Women with mechanical heart valves: management in pregnancy

SIMPSON'S CENTRE FOR REPRODUCTIVE HEALTH;

DEPT OF HAEMATOLOGY, ROYAL INFIRMARY, EDINBURGH

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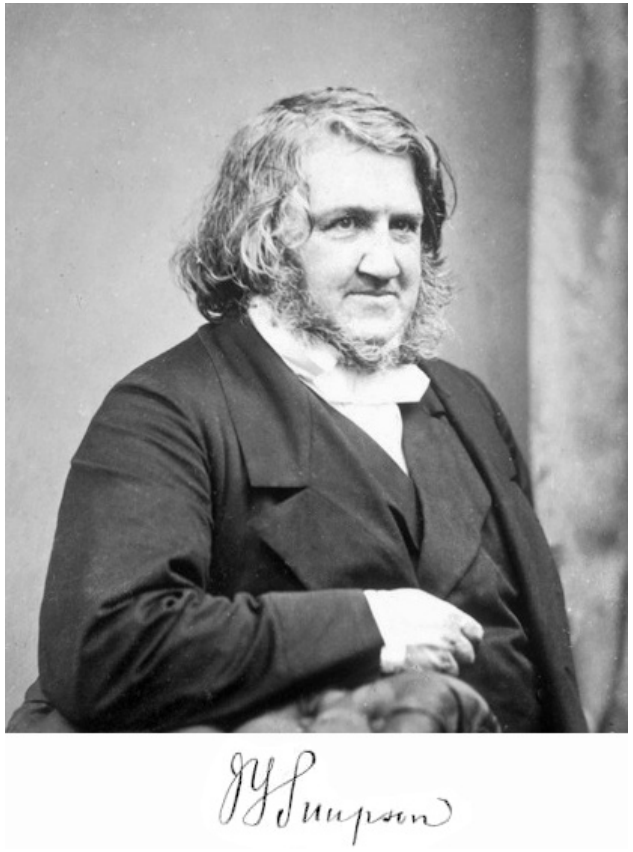
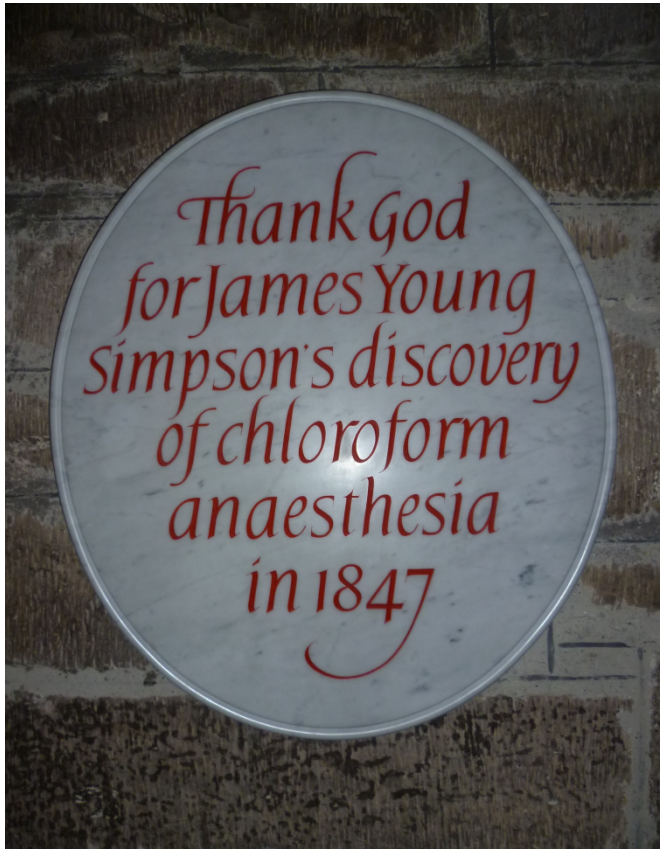
No Disclosures


J Y Simpson


YOUNG SIMPSON
BARONET
K.C.B. D.C.L.
DIED 1870


Thank God
for James Young
Simpson's discovery
of chloroform
anaesthesia
in 1847

Original Simpson's Hospital

Our team

Obstetric anaesthetists

Obstetricians

Haematologists with an interest in haemostasis & thrombosis

Paediatric haematologist

Administrative & clerical support

Thrombosis nurse

Midwife

Specialists of the future Trainees

Coagulation laboratory

Aims of this talk

-Understanding of the handling of different anticoagulants in pregnancy and the puerperium

