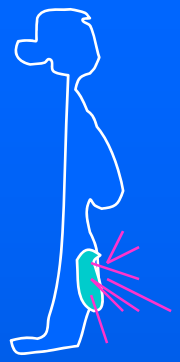

acute venous disease

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thromboembolic disease

- **deep vein thrombophlebitis**
- **superficial thrombophlebitis**
- **phlegmasia cereulea dolens**
- **pulmonary embolism**

some facts

- **over 250,000/yr die of pulmonary embolism**
- **600,000 hospitalizations/yr for DVT**
- **1-2% of hospitalized patients**
- **$1.2-2.4 billion per yr.**

risk factors

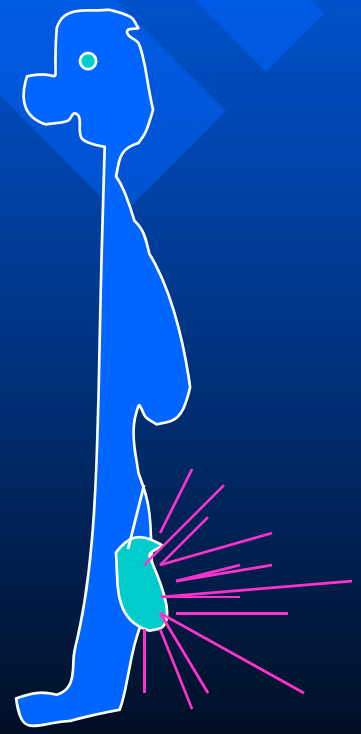
- Hx of dvt, p.e.
- prolonged sitting, standing
- obesity
- recent surgery, trauma
- immobility paralysis
- malignancy
- hypercoaguable state
- smoking
- sepsis
- congestive heart failure
- age >60
- BCPs
- pregnancy (>3)
- venous insufficiency
- copd
- venous incompetence
- nephrotic syndrome

congenital disorders

- atIII deficiency
- protein c, s deficiency
- apc resistance (leiden mutation)
- prothrombin 20210a
- homocystinemia
- heparin cofactor II deficiency
- dysfibrinogenemia
- inc. factor VII
- decreased pa; increased pai g4 gene
- abnormal plasminogen

acquired risk factors

- **heparin induced thrombocytopenia**
- **warfarin induced thrombosis**
- **antiphospholipid syndrome**
- **estrogens**
- **pregnancy**
- **diabetes mellitus**



antithrombin three deficiency

- **antithrombin inhibits factors IX_a, X_a, Xi_a, and XII_a, thrombin**
- **risk of thrombosis increases when functional activity is less than 80%**
- **decreased in liver disease, sepsis, dic, bcps**
- **heparin, ffp, atIII replacement, warfarin**
- **prophylaxis in prothrombotic events**

protein c and s deficiency

- **vitamin k dependant liver proteins**
- **activated by thrombin, bound to endothelial cell thrombomodulin degrades factor V_a and $XIII_a$, decreases tissue pai**
- **protein s is a cofactor**
- **autosomal dominant 1:300**

protein c and s deficiency-2

- **venous thrombosis at early age in heterozygotes (30-70% levels)**
- **prophylaxis with warfarin, heparin**
- **fresh frozen plasma to correct**
- **life long warfarin for thromboses**
- **warning!!! cutaneous necrosis on warfarin more likely**

activated protein c resistance(factor V Leiden)

- **most common inherited cause of thrombosis (3-15% caucasians)**
- **factor V resistance to degradation by activated protein c**
- **7 fold risk of venous thrombosis**
- **life long warfarin**

homocystinemia

- **increased risk of early onset dvt**
- **increased incidence of recurrent dvt**
- **platelet activation, increased factor VII and V, decreased protein c activity, mthfr mutation**
- **39-50% of patients may have normal levels in fasting state**
- **folate (1-15mg/day), B_{12}, B_6**

prothrombin 20210

- **elevated levels of prothrombin**
- **nucleotide change (g to a transition)**
- **arterial thrombosis (coronary and cerebral), warfarin for early and recurrent thromboses**

pregnancy

- 5 fold increased risk of dvt
- increase in factors I, VII, VIII, IX, X, XII, platlets, pai-1,2
- decrease in protein c and antithrombin
- rule out thrombophillic states
- prophylaxis for 2nd pregnancy

antiphospholipid syndrome

- **acquired, drug induced**
- **1-5% of the population**
- **50% of pts over 80**
- **lupus anticoagulants, anticardiolipin antibodies**
- **antibodies against B_2 glycoproteins, prothrombin, platlets, endothelial cells, protein c,s**

antiphospholipid syndrome

- **test for both anticardiolipin and lupus anticoagulant**
- **advise against oral contraception or pregnancy**
- **lifelong warfarin INR 2.0-4.0**

combination of two factors=70-90% risk of vte

treatment goals

- prevent pulmonary embolism
- prevent propagation
- prevent postphlebitic sequellae

dvt diagnosis

- **classic signs**
  - **tumor-swelling, unilateral edema**
  - **dolor-tenderness over the vein course in the thigh, calf muscles**
  - **calor-not usually found**
  - **rubor-if associated with svt**
- **Homans' sign-present in 1/3 of patients with dvt and 1/2 of those without**

diagnosis 2

clinical diagnosis is confirmed in 30-50%

differential diagnosis

- **svt**
- **cellulitis/lymphangitis**
- **muscle or soft tissue injury**
- **achilles tendonitis**
- **asymmetric 2^0 edema**
- **baker's cyst**
- **arthritis**
- **post-phlebitic syndrome**

svt and dvt

- **if you have svt in a patient with varicose veins, 4% chance of dvt**
- **without varicose veins, 40% chance of concomitant dvt**
- **with proximal svt risk of dvt is 10%**

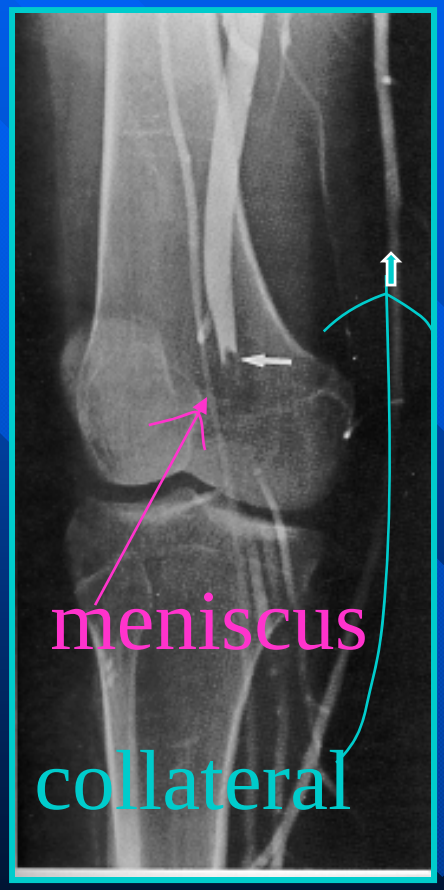
diagnostic tests

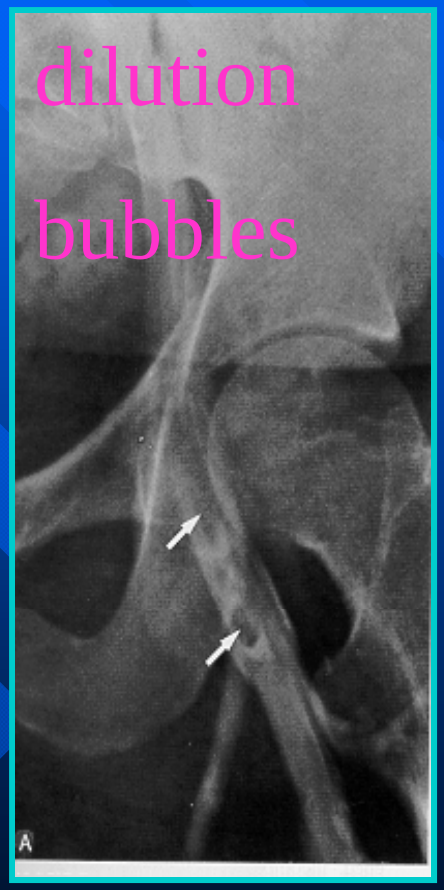
- duplex scan
- d-dimer
- venography
- mri/ct scan

acute dvt diagnosis
ascending phlebography

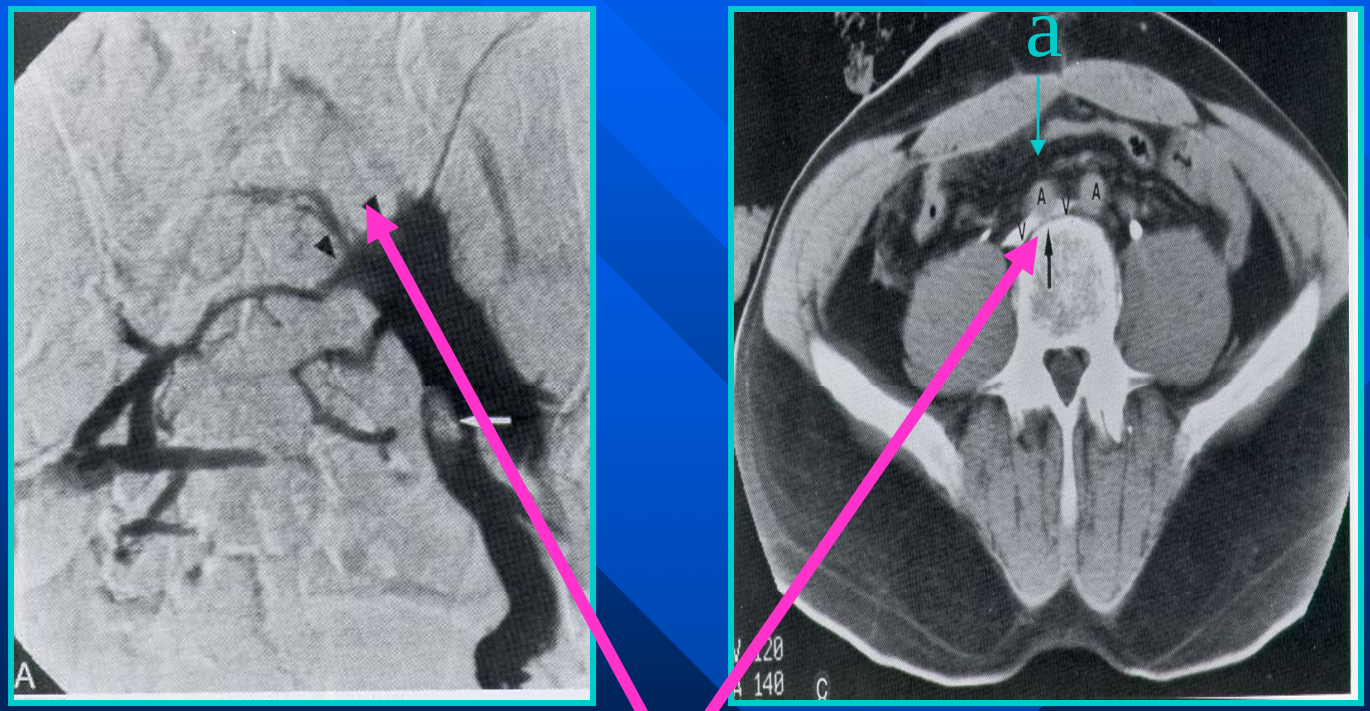
- gold standard
- > 95% accurate
- least accurate in femoral , iliac or foot
- risks of p.e., causing dvt are low
- superficial vein filling preferentially
- site, adherence, extent, age
- observer error

