Aspirin as DVT Prophylaxis in Total Knee Arthroplasty

Thomas D Meade MD

Why am I here?

"The growth of knowledge depends entirely on disagreement"

(Karl R. Popper, 1902-1994)

Change in DVT/PE Prophylaxis

- From:
  - Warfarin (INR <2.0)
  - IPC-Boots
  - Slower mobilization
    - Indwelling epidural
    - Femoral/Sciatic Nerve block
    - General/PCA
    - Longer procedures
    - Intra-medulary violation

Change in DVT/PE Prophylaxis

- To:
  - ASA (325 mg po bid)
  - IPC (boots)
  - Early mobilization
  - Shorter procedure
    - No IM violation
  - Spinal-short acting
    - On-Q pain pump
  - ↓ LOS
    - 20-30% D/C POD #1

Medical Grand Rounds

Physicians Dr Meade Dr Glew

Background

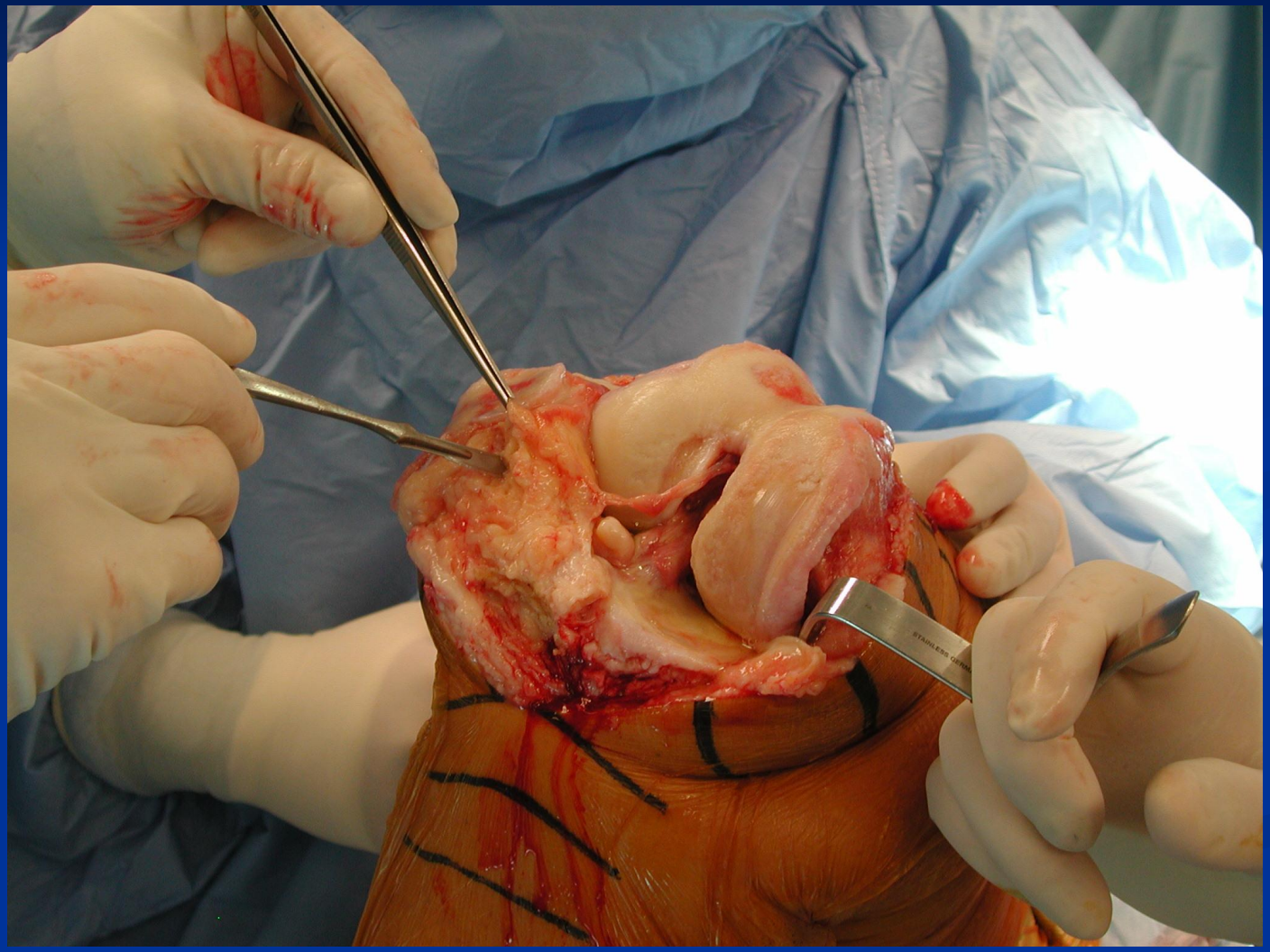
- Limited to Knee Surgery-(>1000 cases annually)
- Advantage evaluate results (+/-)
- Improve processes-CQI

- "Custom Fit Total Knee"-National Advisory Team
  - Hi- Volume-simplified procedure
  - Simplify post-op protocols

One Tray

Exposure

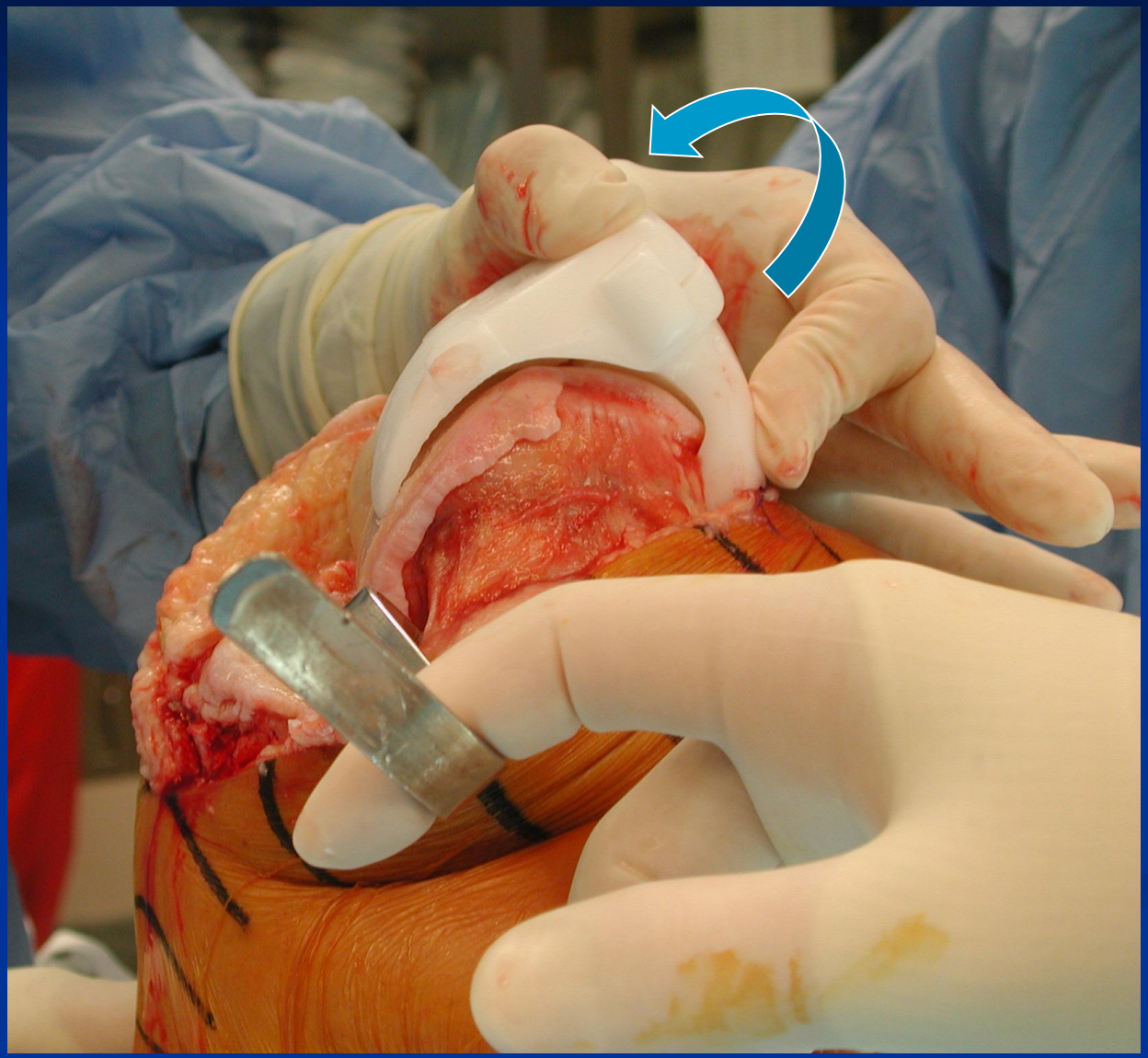
#2



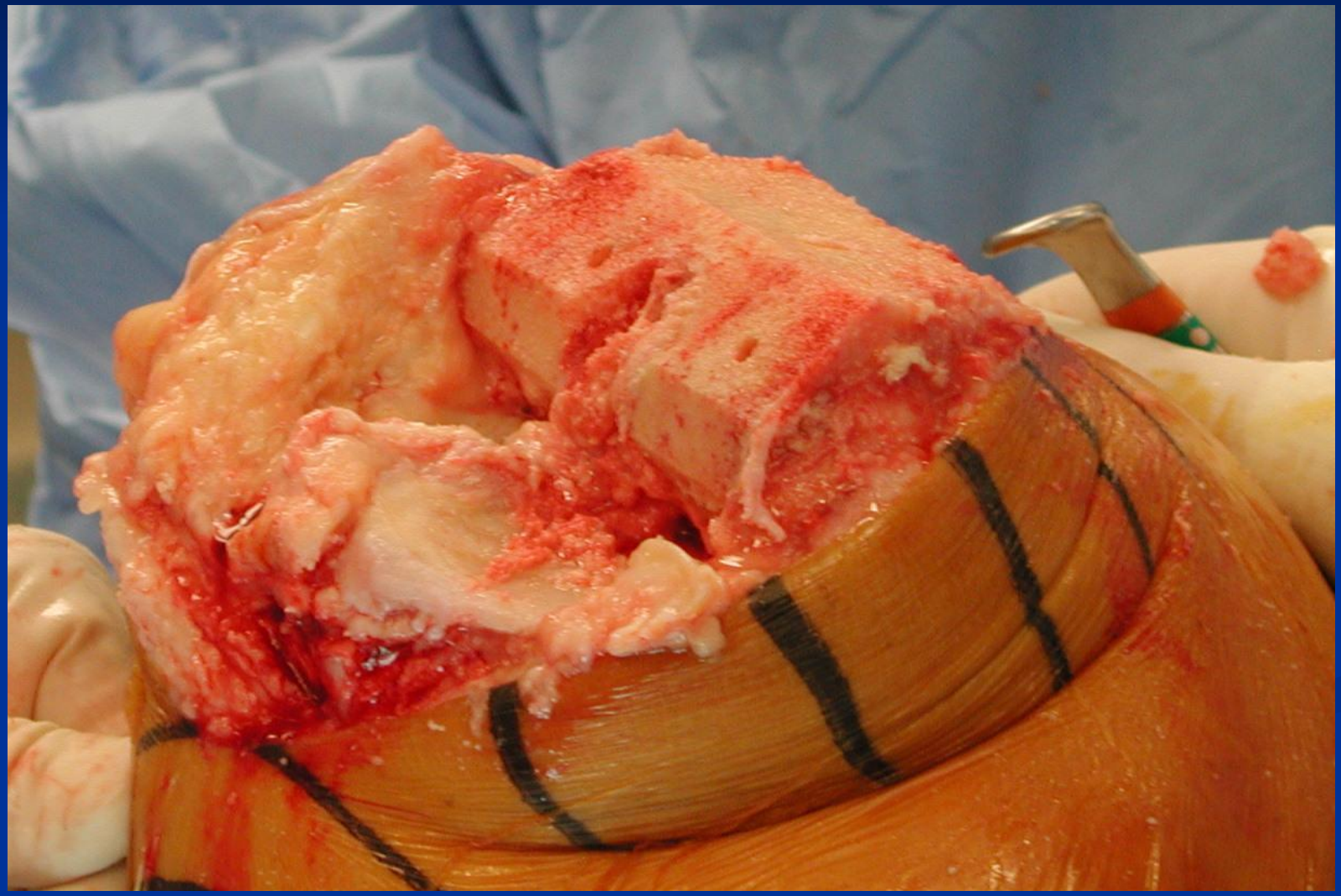
Distal Femur

#3

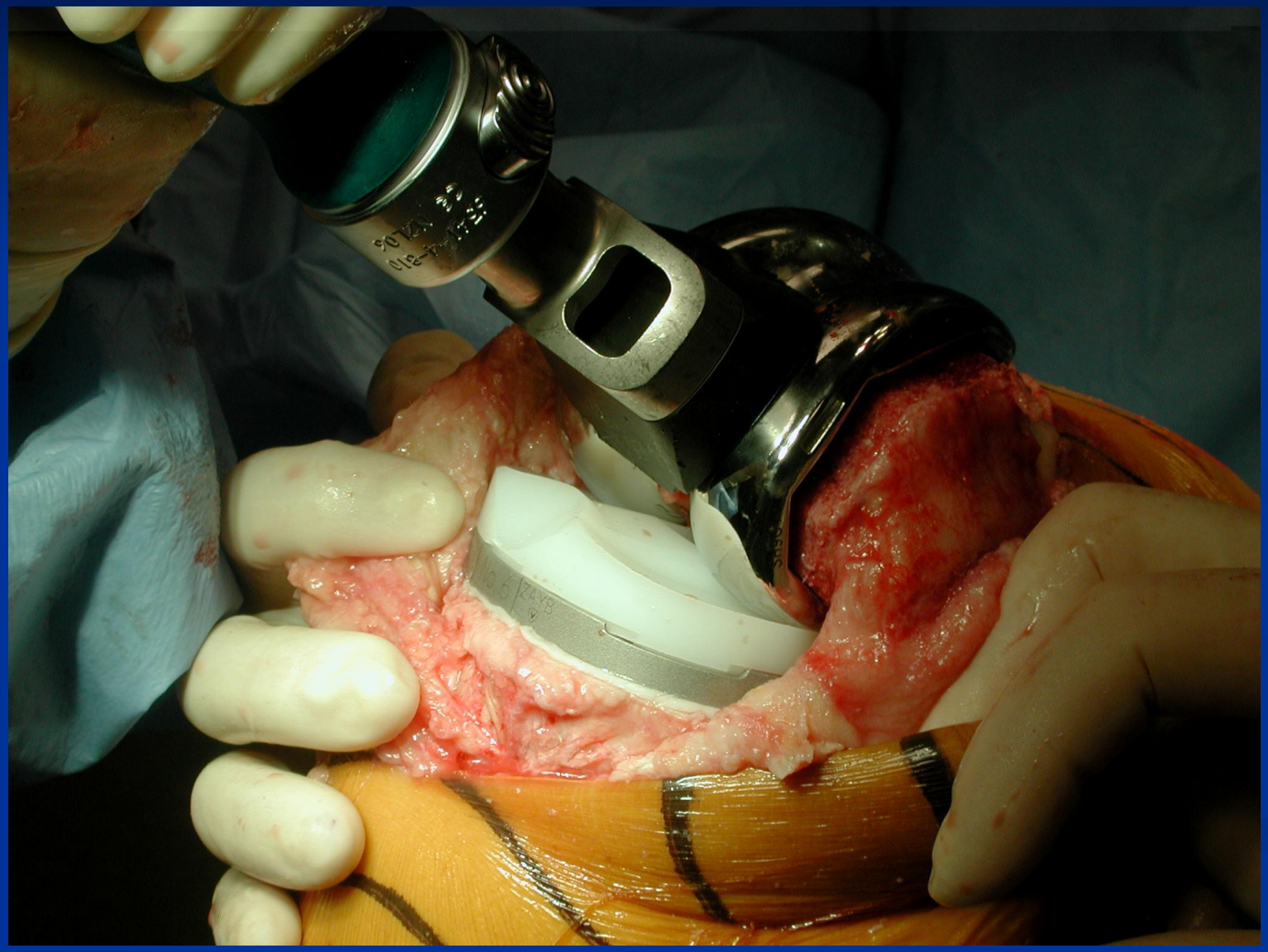
Femoral Jig



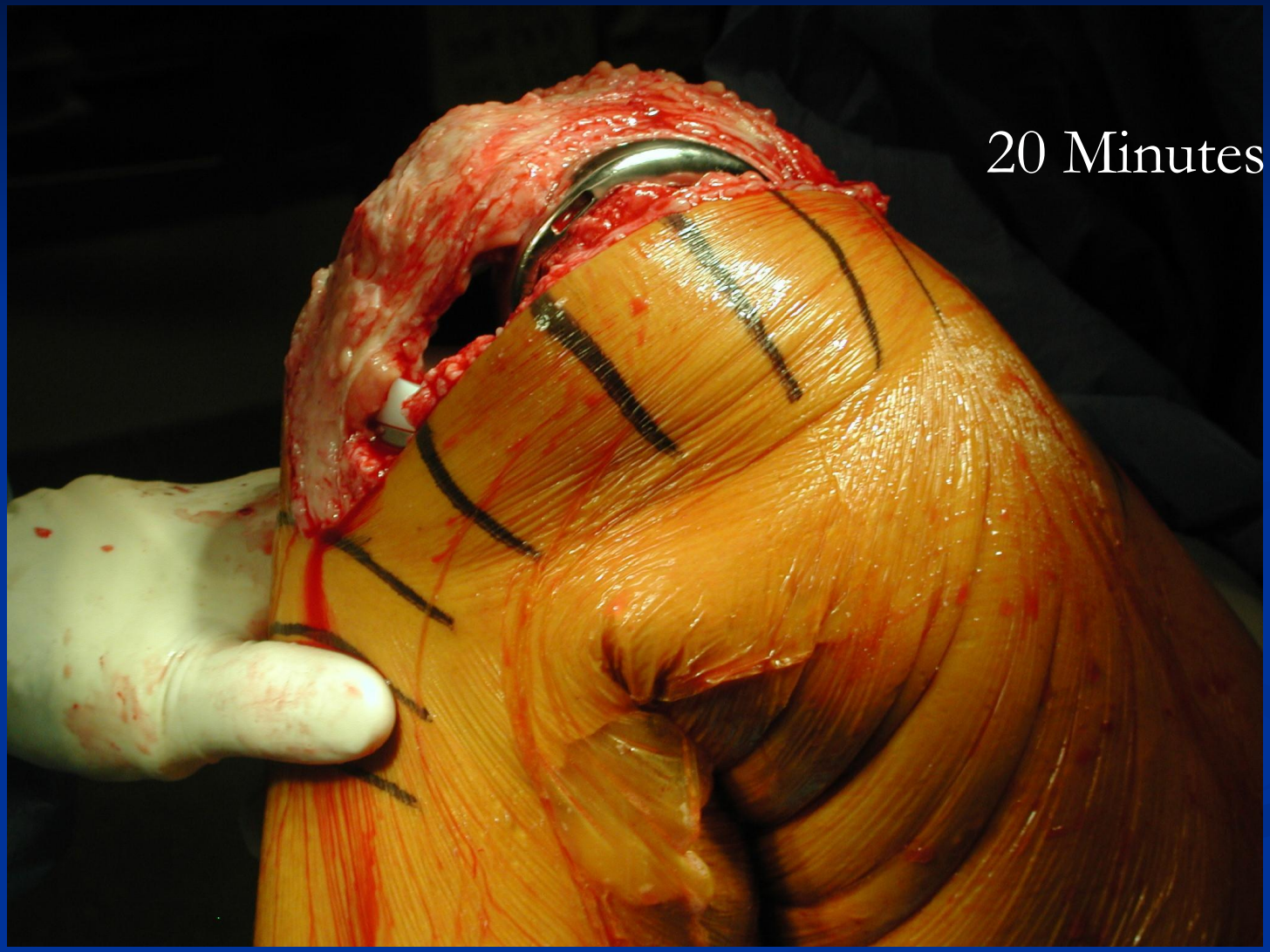
Final Femur



Uncemented Femur



Final

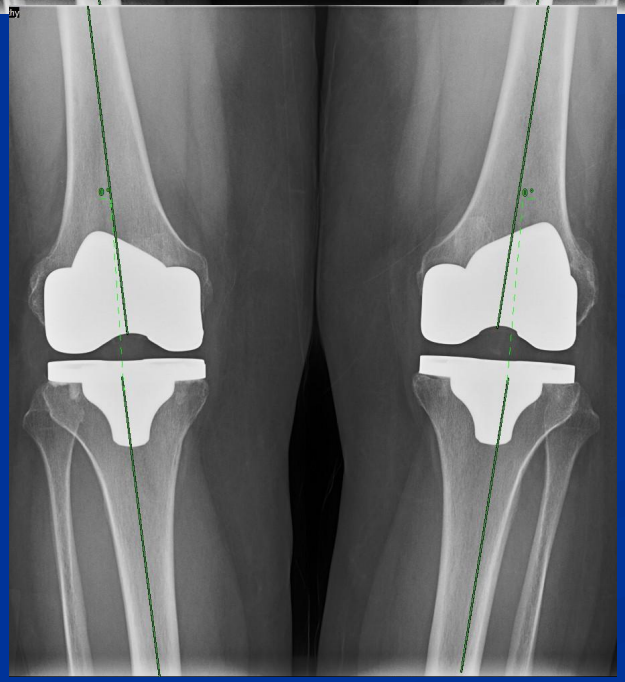


USA's best heart attack care saved his life

- It took 24 minutes for Richard Silverman's doctors at Lehigh Valley Hospital to clear a 100% blockage from his heart's most vital artery.
- That's a third of the 90-minute goal that hospitals strive for.
- LVHN: Encourage, Respects & Promotes hi-tech procedures performed quickly, performed well: successful outcomes

40 Minutes

40 Minutes



Duration of Anesthesia and Venous Thromboembolism After Hip and Knee Arthroplasty

Mayo Clinic

CONCLUSION:

- **Found a marked association between the duration of anesthesia and postoperative VTE in patients undergoing joint arthroplasty.**

