, proximal venous ligation**
  - **Treatment/prevention of infection**
    - **Zinc chloride ( antiseptic )**
    - **Mercury ( syphilis )**
    - **Colchicine ( gout )**
    - **Quinine ( malaria )**

# From the discovery to the development of anticoagulants ( 1920's-1950 )

- **Hirudin: first anticoagulant**
  - **1884 Haycraft: saliva of leeches**
  - **1986: mass production through genetic engineering**

# *From the discovery to the development of anticoagulants ( 1920's-1950 )*

- **Heparin**
  - **1916 McLean: medical student, dog liver**
  - **1933 Charles and Scott: pure crystalline heparin**
  - **1935: first use of heparin in humans**

# *From the discovery to the development of anticoagulants ( 1920's-1950 )*

- **Heparin: first indication for thromboprophylaxis in surgical patients**
  - **1937 Murray, Crafoord: first series for thromboprophylaxis**
  - **1938 Murray, Crafoord: first series for acute DVT**
  - **Bauer (1929-38, 1940-49): *mortality from PE dropped from 18% - 0.4% with 7-10 days IV heparin***

# *From the discovery to the development of anticoagulants ( 1920's-1950 )*

## Heparin: 1940's

- **Effectiveness immediately considered unquestionable**
- **Became standard of care**
- **No randomized placebo-controlled trials**

# DVT: (1271-1940's)

- Surgery, infection, pregnancy
- Associated with fatal pulmonary embolism
- Reduction in morbidity/mortality
  - Treatment of sepsis
  - Bedrest
  - Promotion of venous return
  - Proximal venous ligation
  - IV heparin 7- 10 days

# *From the discovery to the development of anticoagulants ( 1920's-1950 )*

- **Oral anticoagulants: vitamin K antagonists ( VKAs )**
- **Allow prolonged outpatient treatment of DVT**

# Story of VKAs

- **Hemorrhagic disease in cattle, North Dakota/Alberta**
- **Schoefield ( 1921 ): spoiled sweet clover, transfusion**
- **Link ( 1939 ):coumarin oxidized to dicoumarol in moldy hay, reversed by vitamin K**
- ***1941 first use of dicoumarol to treat DVT***

# From the discovery to the development of anticoagulants ( 1920's-1950 ): Story of VKAs

## Link ( 1945 )

- " Vegetating in a santorium "
- Reading articles on the history of rodent control
- Rodent " tasters ": rapid poisons ineffective
- Testing all coumarins synthesized in his lab

# From the discovery to the development of anticoagulants ( 1920's-1950 ): Story of VKAs

## Link ( 1945 )


- 1948 Warfarin launched as ideal rat poison
- Felt too toxic for humans
- Navy inductee suicide attempt:567 mg Warfarin
- *1954 commercialized as therapeutic agent*

# The Modern Era: ambulatory management of DVT and the development of complementary treatments ( since 1950 )

- **Outpatient treatment of DVT: End of bed-rest dogma**
  - **Progress in diagnostics: venography, ultrasound**
  - **Simplicity of anticoagulation**
  - **Compression therapy**
  - **Complementary interventions to decrease mortality and the burden of long term sequelae**

# The Modern Era: ambulatory management of DVT and the development of complementary treatments ( since 1950 )

- **Bed rest**
  - **Mid-1900's: 6 weeks, fear of embolization**
  - **5-7 days during heparin infusion**
  - **1996 Levine: OP LMWH safe as IP unfractionated heparin**