-Understanding of the reversibility of different anticoagulants

-Close work within a multidisciplinary team

-Paucity of evidence on which to base best practice

-Only a few options, lots of guidelines!-

Lots of guidelines

Major Society Guidelines

2014 American Heart Association/ American College of Cardiology (AHA/ACC) valvular heart disease guidelines

Nichimura RA et al. J Am Coll Cardiol 2014 63 e57

2012 American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy

Bates SM et al. Chest 2012 141 e6915

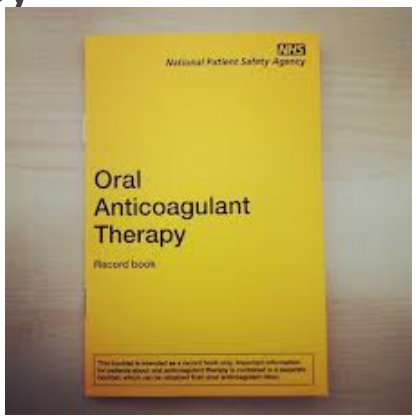
2011 European Society of Cardiology (ESC) Guidelines

Vahanian A et al. Eur Ht J 2012 33 2451

Pre-conception: evaluation & counselling

Mechanical heart valves –

- Increased incidence of thrombo-embolic complications during pregnancy
- Therapeutic anticoagulation required throughout pregnancy
- Various anticoagulant options



- Patients will be on warfarin (or VKA) pre-conceptually
  - How compliant?
  - What is target INR?
  - What is TTR (time within therapeutic range)?
  - How does INR get checked? Warfarin clinic/GP/pharmacy-led clinic? POCT vs venous INR

- Paucity of evidence to guide us about the optimum anticoagulant regimen

Bioprosthetic valves – do not require anticoagulation (some exceptions)

Balance of risks

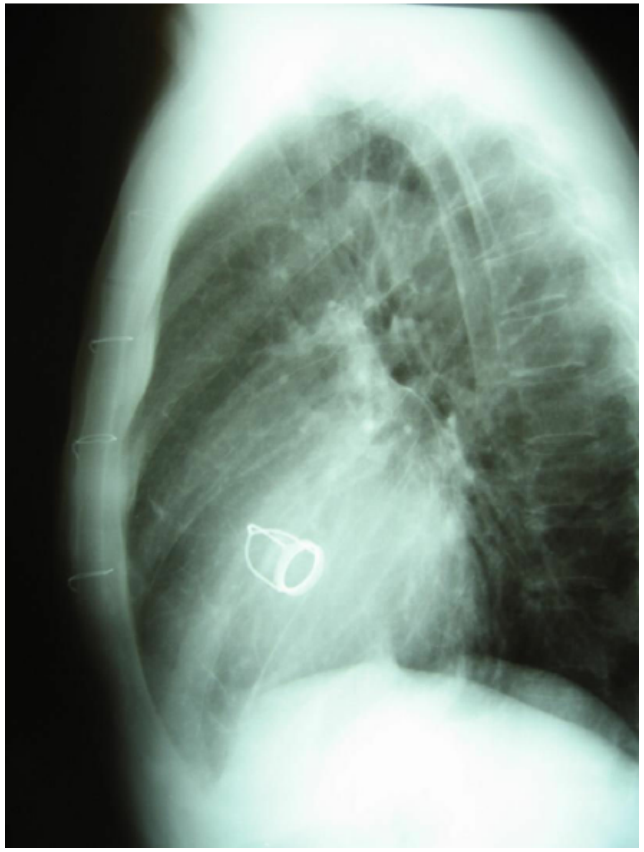
The risk of developing thrombo-embolic complications should be **balanced** against the risk of maternal and foetal complications of anticoagulation

These risks change in the different trimesters

Risk of development of thromboembolic complications

Risk is based on:

- Number – multiple valves
- Type – old style valve
- Site- mitral
- Previous thromboembolic complications
- Atrial fibrillation or atrial flutter