- **Suggest that duration of anesthesia may be an important risk factor for postoperative VTE after orthopedic surgery.**

Innovations-Change Industry

Clayton Christensen-Harvard Business School

- Disruptive Innovations
- Sustaining Innovations

Disruptive Innovation

- New technology
- More affordable
- Simpler to use
- Enables more customers (surgeons) to afford or have skill to use product or service
- Change is so big- it eventually replaces or disrupts the established approach to producing that product

Disruptive Innovation- health care

- Provides solutions patients want & see as better alternatives
  - Is driver for disruption to occur
- Patients want 'custom' or individualization
- Strategies that worked so wonderfully in past no longer suffice
- Disruptive innovation spurs growth/change

Sustaining innovations

- Improve the performance of established products/services

Disruptive Innovations

- …but other benefits: often cheaper, simpler, more convenient to use
- Inexorably get better until they change the game, relegating previously dominant firms to the sidelines in sinking fashion

Simplified post-op process

- Eliminate CPM---No outcome advantage
- Optimized Anesthesia/Pain control
  - Regional- spinal
  - Pain Pumps
  - Intra-articular marcaine/depomedrol
- Mobilize:
  - 20-30% d/c POD #1
  - ↓ LOS

Primary TKA Group

- No fatal PE's
- Increased wound hematoma, hemarthosis,
- Occasional Return to OR wound evacuation
- INR- variability on warfarin
- 'Severe" complications on post op heparin/LMWH

Local/Regional Accepted Practices

- U of P: ASA/boots/mobilize
- Jefferson: ASA/boots/mobilize
- Riddle/Main Line ASA/boots/mobilize
- Pennsylvania Hospital ASA/boots/mobilize
- Hospital For Special Surgery –ASA (low risk)
- LVHN– formalize ASA community standard

Controversy : Optimal Antithrombotic (DVT/PE) Prophylaxis TKA

- Surgeon vs Hospitalist/Medical Consultant
- ACCP-Clinical Practice Guidelines-Antithrombotic & Thrombolytic Therapy
- AAOS-Prevention of PE in THA/TKA-Clinical Guidelines

Disclaimers

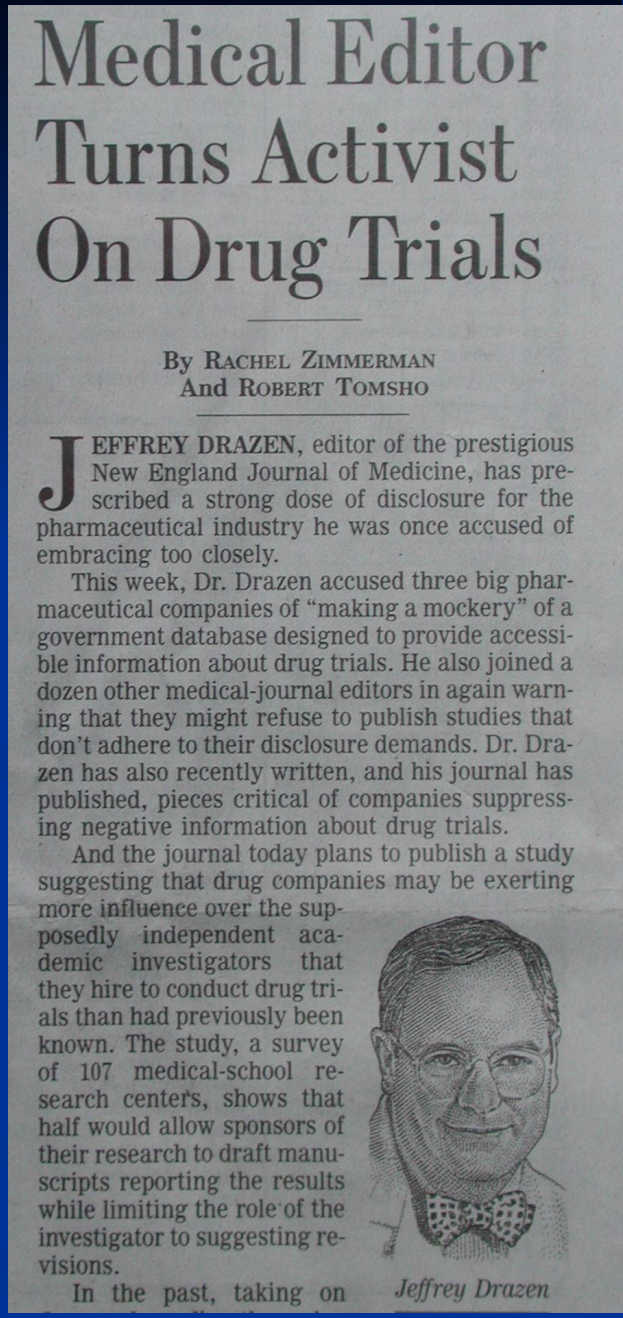
- ACCP- (1000)pages—2006 supplement
  - Guidelines: General info only-NOT Medical Advice
  - Do not replace professional medical care & physician advice
  - May not be complete or accurate
  - ACCP disclaim all liability for accuracy and completeness of guidelines
  - Guidelines-data existing literature (1980's, 1990's)

Literature: Imperfect/ Tainted

Dr Jeffery Drazen:Harvard Pulmonologist- Editor NEJM-5/2005

"…..he sees the ugly side that he hasn't seen before-

…….. the suppression of results that they don't like, the spin of unfavorable results"



Medical Editor Turns Activist On Drug Trials

By Rachel Zimmerman And Robert Tomsho

JEFFREY DRAZEN, editor of the prestigious New England Journal of Medicine, has prescribed a strong dose of disclosure for the pharmaceutical industry he was once accused of embracing too closely.

This week, Dr. Drazen accused three big pharmaceutical companies of "making a mockery" of a government database designed to provide accessible information about drug trials. He also joined a dozen other medical-journal editors in again warning that they might refuse to publish studies that don't adhere to their disclosure demands. Dr. Drazen has also recently written, and his journal has published, pieces critical of companies suppressing negative information about drug trials.

And the journal today plans to publish a study suggesting that drug companies may be exerting more influence over the supposedly independent academic investigators that they hire to conduct drug trials than had previously been known. The study, a survey of 107 medical-school research centers, shows that half would allow sponsors of their research to draft manuscripts reporting the results while limiting the role of the investigator to suggesting revisions.

In the past, taking on

Jeffrey Drazen

Evidenced Based Journal Articles?

WSJ.com

New Protocol

Worrisome Ailment in Medicine: Misleading Journal Articles

Editors Demand More Data To Ensure Full Disclosure Of Drug Risks, Trial Gaps

Sarbanes-Oxley for Professors

By Anna Wilde Mathews

Doctors and patients who rely on articles in prestigious medical journals for

JAMA

THE NEW ENGLAND JOURNAL of MEDICINE

Moving Goalposts

The main goal of a study may change between th original design and final publication. What some authors do, according to a sampling of articles:

- May 2005-WSJ Front pg article
  - Omit key findings of trials about a drug's safety and efficacy

- NEJM-5/2005
  - Survey 107/122 Med Schools
    - 50% allow Pharm Co. draft articles
    - 25% allow Pharm Co.supply results
  - Conflict of interest
  - Recent controversies
    - Paxil/Vioxx suppressing neg results
  - AMA –working to eliminate gag clauses

Survey: Drug companies control much of medical studies' results

Drafting journal articles, supplying data OK with many in academia.

By Alicia Chang
Of The Associated Press

Many U.S. medical schools are willing to give companies that sponsor studies of new drugs and treatments considerable control over the results, according to survey results that some doctors found troubling.

Half of the schools said they would let pharmaceutical companies and makers of

of Public Health, appears in today's New England Journal of Medicine.

Harvard researchers sent surveys to the nation's 122 accredited medical schools to gauge what kinds of standards exist between researchers and sponsors. All but 15 responded.

The researchers did not directly establish exactly how much control universities actually give to companies.

But the medical schools overwhelmingly agreed that they would not enter into contracts that would allow companies to edit research articles or suppress negative

tary research guidelines stating that companies will sometimes help analyze and interpret results and have the right to review articles before publication. The guidelines also note that sponsors own the data and have sole discretion over who has access to the information.

Recent controversies involving companies accused of suppressing unfavorable results have led to demands for more public disclosure of industry-sponsored research. Drug manufacturers GlaxoSmithKline and Merck were recently accused of hiding information about the antide

"disastrous inadequacy of lesser evidence"-Sackett. Oxford-2002

- A misguided attempt to do good, advocate 'preventative' maneuvers that have never been validated in rigorous randomized trials.
- Not only do they abuse their positions by advocating unproven 'preventives' they also stifle dissent
- HRT: --caused far more harm than good
  - increased Hrt disease, breast cancer, stroke, dementia

"disastrous inadequacy of lesser evidence"

- If a drug prevents heart disease but can cause cancer, the benefits may not be worth the risk.

- If a drug decreases DVT but can increase bleeding risk– it may not be worth the risk– esp if it does not decrease the incidence of fatal PE.

ACCP-Conflict of Interest Disclosures

- Dr Hirsh-Chair: Support 2 books-Fondaparinux; LMWH
- All Co-Chairs: Astra, Bristol-Myers Squibb, Sanofi,Aventis, Abbott, Baxter, GlazoSmithKline,Merck, Bayer,Wyeth,Titan, Novartis, Peregine, J&J, Eli Lilly, AstraZeneca, Genzyme,…….

ACCP- Elective Knee Replacement

- Routine LMWH, fondaparinux, or VKA (2.5INR)
- For pt's undergoing TKA the Optimal use IPC is an **alternative option** to anticoagulant thromboprophylaxis
- Recommend AGAINST singular use:
  - Aspirin
  - LDUH-lo dose unfractionated heparin
  - VFP-venous foot pumps

ACCP –Elective Knee Replacement

- Hi Risk Bleeding
  - Optimal use IPC
  - VFP
- Hi Risk Decreases
  - Return pharmacologic thromboprophylaxis

AAOS Guidelines-PE Prevention

(63 pages)-2007 (data >1996)---Revision planned 2010

- Disclaimer
  - AAOS physician volunteer Work Group
    - Only One Dr Conflict: DePuy—no pharmaceuticals
  - Educational tool based on an assessment of the current scientific and clinical information and accepted approaches to treatment.
  - Not intended to be a fixed protocol
  - Some patients may require more or less treatment.
  - Patient care and treatment should always be based on a **clinician's independent medical judgment** given the individual clinical circumstances

Burden of Disease

- ACCP: Hospital acquired DVT
  - 10-40% med/surg pt's
  - 40-60% orthopaedic pt's
- Widely accepted DVT proxy measure of PE risk
- Thus: ↓ DVT would ↓ PE
- **FACT**: Rate PE all prophylactic modalities not statistically different

"The great tragedy of Science-the slaying of a beautiful hypothesis by an ugly fact."

(Thomas Huxley, 1825-1895)

AAOS: Available evidence

- No differences among the interventions in rates of
  - PE
  - PE-related death
  - total death
  - major bleeding
  - bleeding-related death
  - rehospitalization.
- This lack of adequate evidence holds true for the broader comparison of systemic interventions (fondaparinux, LMWH, and warfarin) and mechanical devices or aspirin alone.
- Exception: major bleeding was very rare among patients receiving aspirin or mechanical devices alone (1 case in 697, or 0.14%, exact 95% CI 0.03-0.8%)

AAOS-Recommendations

***based on systemic literature review by Center for Clinical Evidence Review-Tufts**

- Standard risk PE, bleeding-(Majority)
  - Aspirin, LMWH, synthetic pentasaccarides, warfarin
- Elevated risk PE, Std risk bleeding
  - LMWH, synthetic pentasaccarides, warfarin
- Std risk PE, elevated risk bleeding
  - Aspirin, Warfarin, none
- Elevated risk PE & Bleeding
  - Aspirin, Warfarin, none

Pre OP-Risk Factors for Venous Thromboembolism

- Immobility
- Paresis
- MalignancyCancer therapy
- Previous venous thromboembolic disease
- Inflammatory bowel disease
- Nephrotic syndrome
- Myeloproliferative Disorders
- Paroxysmal nocturnal hemoglobinuria
- Smoking
- Varicose veins
- Inherited or acquired thrombophilia

Pre Op-Risk of PE

- No evidenced based risk stratification system
  - History of DVT/PE
  - Cancer
  - Hypercoaguable states : polycythemia,SCI,
  - No lab test
  - Cornerstone of PE Risk Mgmt:
    - Careful H&P
    - **Clinical Judgment**/ Risk factors

Pre OP-Major Bleeding Risk

- Hx uncontrolled bleeding
- Known coagulation factor deficiency
- Recent GI bleed
- Recent hemorrhagic stroke
- Routine serologic tests: only if hi level clinical suspicion

AAOS- additional recommendation

*** based on consensus development methods only**

- Pre-op assessment PE/bleeding risk
- Know contraindications for anti-coagulation t/c vena cava filter
- Pt's considered for intra/immed post op mechanical prophylaxis
- Consider regional anesthesia
- Mechanical prophylaxis til d/c
- Mobilize asap

DVT vs PE

- Statistical differences in DVT rate- selected Rx
- No statistical difference in PE rate-selected Rx

- Why: Studies w DVT as endpoint underpowerd to demonstrated PE as endpoint

Relevant issue

- Selection of appropriate PE prophylaxis in THA/TKA …….balance
  - Bleeding risk vs symptomatic PE
  - Regime decrease DVT does not imply risk benefit ratio has been optimized

PE

- 60 d PE mortality 67,584 THA – 0.37%
  - Need 30,000 pt study to demonstrate a 50% reduction between 2 competing agents—cost prohibitive
  - May be other risk factors that control PE rather that sheer evidence of DVT

In any case…..

- presumed direct pathophysiologic link between DVT and PE
  - has not been proven by clinical observation,

...at least in the case of total hip and knee replacement.

PE THA/TKA …..Rare

- 90 d non-fatal PE THA-medicare pt's
  - With/without dvt prophylaxis-0.93% (58,521)
- 90 d fatal-PE---even lower
  - (0.22%) 44,578
- Fatal & Non-fatal PE TKA—EVEN LESS
  - 0.41% non fatal (>222,000)
  - 0.15% fatal (>27,000)

AAOS –additional recommendations

- Routine post-op DVT screening-not cost effective
- Increase mobility at home
- Educate pt common DVT & PE symtoms

PE rate remarkably stable 10-15yrs

- Despite significant changes in DVT prophylaxis and surgical techniques

Major Bleeding: THA/TKA

- Deleterious
- Chronic stiffness
- Infection
- 1-3% all TJA
- Common cause –return OR

Early Return to Surgery for Evacuation of a Postoperative Hematoma After Primary Total Knee Arthroplasty (Nov 2008 JBJS-Mayo)

- **Conclusions: RT OR <30 d**
- **13% 5 yr risk infection or revision vs 0.15% fatal PE**
- **These results support all efforts to minimize the risk of postoperative hematoma formation.**

Underestimate of bleeding

- Literature non-standardize in defining, identifiying & confirming Major Bleeding episodes

Legitimate question??

- Are the resources available to prevent serious throboembolic complications after THA/TKA being appropriately and cost effectively utilized??????

…..considering a 10-100X inc risk bleeding complication

Optimal prophylactic regime

- Balance of clinical judgment on the risks of both major bleeding vs symptomatic PE

Evidenced based risk stratification

- Difficult: all Orthopaedic pt's high risk DVT
- ..for PE & Bleeding require far more pt's studied rigorously, longer period than exists in literature now
- Randomized studies exclude 'high risk' pt's which need to be included
- Studies conducted in 'real world' setting – more robust data
- Joint registries—helpful link risk factors surgical outcomes

Grading the Recommendations-AAOS

- A: Good evidence (Level I Studies with consistent finding) for recommending intervention.
- B: Fair evidence (Level II or III Studies with consistent findings) for recommending
- intervention.
- C: Poor quality evidence (Level IV or V) for recommending intervention.

Guideline Recommendations

- **Recommendation 1. Pre-operative Care**
- **1.1** All patients should be assessed pre-operatively for elevated risk (greater than standard
- risk) of pulmonary embolism. The following patients are examples of those considered to
- be at elevated risk:
- • Hypercoagulable states
- • Previous documented pulmonary embolism
- **Level of Evidence: III**
- **Grade of Recommendation: B**
- **Note: This Grade of Recommendation was reduced from B to C because of the lack**
- **of consistent evidence in the literature on risk stratification of patient populations.**
- **C**

- **1.2** All patients should be assessed pre-operatively for elevated risk (greater than standard
- risk) of major bleeding. Patients with the following conditions are examples of those
- considered to be at elevated risk:
- • History of a bleeding disorder
- • History of recent gastrointestinal bleed
- • History of recent hemorrhagic stroke
- **Level of Evidence: III**
- **Grade of Recommendation: C**

- **1.3** Patients with known contraindications to anticoagulation should be considered for vena
- cava filter placement.
- **Level of Evidence: V**
- **Grade of Recommendation:**

Expert Opinion: Omega-3 Fatty Acids and Bleeding—Cause for Concern?

William S. Harris, PhD

Omega-3 fatty acid ethyl esters have well-known triglyceride-lowering properties and were shown >30 years ago to inhibit platelet function. With the recent US Food and Drug Administration (FDA) approval of these agents for treating severe triglyceride elevations, concerns about excess bleeding naturally arise. However, an objective assessment of the evidence for clinically significant bleeding reveals that such concerns are unfounded. As such, the benefits of triglyceride lowering with omega-3 fatty acids more than outweigh any theoretical risks for increased bleeding. (Am J Cardiol 2007;99[suppl]:44C–46C)

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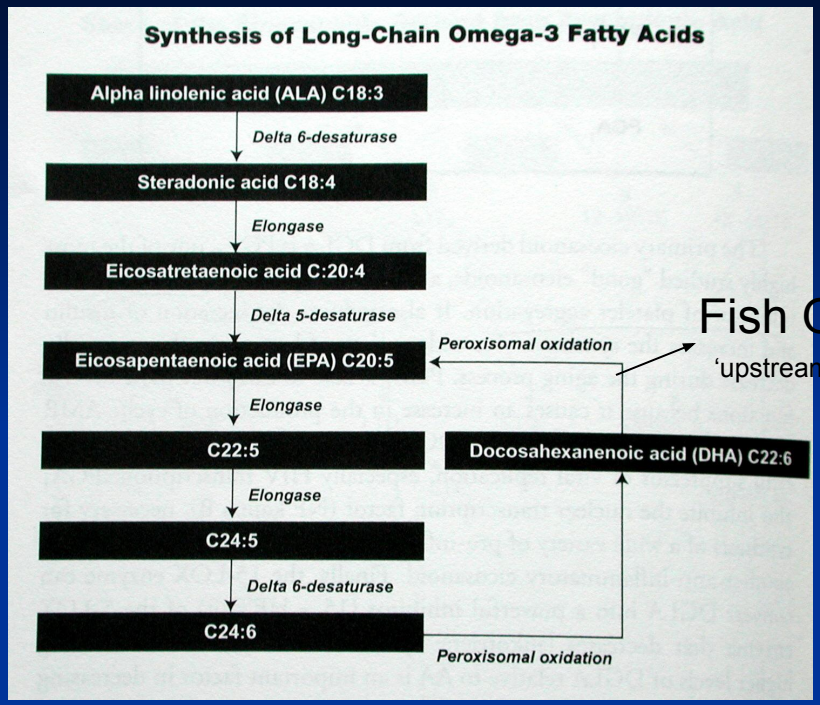
Phospholipids

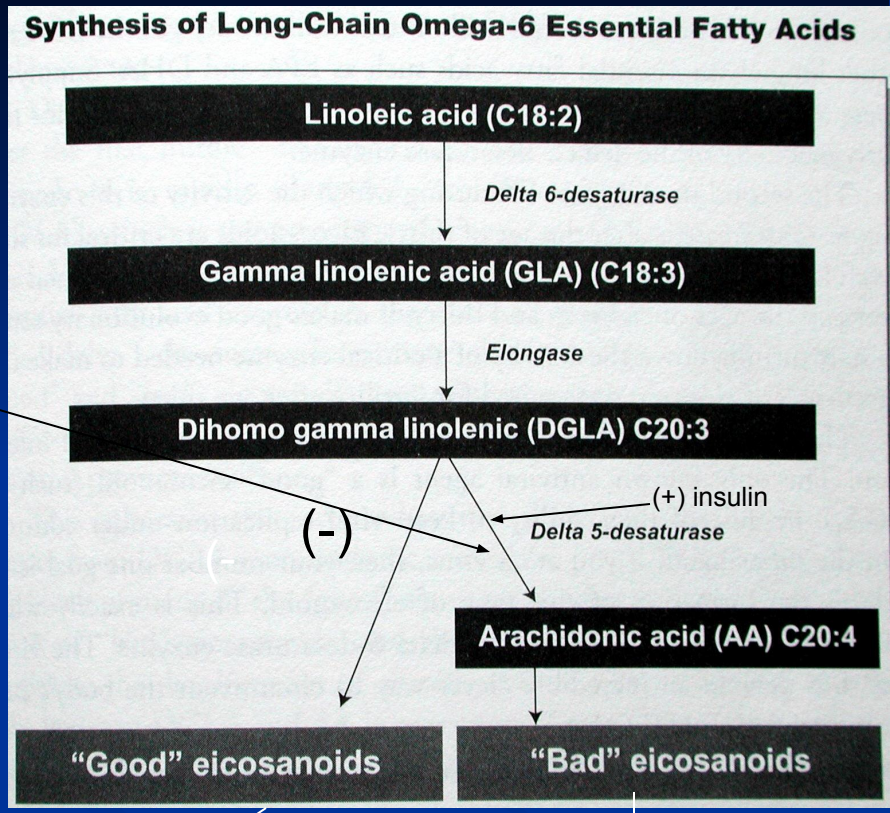
Steroids - Phospholipase A2

20

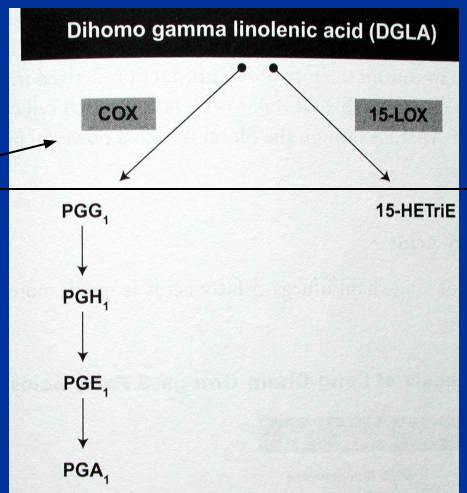


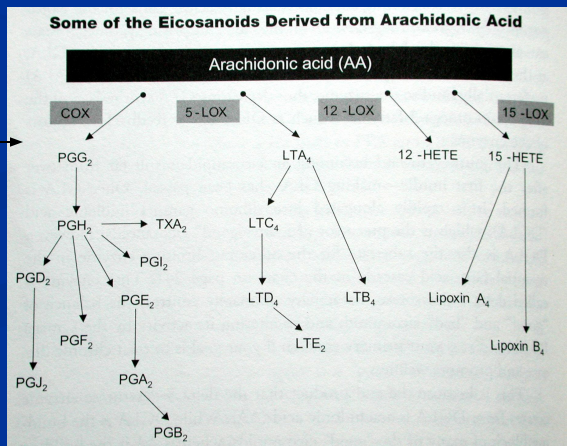
Fish Oil

'upstream'



NSAID's/COX Inhib





The Joint Commission

Sentinel Event Alert- (9/08)

- Anticoagulants: a top 5 drug asso w/ pt safety issues in US
- 7% of all medication errors
- 3% caused harm/death
- Heparin (2/3), Warfarin, Enoxaparin
- Wrong drug; wrong dose; Improper monitor; pump error, no order

AAOS –Study 2008

- 93,840 TKA patients @ 300 hospitals (2003-05)
- Compared ASA vs guideline approved therapies
- ASA: fewer risk factors for blood clots before surgery and lower odds for blood clots than those on warfarin
- Risk of blood clot in ASA was similar to those on injectables to prevent clots
- No difference in bleeding risk or mortality
- Surgical techniques have changed, pt's are likely to be younger & healthier today than when guidelines were developed
- More research needed

Future Research

- Powered studies to detect superior PE protection: costly
- DVT more attractive proxy to study
- HOWEVER: relationship- not linear.
  - ($\downarrow$ DVT $\neq \downarrow$ PE)
- Need: research better describes this relationship
- Better PE risk stratification
- Post op bleeding: more uniform and standardized reporting

AAOS -Conclusions

- Major limitations in evidence
- Lg clinical heterogeneity; other procedures/interventions; doses, study populations, f/u times;
- Major bleeding: definition?
- No study designed to study PE as primary outcome
- PE related events: incomplete/vague

Personal Philosophy

- ASA is effective in majority of pt's
- Not militant!!!
- Quick to resort to my second favorite: Warfarin

- Bleeding event: profound effect on QOL

ACCP

- Misguided in ortho recommendations
- Bias toward DVT reduction at expense higher wound complications
- INR recommendation 2-3:
  - Few ortho surg do this: too hi risk bleed
  - Higher in obese

AAOS-Guidelines

- Accept a higher risk asymtomatic DVT
  - Post thrombotic syndrome rare
- Favors lower risk wound complications given the equivalency of PE across a variety of anticoagulants

U of P Study

- 3500 primary TKA's
- ASA without IPC
  - Fatal PE **0.06%**
  - Non-fatal PE 0.26%
  - Symtomatic DVT 0.2%

ASA

- Slightly less effective in preventing DVT
- **Similar fatal PE rate**
- Lower Bleeding Risk
- Easy, effective, inexpensive
- Pt's prefer it
- No monitoring
- Attractive risk profile
- AAOS supports it…. As do the data

At the end of the day…

- Decide to reduce DVT risk at expense of bleeding complications

- Or accept higher DVT-
  - reduce equivalently the incidence of PE (fatal & non-fatal)…
  - reduced tendency wound complications

Our Standard regime

- ASA 325 mg po bid X6 weeks
- IPC in hospital/rehab
- Early mobilization
- Regional anesthesia
- Short surgical times
  - Less tissue trauma, no IM violation
- Essential Fatty Acids (Omega-3)
- Lo threshold to resort to Warfarin

That's my story

& I'm stickin to it!!!!

Thank You!!!!!

Why are Orthopaedists interested in Obesity???