# The Modern Era: ambulatory management of DVT and the development of complementary treatments ( since 1950 )

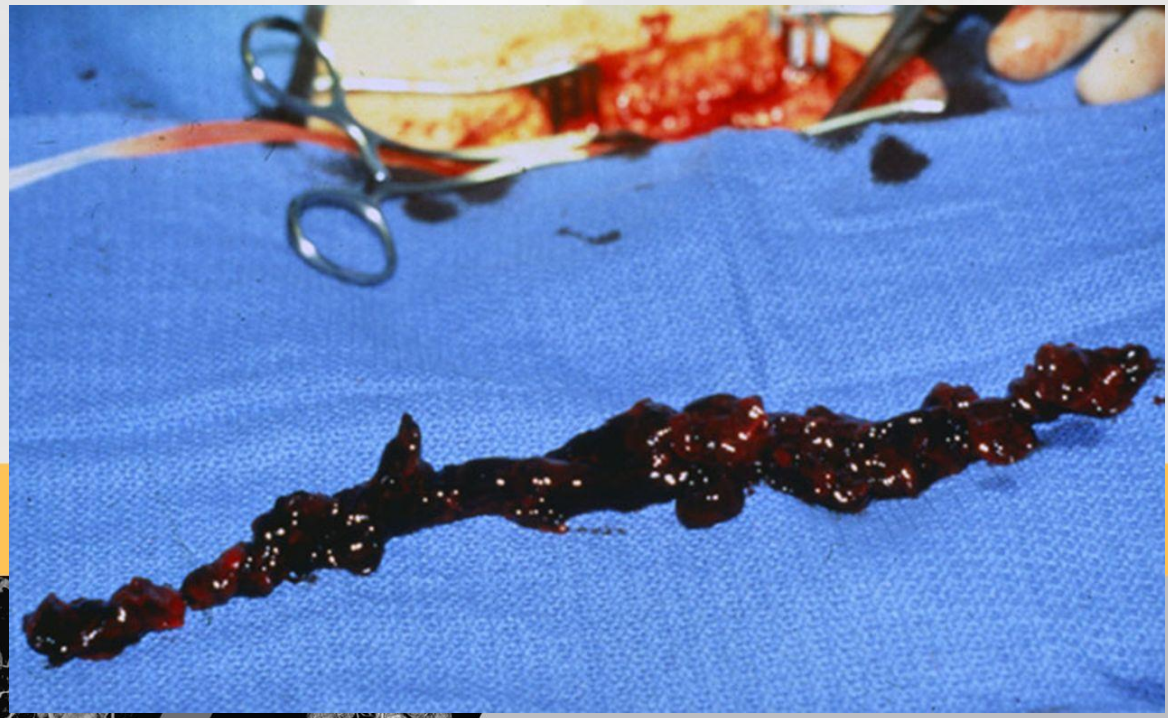
- **Compression Therapy**
  - **Hippocrates: compression bandages to treat ulcers**
  - **More widely used when anticoagulants became available**
  - **Usually administered after completion of heparin administration**
  - **Late 19th century Fischer, Lasker: rapid resolution of superficial thrombosis**
  - **1996 Partsch ( randomized trial ): no increased risk of PE and decreased pain, edema with early ambulation and compression hose**
  - **1997 Brandjes: early application of compression hose useful in decreasing post thrombotic sequelae**

# Complementary treatments: embolization/PE ( 1950's)

- Unfractionated heparin treatment of choice
- High incidence of embolization, pulmonary embolism
- Proximal surgical ligation: femoral, iliac, IVC
- 14% mortality rate

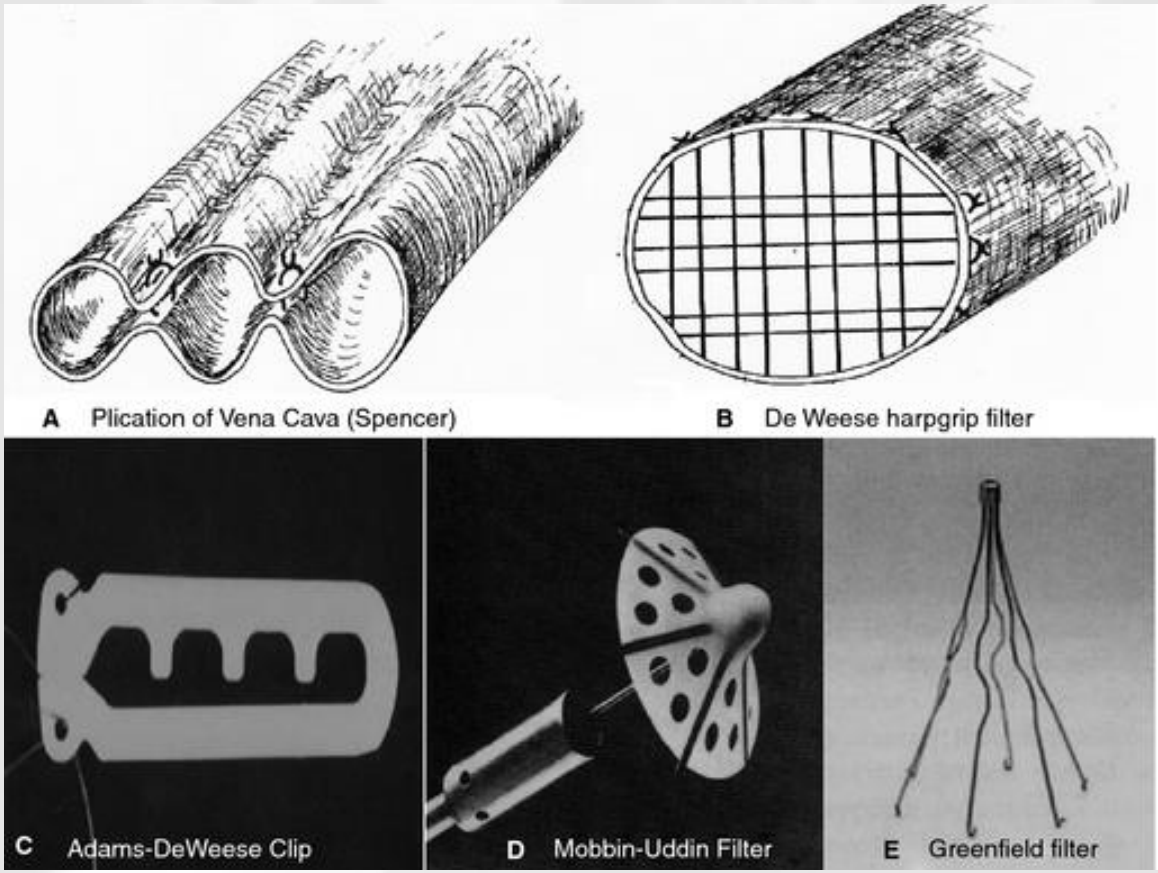
# The Modern Era: ambulatory management of DVT and the development of complementary treatments ( since 1950 )

- **Venous thrombectomy: clot burden**
  - **Lawen ( 1938 ): first description**
  - **Mahorner, Fontaine ( 1950's ): with anticoagulation, manual compression**
  - **Fogarty ( 1963 ): balloon thrombectomy, early post-op occlusion**
  - **Transient A-V fistula ( 1974 )**



# The Modern Era: ambulatory management of DVT and the development of complementary treatments ( since 1950 )

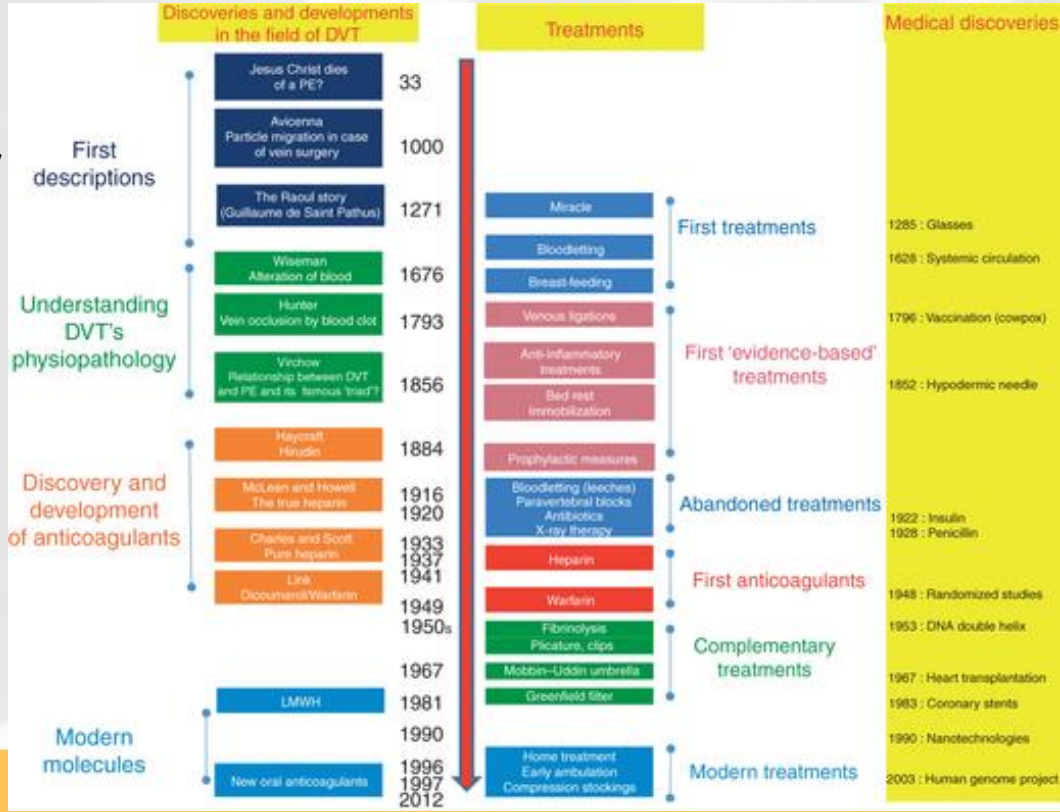
- **IVC interruption**
  - DeWeese ( 1958 )
  - Spencer ( 1960 )
  - Adams-DeWeese ( 1966 )
  - Mobbin-Uddin ( 1967 ): local heparin coating
  - Greenfield ( 1981 ):percutaneous
  - Temporary IVCF's




# The Transformation of Deep Venous Therapies

## Most breakthroughs in last 100 years

- Simplification of anticoagulation: oral
- Aggressive use of compression therapy
- Elimination of bed-rest dogma
- Shift to ambulatory management
- Complementary treatment
  - IVCF's- percutaneous, retrievable
  - Thrombolysis- percutaneous
    - Mechanical
    - Pharmacologic




# The Transformation of Deep Venous Therapies

## Unresolved debates

### When is use of complementary therapy appropriate?

- Management of large clot burden: how much is too much?
- Protection from pulmonary embolism: when and with what?
- Treatment of pulmonary embolism: when and how?