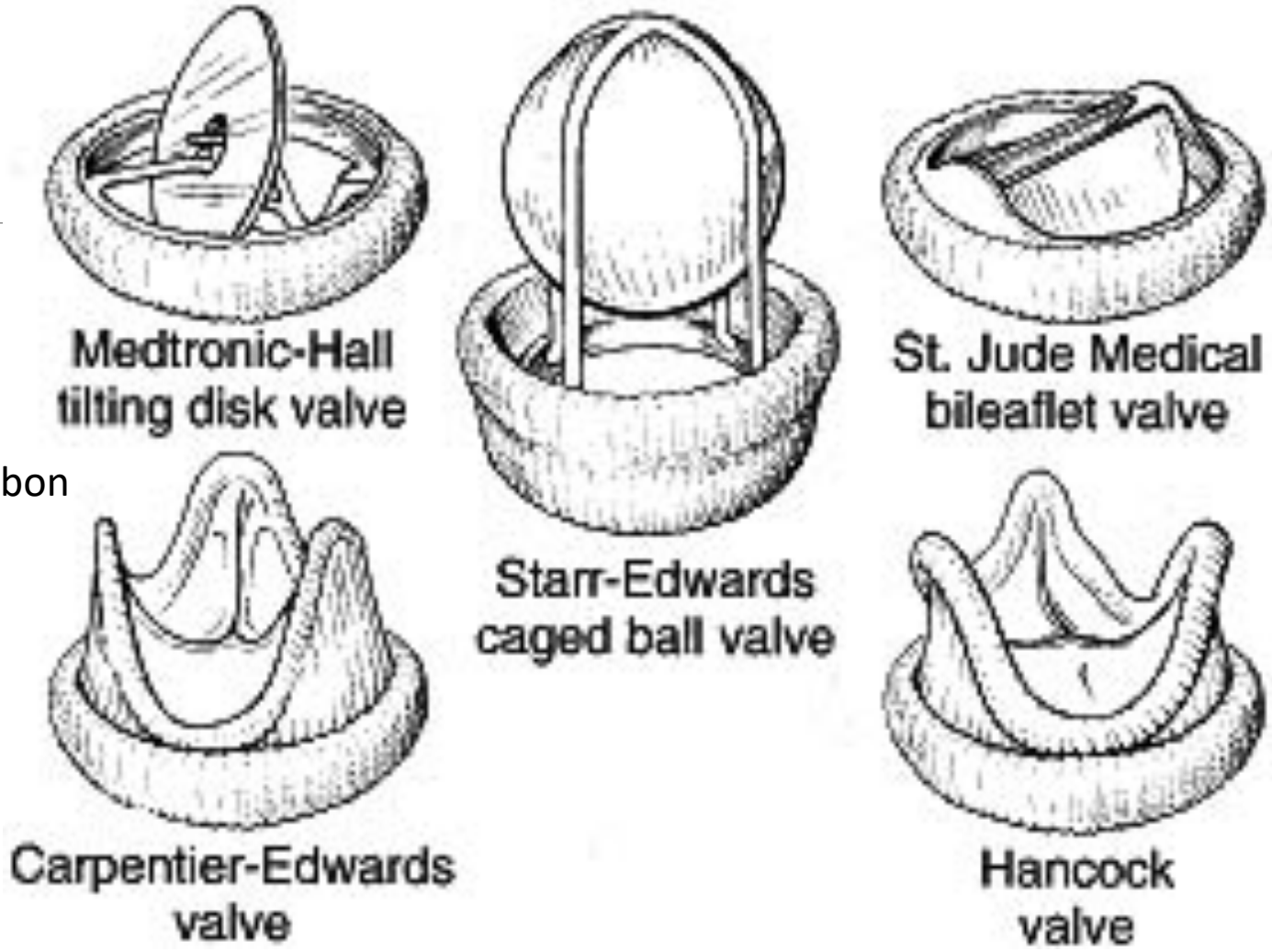
Pre-operative CXR with Starr-Edwards caged ball valve

Mechanical prosthetic heart valves

Ball and Cage: Starr-Edwards

Single Disc: Medtronic-Hall, Bjork-Shiley

Bileaflet: St Jude Medical, Carbo Medics, Sorin bicarbon



Development of the original ball and cage valve design attributed to the bottle stopper in 1858;
In the early 1950's it led to the idea of a prosthetic heart valve consisting of a cage with a mobile spherical poppet

Handling of anticoagulants in pregnancy

Anticoagulant	First trimester	Second trimester	Third trimester	Breast-feeding	Comments
Warfarin	Avoid weeks 5-12; risk of embryopathy	Can be given	Consider switch from 36 weeks	safe	Reversible with vit K and PCCs
Low molecular-weight heparin (LMWH)	safe	safe	safe	safe	Partially reversible with protamine
Unfractionated heparin (UFH)	safe	safe	safe	safe	s/e: osteoporosis, HIT(T); reversible
Fondaparinux	safe	safe	safe	safe	Not much experience in general; would not be appropriate for use in mechanical valves outwith or in pregnancy
Direct oral anticoagulants (DOACs) (oral)	uncertain risk: avoid	avoid	avoid	Uncertain - avoid	Risk unclear; would not be appropriate for use in mechanical valves outwith or in pregnancy

warfarin

Warfarin freely crosses the placental barrier and can adversely affect foetal development

Associated with a high incidence of spontaneous abortion, prematurity, still birth, and foetal bleeding

Can cause neonatal intracranial haemorrhage or a retroplacental haematoma

Considered safe in breast feeding

Warfarin: emergency reversal

1. Stop warfarin

2. Intravenous vitamin K 5mg

3. Prothrombin complex concentrate e.g. Beriplex, Octaplex

Dose-dependent fetal complications of warfarin in pregnant women with mechanical heart valves
Nicola Vitale, Marisa De Feo, Luca Salvatore De Santo, