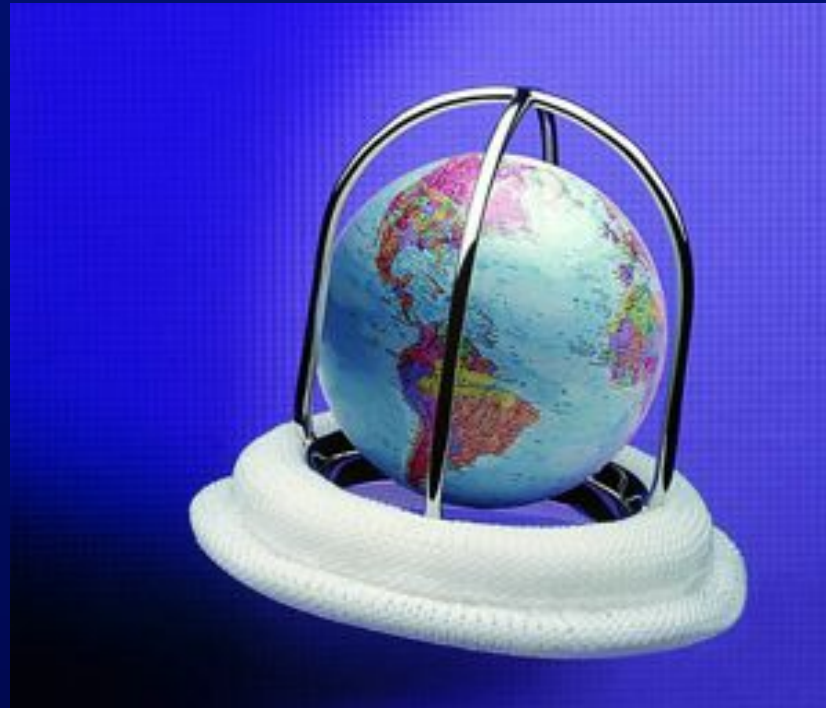


# LWMH is the Anticoagulant of Choice in Pregnant Women with Mechanical Heart Valves



**For Cardiac Problems in Pregnancy  
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- My abstract is published in the program book.

# The Problem with Mechanical Heart Valves

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- High risk of valve thrombosis
- Risk of embolization with stroke
- Require life-long anticoagulation with warfarin

mitral – INR 2.5 - 3.5

aortic – INR 2.0 - 3.0

# Physiological Changes in Pregnancy

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- 50% increase in cardiac output → increased risk of cardiac decompensation
- Hypercoagulability with 4 to 5-fold → increased risk of thrombosis



# The Problem with Mechanical Heart Valves in Pregnancy

1, Vural et al, 2003

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- High risk of valve thrombosis (up to 50% in those not anticoagulated<sup>1</sup>)

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- Valve thrombosis can result in subsequent stroke

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# The Problem with Mechanical Heart Valves in Pregnancy

- High risk of valve thrombosis (up to 50% in those not anticoagulated<sup>1</sup>)
- Valve thrombosis results in subsequent stroke
- Pregnancy presents bleeding challenges:
  - miscarriage
  - childbirththat are compounded by anticoagulation

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# The Problem with Mechanical Heart Valves in Pregnancy

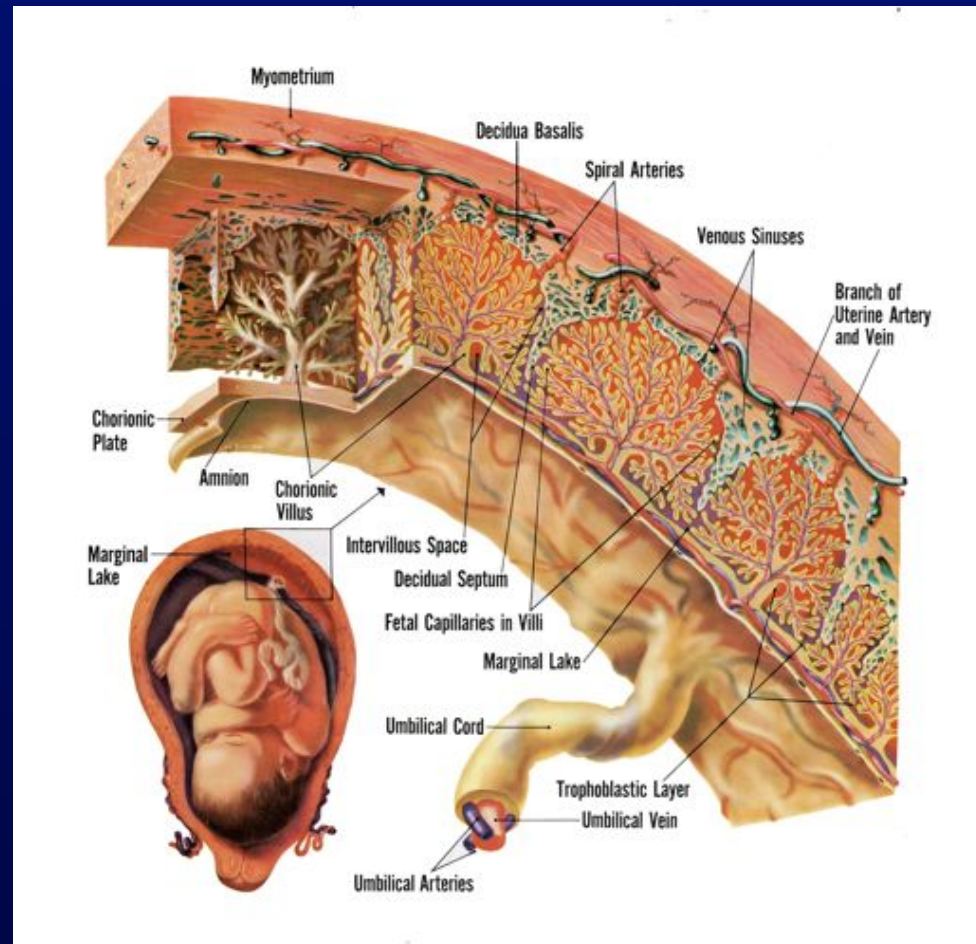
- High risk of valve thrombosis (up to 50% in those not anticoagulated<sup>1</sup>)
- Valve thrombosis results in subsequent stroke
- Pregnancy presents bleeding challenges:
  - miscarriage
  - childbirth
  - that are compounded by anticoagulation
- Warfarin crosses the placenta

1, Vural et al, 2003



# Heparins

- Parenteral administration
- 1-2% risk of major bleeding<sup>1,2</sup>
- Do not cross the placenta



1. Ginsberg et al 1989; 2. Sanson et al 1999

# Low-Molecular-Weight Heparins (LMWH)

Advantages of LMWH compared to UFH:

- Duration of action
- Convenience of use
- Reduced risk of bleeding
- Reduced risk of HIT – no confirmed cases in 2 large reviews of LMWH<sup>2,3</sup>
- Osteoporosis – earlier concerns of osteoporosis not confirmed in recent studies<sup>4,5,6</sup>



1. Ginsberg et al 1989; 2. Sanson et al 1999 3. Leperq et al 2001 4. Casele et al , 2006; 5. Carlin et al, 2004; 6. Rodger et al, 2007

# Maternal Risks

	Bleeding	Thrombosis	Mortality
Heparin <sup>1</sup>	2.5%	33%	15%

1. Chan et al *Arch Intern Med* 2000
2. James et al *J Matern Fetal Neonatal Med* 2006
3. McLintock et al *BJOG* 2009

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Warfarin <sup>1</sup>	2.5%	4%	2%

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# Fetal Risks

	Miscarriage	Birth Defects	Fetal ICH	Neuro abnormality	Low IQ
Warfarin <sup>1</sup>	15-56%	0-30%	2%	14%	4%

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# Severe Facial Cleft



# Fetal Risks

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Warfarin <sup>1</sup>	15-56%	0-30%	2%	14%	4%
Heparin <sup>2</sup>	15%	0%	-	-	-
LMWH <sup>1</sup>	11%	0%	-	-	-

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2. Chan.et al *Arch Intern Med* 2000

## Legal Risks

“If you were taking coumadin at the time you became pregnant, or if your doctor prescribed coumadin during your pregnancy and your baby was subsequently born with birth defects, you are urged to talk to an attorney promptly. Medical malpractice lawyers of Morgenstern & Herd, P.A., handle birth injury cases involving birth defects apparently caused by coumadin.”



## In Conclusion

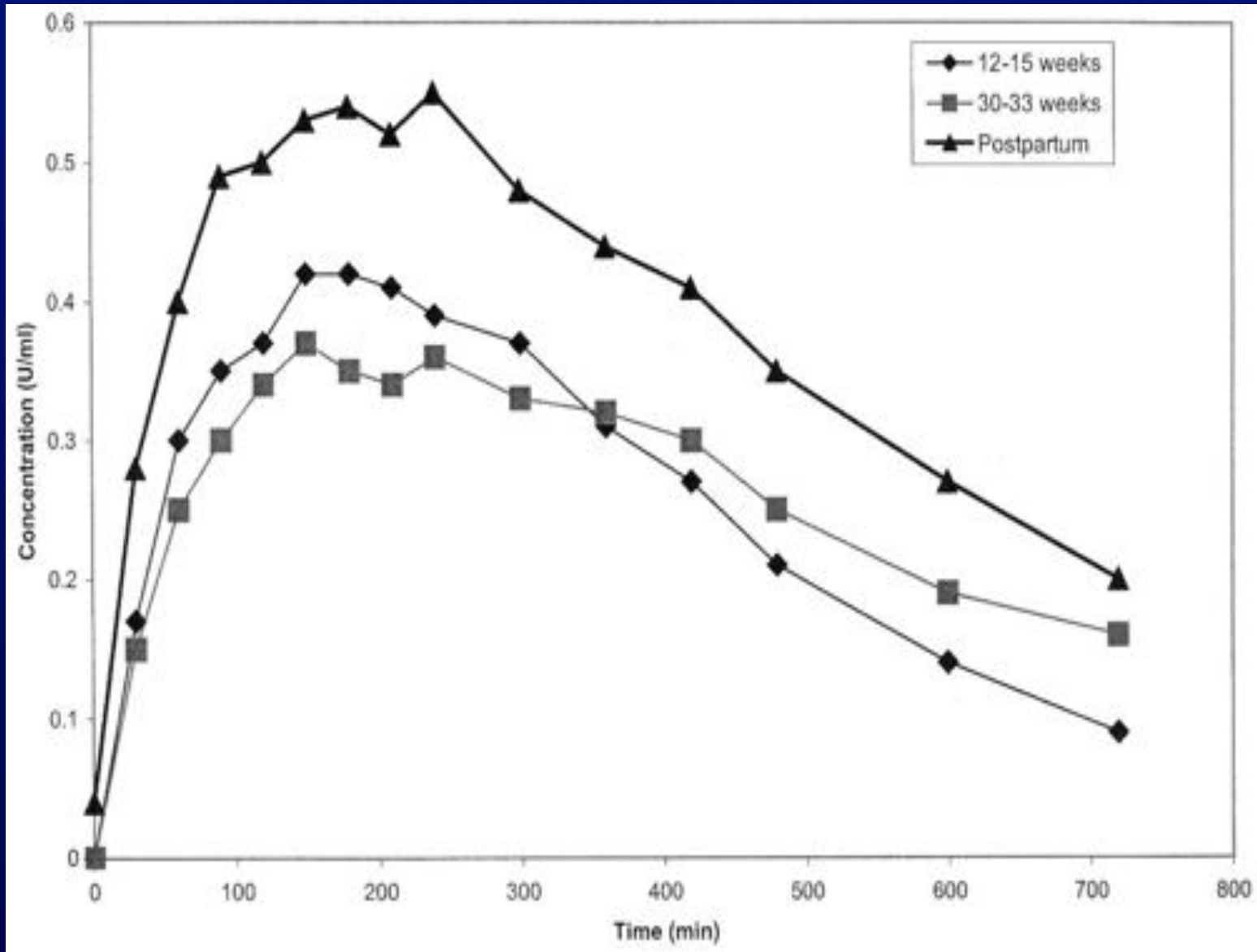
- These are extremely high risk pregnancies with potentially adverse outcomes.
- Counseling regarding the risks of continuation of pregnancy is essential.
- No single anticoagulation option ensures against adverse outcomes.
- When counseled about fetal risks, many women refuse warfarin.

## In Conclusion

- Even women maintained on warfarin are not maintained on warfarin for the duration of pregnancy.
- Therefore, low-molecular-weight heparin, which has fetal outcomes closer to those of the general population, may be the best alternative in this difficult situation.



# Enoxaparin concentration



Casele et al, Am J Obstet Gynecol, 1999

# European Guidelines on the Management of Valvular Heart Disease<sup>1</sup>: Classes and Levels of Evidence

- Class I – consensus that treatment is beneficial
- Class II – conflicting evidence that treatment is beneficial
  - IIa – weight of evidence is favorable
  - IIb – efficacy less well-established
- Levels of evidence, same as ACC/AHA

1. Published January 26, 2007 by the European Society of Cardiology (ECS)

# ECS Recommendations Regarding Anticoagulant Management

- Warfarin is the favored anticoagulant therapy during the second and third trimester until the 36<sup>th</sup> week of gestation.(IC)  
(Data are lacking about other vitamin K antagonists.)
- Warfarin is favored during the first trimester if dose is  $\leq 5$  mg/24h, after patient information.  
(IIaC)

# ACC/AHA Guidelines for the Management of Valvular Heart Disease<sup>1</sup>: Levels of Evidence

- A - multiple randomized trials
- B - one randomized trial or other non-randomized studies
- C - case studies or expert opinion

1. Published August 1, 2006

# ACC/AHA Guidelines: Definite Recommendations

- Continuous anticoagulation (B)
- Preconceptional counseling (C)
- Close monitoring for pregnancy (C)
- If warfarin is stopped weeks 6-12, then initiation of:
  - dose adjusted IV heparin (C)
  - dose-adjusted SC heparin, or (C)
  - dose-adjusted SC LMWH (C)

## If Warfarin is Used

- Maintenance of INR between 2.5 and 3.5 (C)
- Conversion to IV heparin 2-3 weeks before planned delivery (C)

## If Dose-Adjusted Heparin is Used

- Counseling regarding increased risks of thrombosis, embolization, osteoporosis, HIT and infection (with continuous intravenous heparin) (C)
- Maintenance of PTT at twice control (C)

## If LMWH is Used

- Twice daily injections to maintain anti-factor Xa level between 0.7 and 1.2 four hours after administration (C)

# ACC/AHA Guidelines: Reasonable Recommendations

- For fetal reasons, avoid warfarin 6-12 weeks gestation (C)
- Add low-dose aspirin (75 to 100 mg per day) in the second and third trimesters (C)
- Resume heparin 4-6 hrs postpartum and resume warfarin if no significant bleeding (C)

# ACC/AHA Guidelines: Recommendations **Against:**

- Administration of LMWH without monitoring anti-factor Xa levels (C)
- Substitution of dipyridamole for low-dose aspirin (B)

# ACCP Guidelines

The grading scheme classifies recommendations as:

- strong (grade 1) or
- weak (grade 2)

according to the balance among benefits, risks, burdens, and possibly, cost.

The system classifies quality of evidence as:

- high (grade A)
- moderate (grade B), or
- low (grade C)

according to factors that include the study, design, and the consistency of the results.

# ACCP Guidelines

- Adjusted-dose bid LMWH or UFH throughout pregnancy (Grade 1C) *or*
- Adjusted-dose bid LMWH or UFH until the 13<sup>th</sup> week with substitution by vitamin K antagonists until LMWH or UFH are resumed are resumed close to delivery (Grade 1C)
- The latter is preferred for women with older-type valves in the mitral position (Grade 2C)