phlebography





may-thurner syndrome



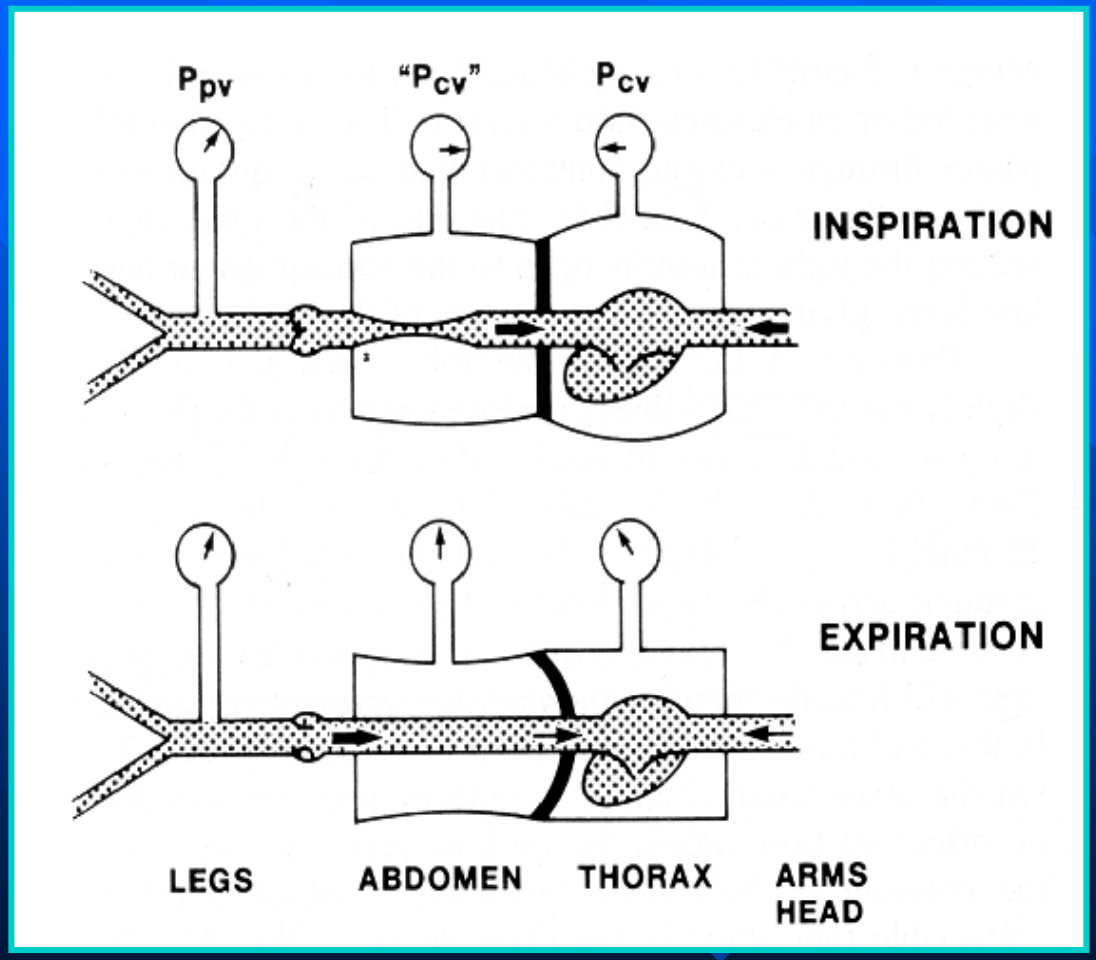
left iliac venous occlusion by crossing rt. iliac artery

venography
infiltration

doppler

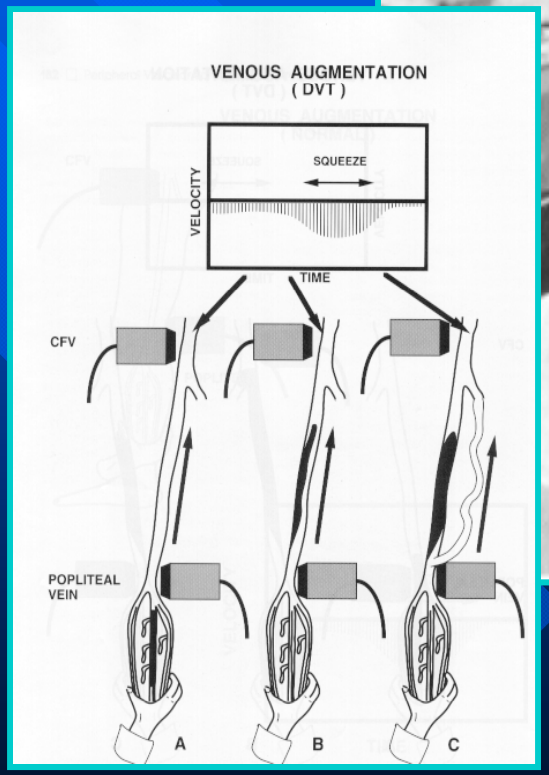
- wave:
  - continuous if hand held
  - pulsed on duplex
- 5 MHZ probe, 60 degree angle
- listen for:
  - spontaneous flow
  - respiratory variation
  - segmental augmentation
  - competency of valves
  - pulsatility

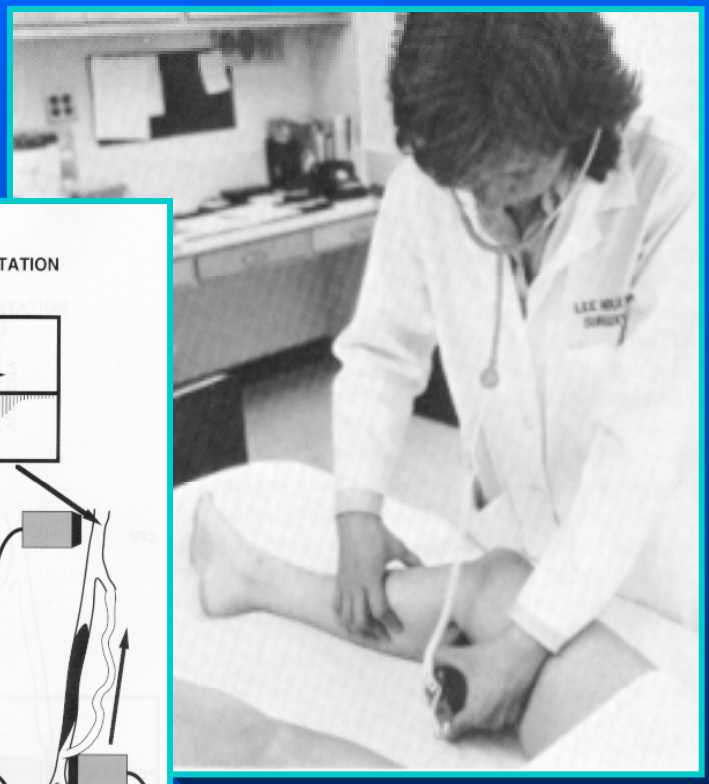
respiratory variation



augmentation

- position important
- evaluate
  - tibials
  - popliteal
  - sfv
  - cfv
  - iliac
  - saphenous



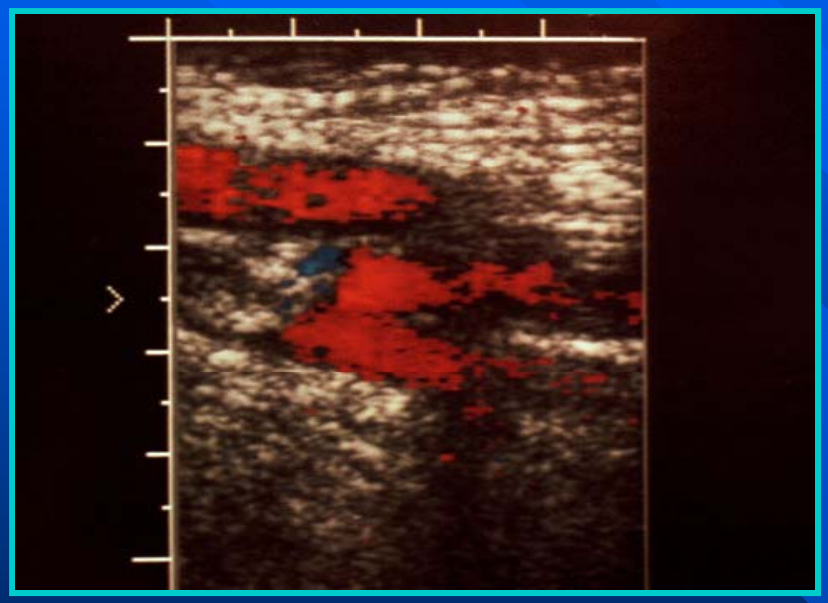


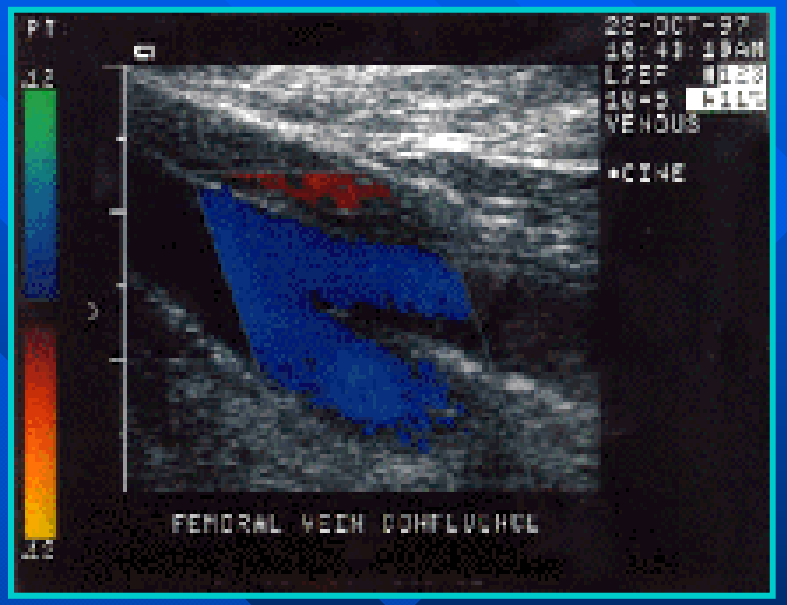
reflux

duplex scan

- B mode 4-8 MHZ linear array probe
- color to demonstrate flow
- grey scale to assess chronic changes
- assesses the iliac / vena cava better

duplex femoral vein

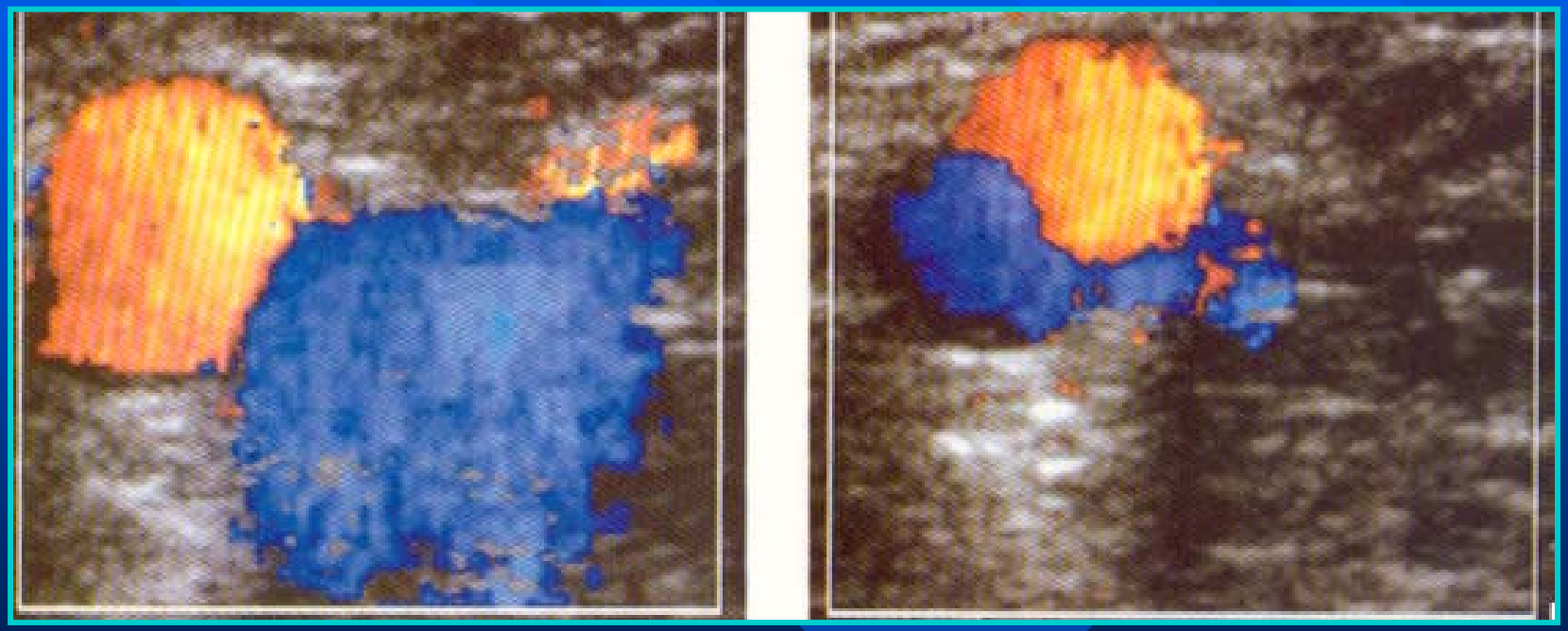




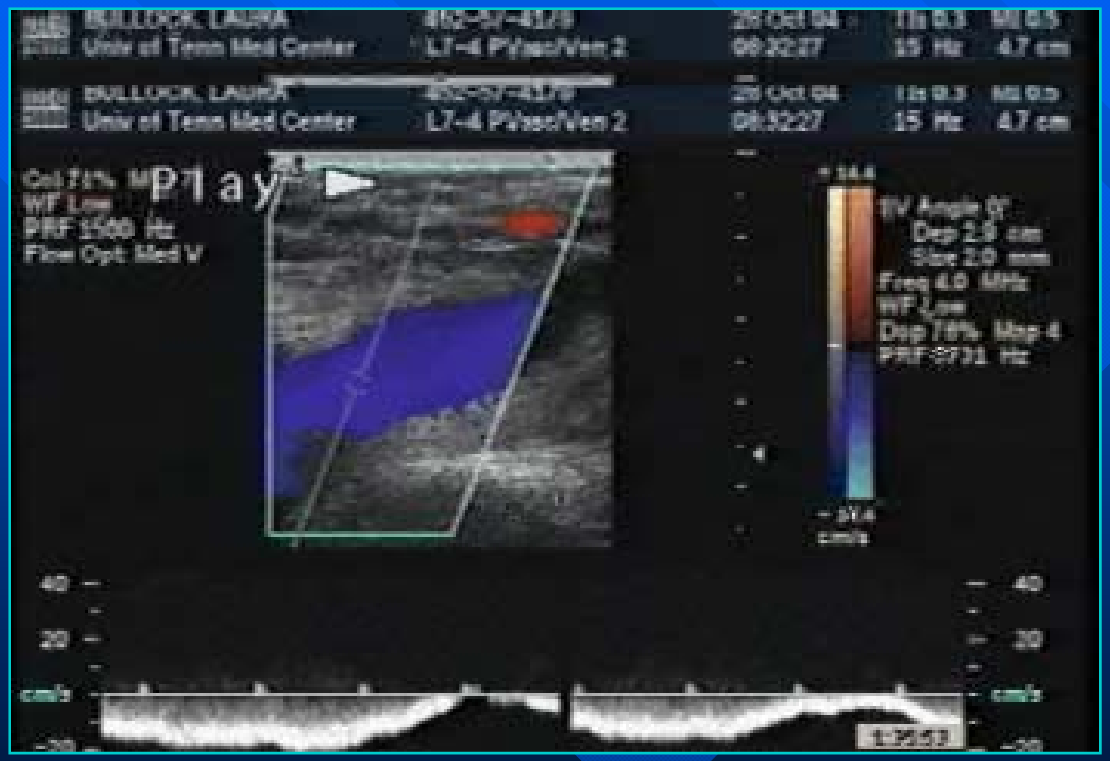
duplex scan criteria

- compressibility
  - deep femoral
  - superficial femoral at adductor hiatus
  - posterior tibialis at ankle
- augmentation
  - competent
  - phasic

compressibility



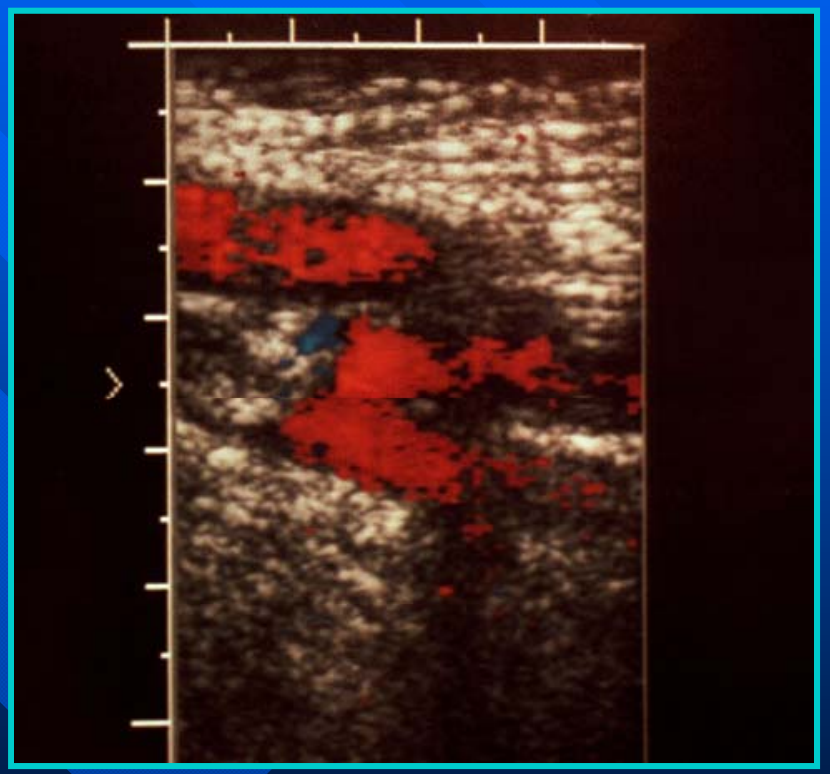
venous hemodynamics



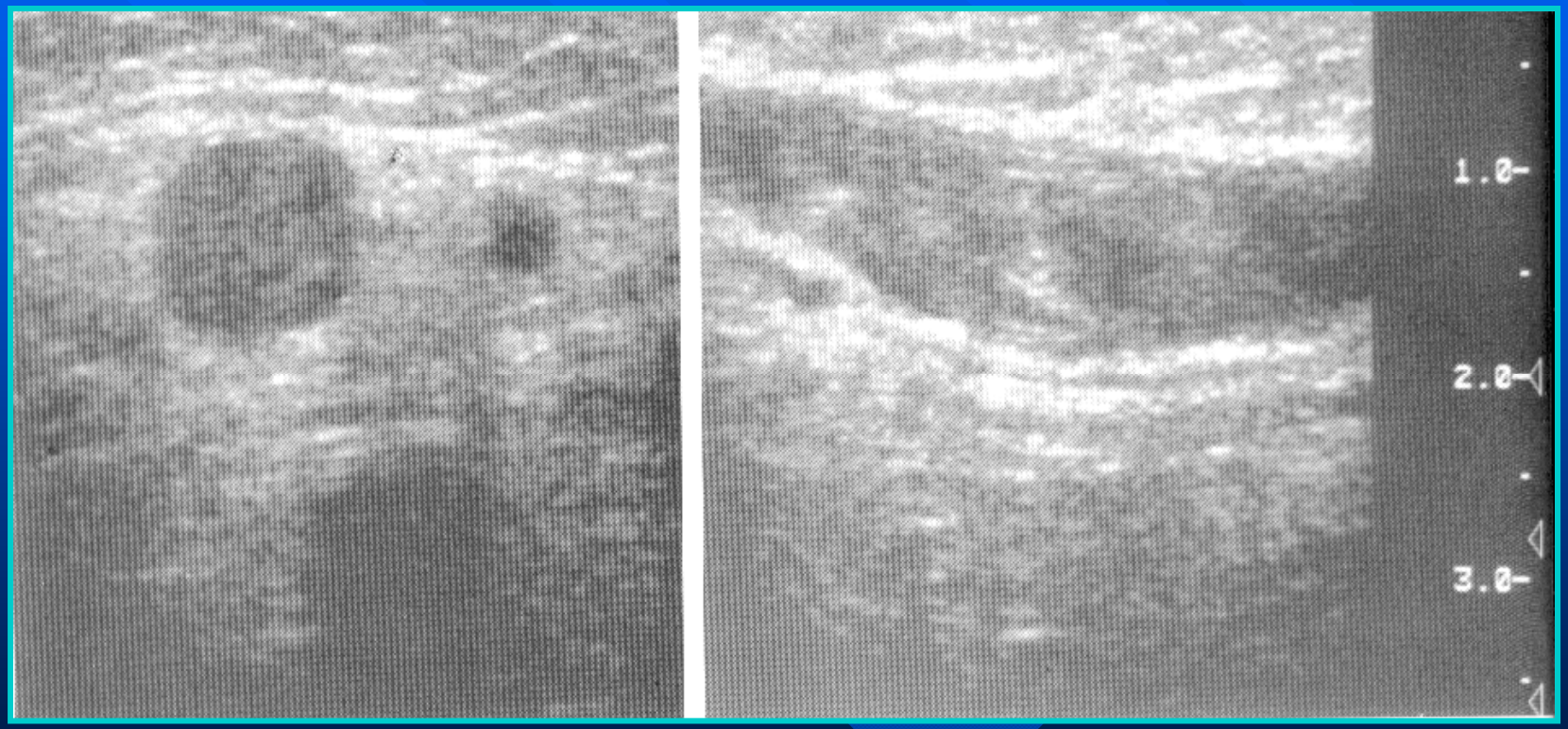
dvt acute vs. chronic

acute

- Less echogenic
- Vein distension
- Homogeneity
- Free floating



dvt acute vs. chronic



dvt acute vs. chronic

chronic

- echogenic
- vein retraction
- heterogeneity
- clot retraction
- collaterals
- recanalization

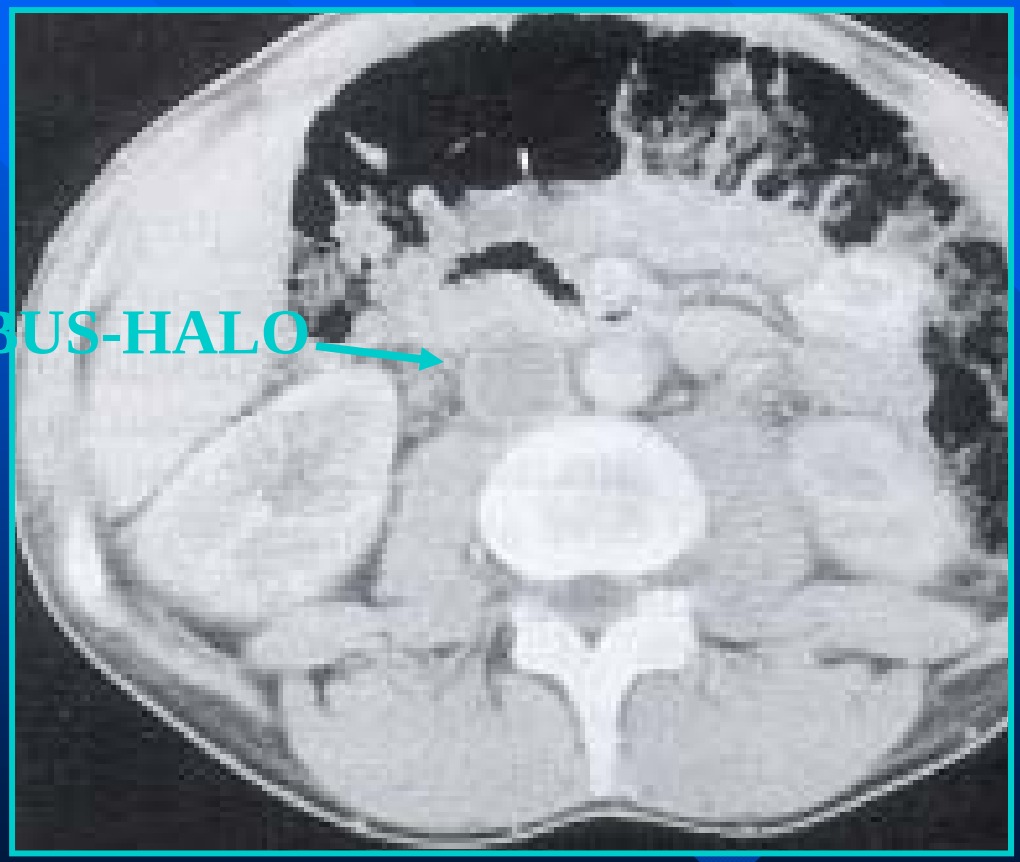
duplex
rationale

- duplex least accurate in infrapopliteal veins
- incidence of P.E. from infrapopliteal veins low
- often don’t treat calf thromboses
- incidence of progression >35% to popliteal in 24 hrs

duplex scan accuracy

	SENSITIVITY (%)	SPECIFICITY (%)
FEMORAL POPLITEAL	89-100	98-100
POPLITEAL/UPPER CALF	63-91	83-100
TIBIOPERONEAL	73-100	86-100

computed tomography



Hey you!!

YEAH , YOU IN THE THIRD ROW!!!!!!!!

WAKE UP!

d-dimer

- products of degradation of cross linked fibrin by plasmin
- up to 98% sensitive to diagnosis of DVT
- low as 38% specific

  malignancy, recent surgery, hospitalized for>3 days
- high Negative Predictive Value (if it's negative it ain't there)

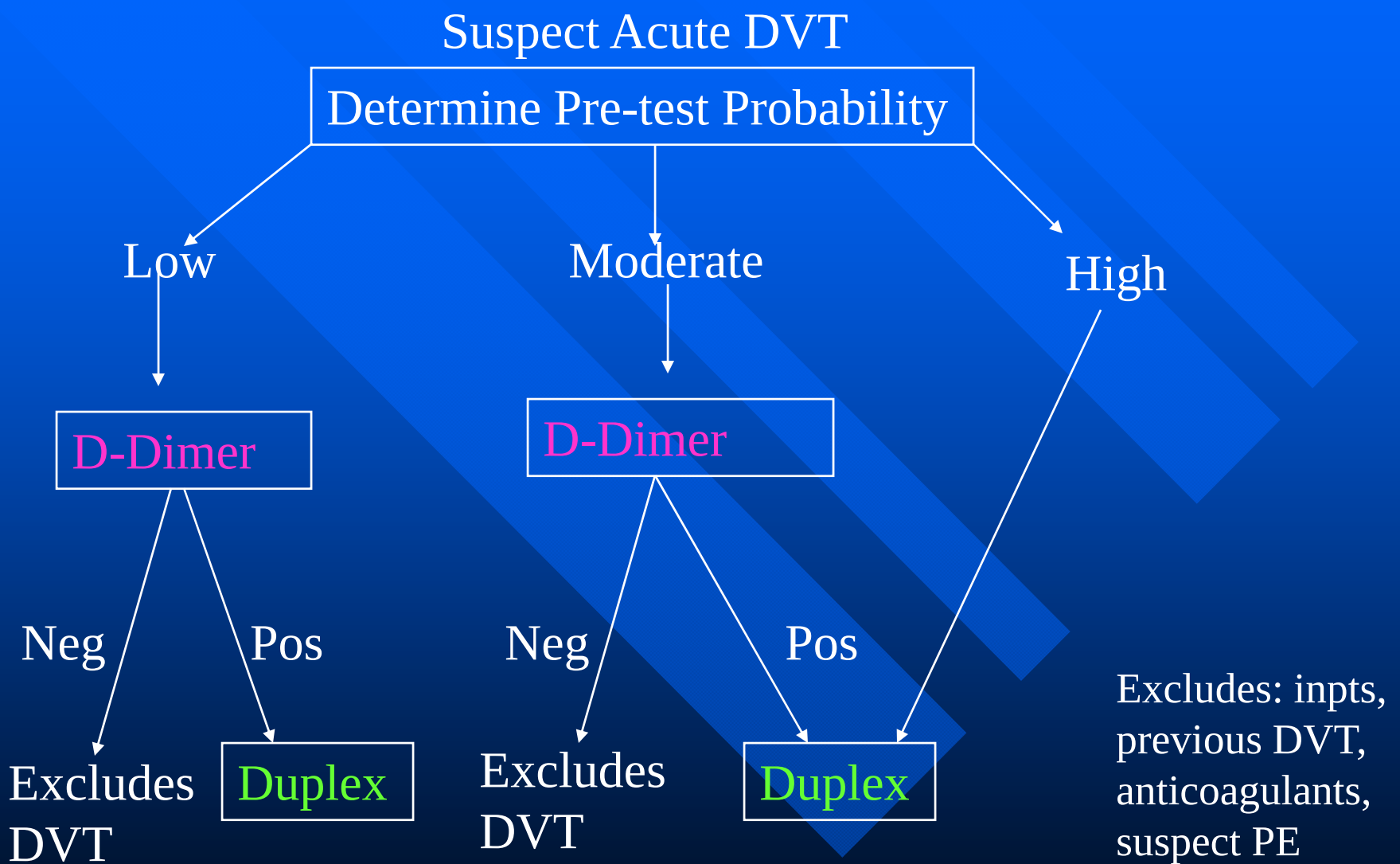
pre-testing stratification

Clinical Feature	Pts
Active cancer	1
Paralysis, paresis, immobilization	1
Bed ridden >3days/Surgery<4 weeks	1
Tenderness along deep veins	1
Entire leg swollen	1
Swelling >3 cm vs other leg(10cm below tuberosity)	1
Pitting edema	1
Non-varicose superficial collateral veins	1
Alternative diagnosis likely	minus 2

Probability: Low≤0, Moderate 1-2, High≥3

Lancet 350:1795, ’97

diagnostic algorithm for outpatients



Prophylaxis-Hospitalized

- Low Risk — Early and continuous ambulation, graduated stockings
- Moderate Risk — Compression Device, s.c. low dose UFH or LMWH
- High Risk — low dose UFH or LMWH once or twice daily, or oral anticoagulant,

and/or — IPCD

dvt treatment

- **tibio-peroneal**
- **fem-pop/iliofemoral**
- **recurrent**
- **phlegmasia cereulea dolens**

tibio-peroneal dvt

- **controversial**
  - **to heparinize or not**
  - **if you do, use outpt therapy with LMWH**
  - **if you don't, use nonsteroidals**
- **ambulation**
- **support hose**
- **restudy for propagation**

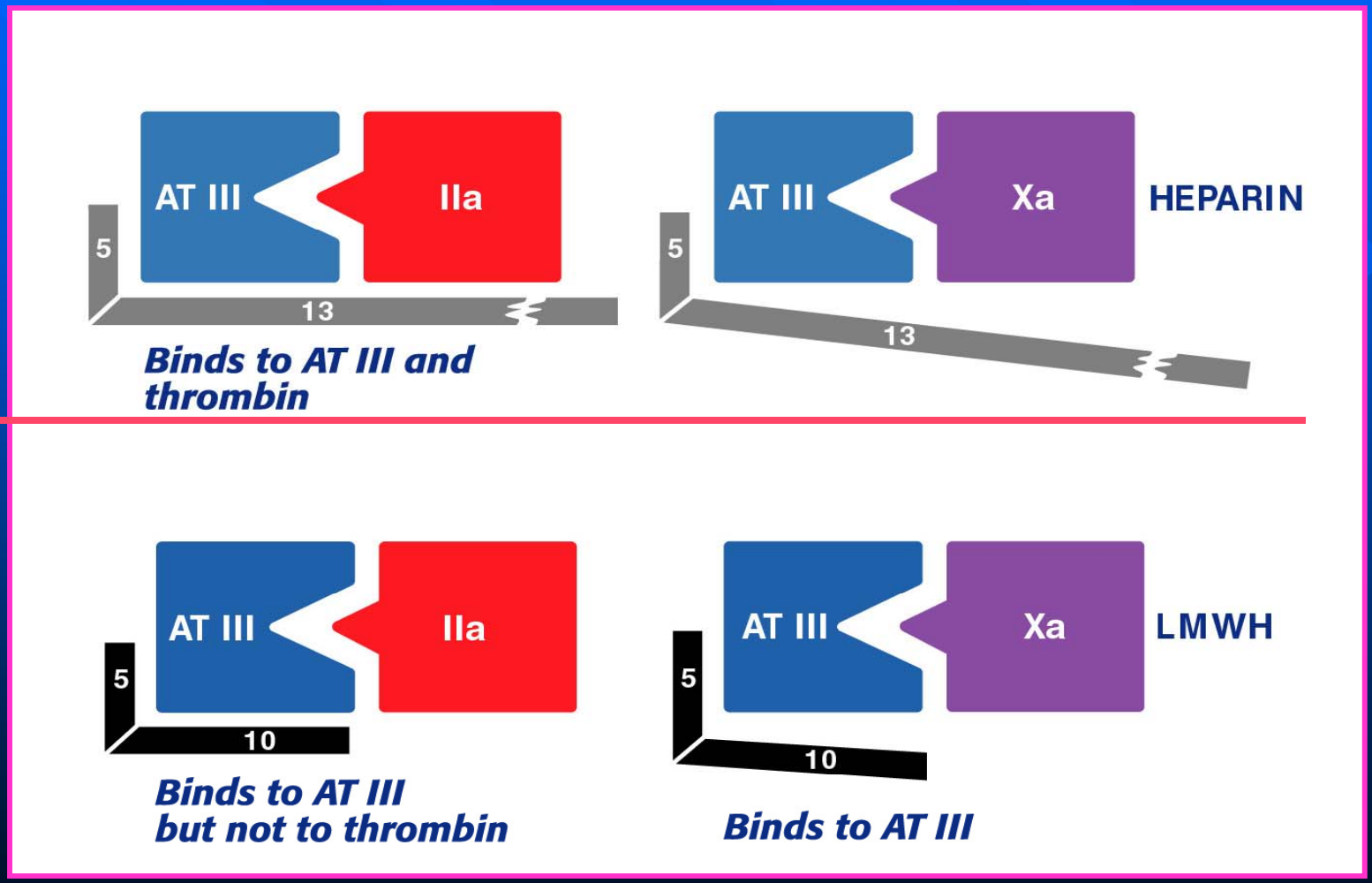
ilio-fem-pop dvt

- **20% of popliteal untreated propagate**
- **LMWH or unfractionated heparin**
  - **rate of propagation and p.e. same**
- **ambulation early**
  - **bed rest increases propagation 20 to 1**
  - **swelling diminished sooner with ambulation and….**
- **support hose-class II**
- **early warfarin**

recurrent dvt

- look for HCS or other reason
- if already on coumadin, add ASA/plavix
- retreat if not on anticoagulants
- consider lifelong coumadin
- Up to 20% recurrence

Differential Effects of UFH and LMWH on Factor Xa and Thrombin



Hirsh J, Levine MN. *Blood*. 1992; 79: 1-17

UFH vs LMWH

high mw (15,000)	low MW (4500-6000)
bioavailability <30%	>90%
short $t_{1/2}$	longer
low Anti-Xa/IIa	high Anti-Xa/IIa ratio
drug interactions	fewer
continuous/inpatient	intermittent/outpatient

UFH vs LMWH

recurrence	**6.7-8.5 (%)**	**5.3-6.9**
bleeding	**1.2-2.0(%)**	**0.5-2.0**
death	**6.3-8.0 (%)**	**4.0-6.9**
HIT	**1-2(%)**	**1-2**

patients not suitable for outpatient therapy

- **severe liver disease**
- **thrombocytopenia**
- **renal disease**
- **high risk of falling**
- **acute p.e.**
- **other reasons for hospitalization**

inpatient therapy

- **LMWH or**
- **continuous iv heparin by nomogram**
- **loading dose of 80-100U/kg**
- **15-20 U/kg/hr**
- **check aPTT**

<35 sec rebolus and 4U/kg/hr

45-70 sec ok

>70 sec decrease or stop for 2 hrs

long term therapy

- **start coumadin when aPTT therapeutic or after 2 days of LMWH**
- **overlap of at least 5 days or until therapeutic**
- **INR of 2-3**
- **3-6 mo. reduces the frequency of recurrence over 1-2mo (6% vs 11-18%)**
- **check venous hemodynamics**

alternatives to coumadin

- ximelagatran(oral iia)
  - max level 1.5-2.5 hrs
  - vte prophylaxis, decreased recurrent dvt vs lmwh +warfarin
  - acute coronary syndrome with asa
  - transient liver toxicity
- dabigatran (oral iia)
  - vte prophylaxis phase iii
  - equivalent to enoxaparin
  - peak =2hrs; t ½ =15 hrs

alternatives to coumadin

- razaxaban
  - factor xa inhibitor
  - s.c. administration
  - liver metabolized
  - randomized knee replacement
    - » dose dependant reduction in vte compared to lmwh
    - » dose dependant increase in bleeding

HIT

- ufh acts as a hapten between platelet membrane and pf-4
- uncommon in dialysis pts-why?
- monitor pt ct every other day for 14 days
- lmwh 1/10th incidence of hit
- 50% fall in platelets or below 150,000/ul
- argatroban (2.0 ug/kg/min)

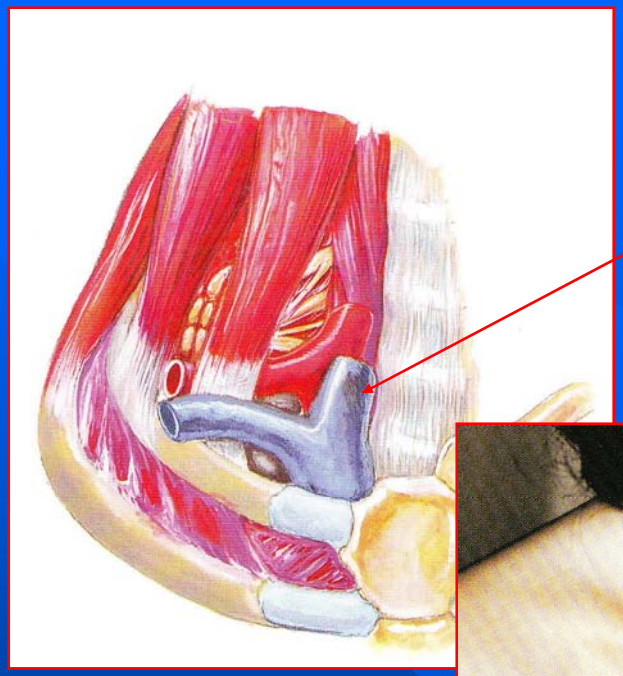
argatroban

- direct thrombin (iia) inhibitor
- synthetic analog of hirudin (smaller molecule)
- t ½ =30-60 mins.
- hepatic clearance
- i.v. administration
- monitor aptt

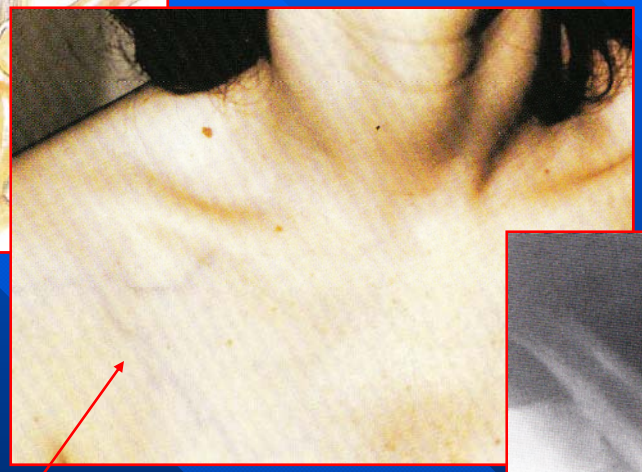
primary axillary/subclavian vein thrombosis (Paget-Schroetter)

- **2º to hypertrophy of the scalenus muscles or an abnormal rib**
- **duplex and venography, MVOV**
- **heparinization ⇒ thrombylysis ⇒ look for causes repair ⇒ anticoagulation →**
- **without repair-chronic problems and → recurrence**
- **repair of anomalies should be done within a wk after lysis**

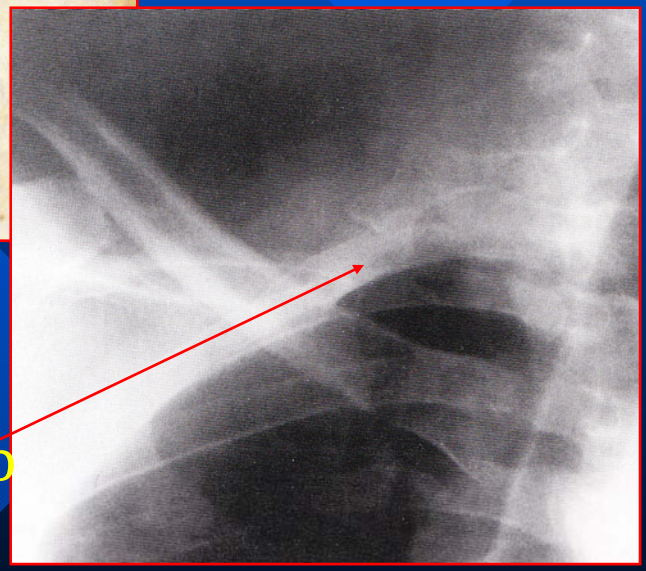
Paget-Schroetter Syndrome TOS



thoracic outlet

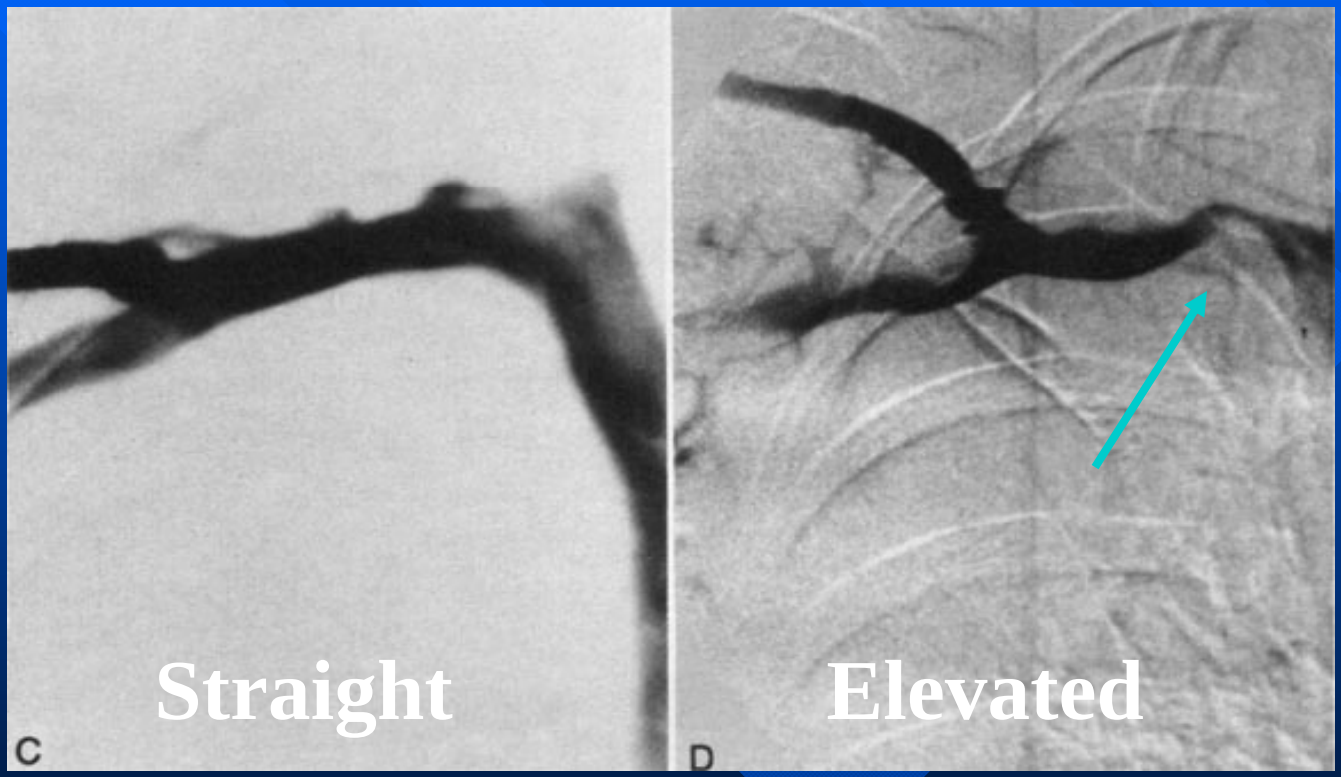


dilated superficial veins



cervical rib

Paget-Schroetter



secondary axillary/subclavian vein thrombosis

- **prevention-use I.J. preferentially**
- **avoid long termed central lines, pic lines**
- **surveillance**
- **thrombolysis early followed by anticoagulation**
- **catheter removal depends on necessity vs symptoms**

phlegmasia

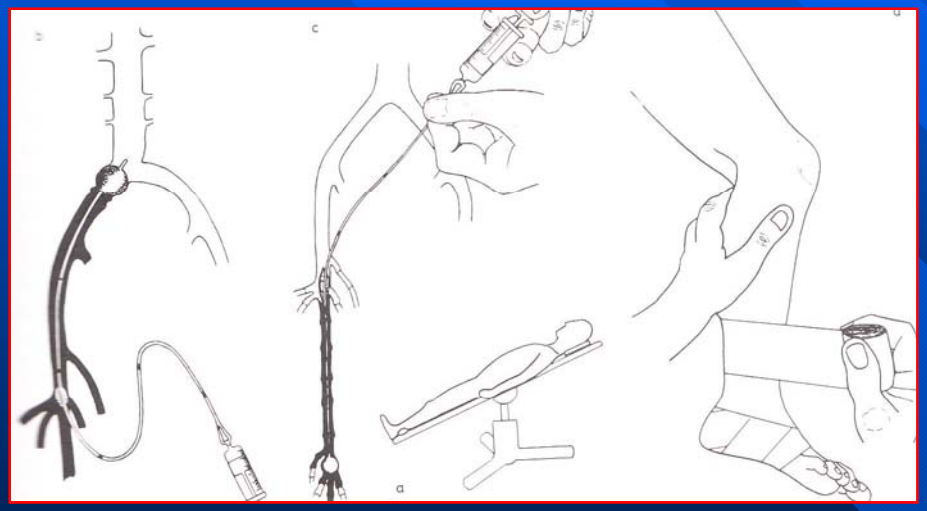
- **iliofemoral thrombosis**
- **thrombectomy vs thrombolysis**
  - **contraindication to lysis**
  - **viability of limb (alba)**
  - **popliteal approach for lysis**
  - **with or without fistula**
- **post thrombotic sequellae**
- **anticoagulation**

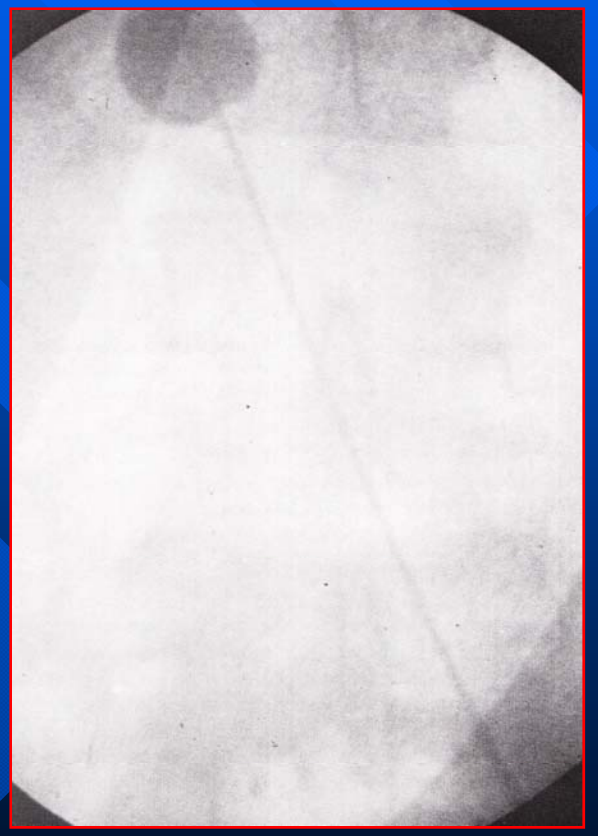
phlegmasia cereulea dolens

phlegmasia cereulea dolens

- if no “P’s” anticoagulate, elevate/ambulate, stockings
- “P”
  - Pain -Pulseless
  - Pallor -PARESTHESIA
  - Poikilothermia -PARALYSIS
- even in the presence of arterial flow if the two big “P’s” are present, thrombectomy and fasciotomy are necessary

thrombectomy





Thrombolysis

- systemic/regional
  - better venous patency and less post thrombotic syndrome
  - bleeding, long treatment times
- catheter directed
  - patency and function improved over systemic
  - possibly decreased bleeding
  - life function better
- mechanical
  - often needs thrombolytic therapy after

Thrombolysis

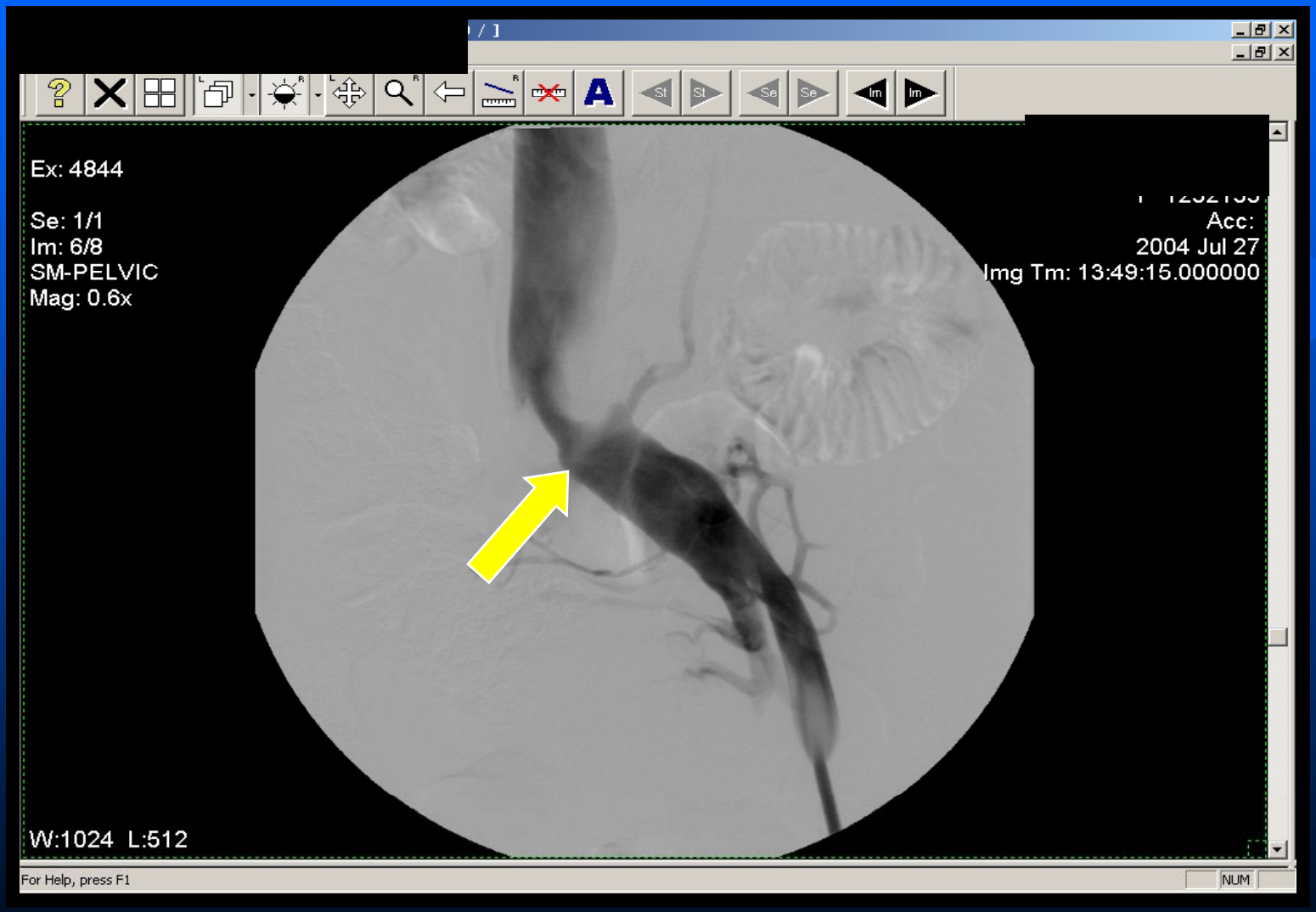
- pharmacomechanical
  - seed with tpa
  - mechanical thrombectomy
  - increases clearing of clot
  - fewer pts need regional or catheter thrombolysis for shorter times

phlegmasia-thrombolysis

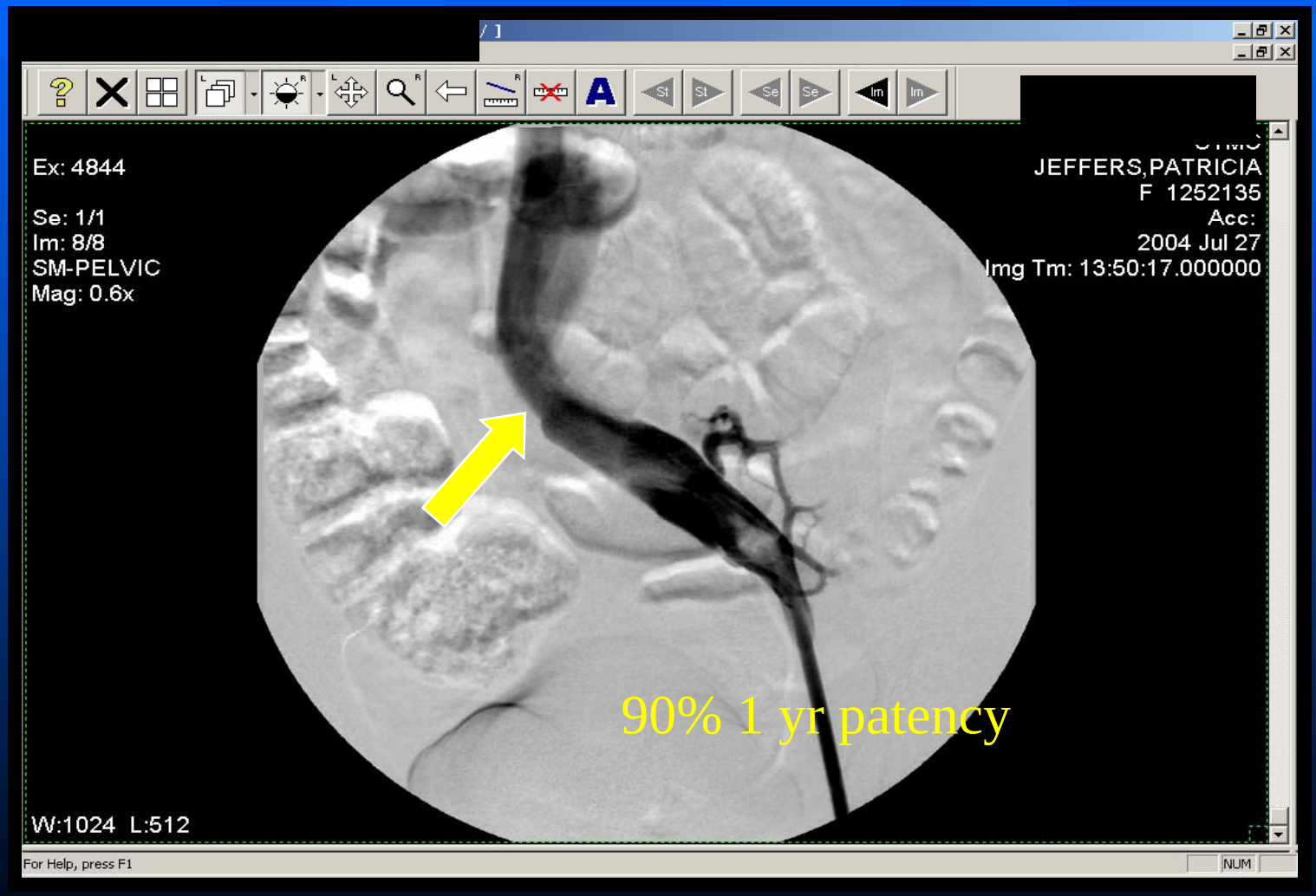
Phlegmasia-thrombolysis

popliteal access →

adjunctive measures may-thurner



may-thurner after stent

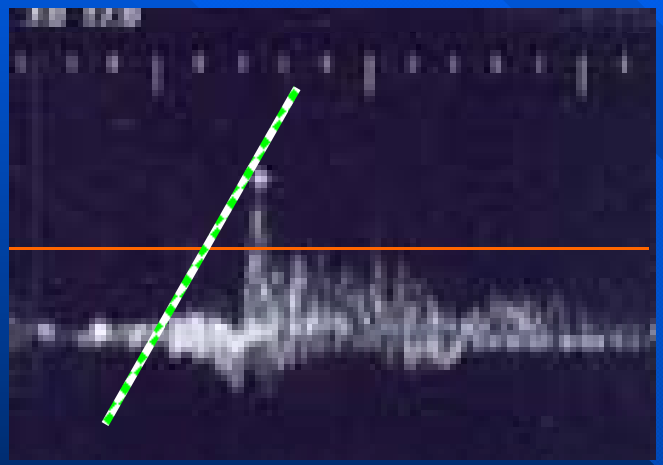


Maximum Venous Outflow Velocity

- Evocative test measuring venous outflow velocity using a standardized thigh blood pressure cuff pressureand duplex obtained femoral vein velocities upon release to detect venous outflow obstruction.
- Lebow et al (UTMCK): MVOV is significantly decreased on the left side in a sample of normal female volunteers and can be used as a preliminary test to Dx functional venous outflow obstruction.

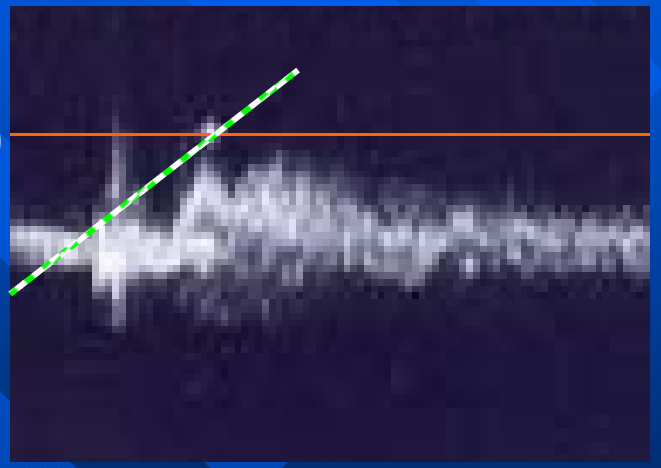
Left Venous Outflow Obstruction

MVOV 82 cm/sec



R

MVOV 40 cm/sec



L

a myth

“bed rest in acute dvt reduces the risk of pe, alleviates pain, and decreases swelling”

no difference in pe between lmwh and bed rest and lmwh and 4 hrs ambulation a day and compression

clinically asymptomatic pe was found by scan in ½ of pts at the time of dvt diagnosis

ambulation and compression reduces stasis and thrombus propagation (26% vs 1%)

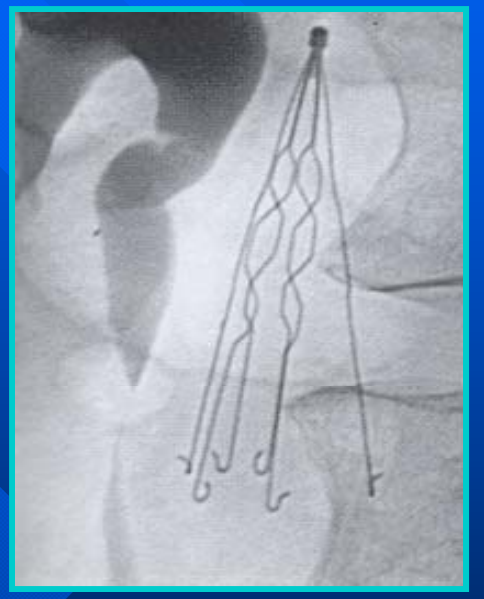
ambulation and compression leads to faster pain relief and less swelling

Reduces the frequency and severity of post thrombotic syndrome

ivc filters

Indications (classical)

- **major p.e.**
- **p.e. on adequate anticoagulation**
- **loose clot**
- **respiratory insufficiency**
- **can't anticoagulate**

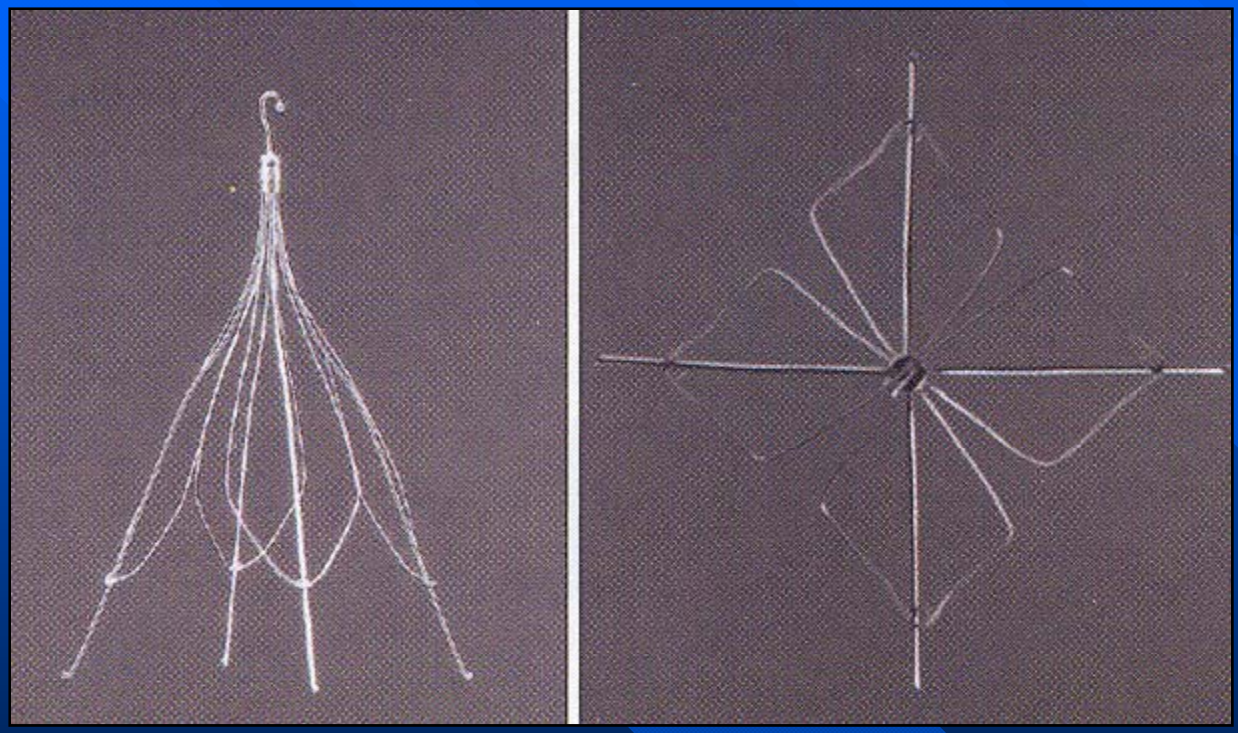


1-4% recurrence

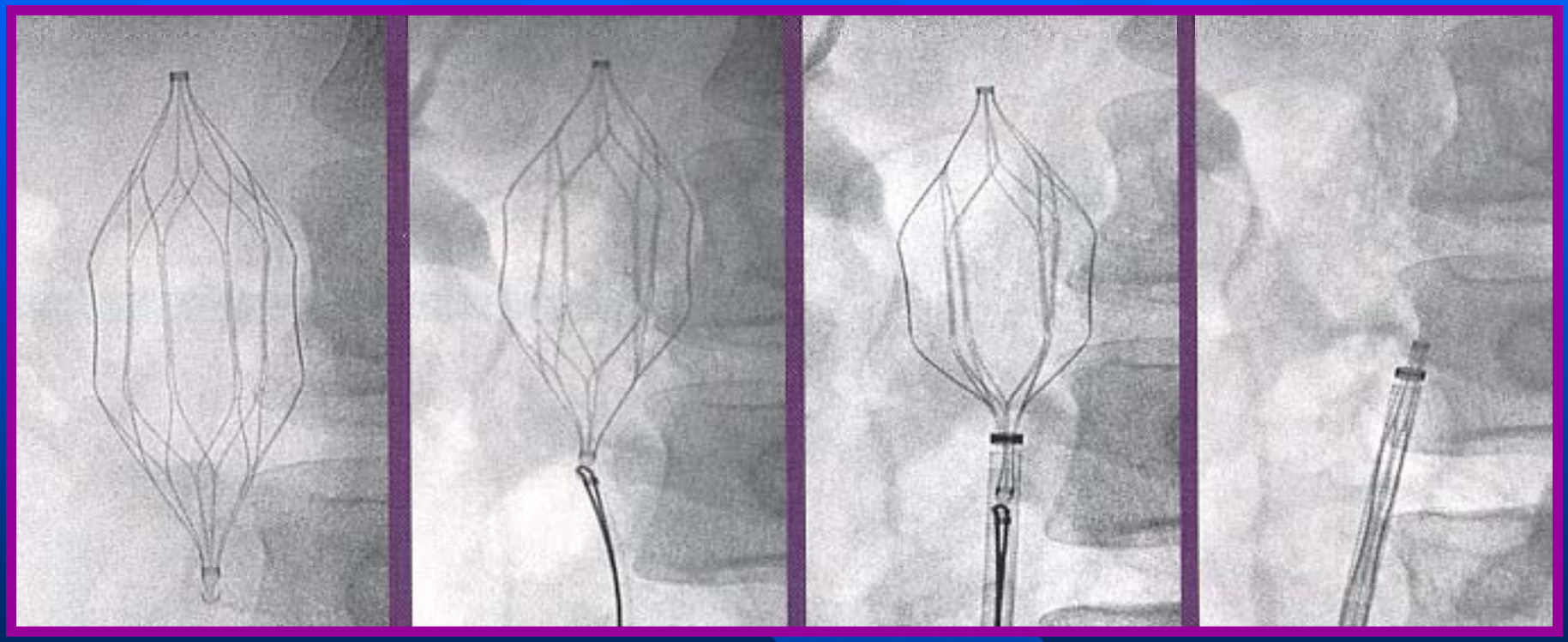
ivc filters

- not so classical reasons
  - cancer
  - surgery and dvt
  - hit
  - trauma
  - free floating
  - morbid obesity surgery
  - venous reconstruction, endovascular procedures

removable filters



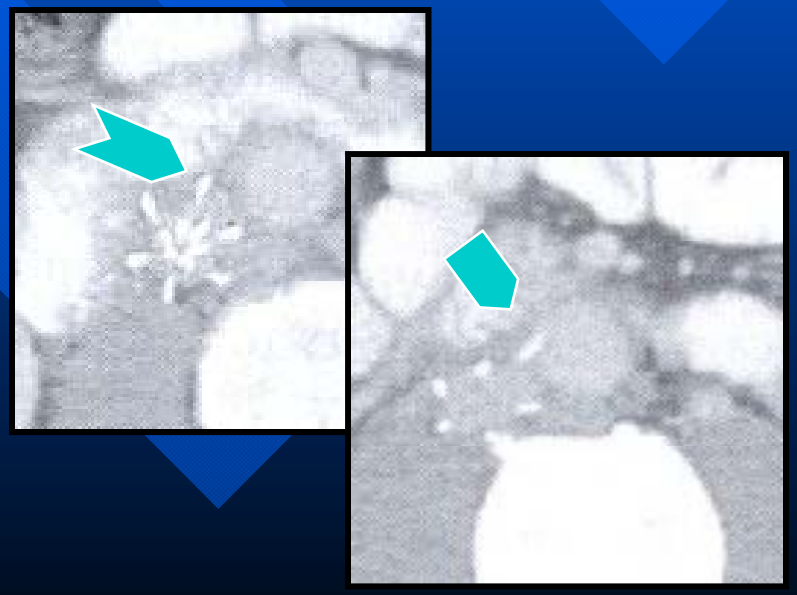
removable filters



Opt-Ease

rationale

- higher incidence of dvt after filter
- ivc thrombosis
- migration
- strut fracture ( )
- Penetration ( )
  - Duodenum, ureter, aorta
- infection
- trauma
- pregnancy
- short termed prophylaxis



removable filter

as yet, no clear-cut indications for use

summary-what's new since I last gave grand rounds on this subject over two years ago

- d-dimer
- lMWH outpt therapy
- replacement for heparin-argatrobans
- replacement for coumadin
- thrombolysis
- ct diagnosis of pe
- removable filters
- MVOV


SO LONG AND
THANKS FOR
ALL THE FISH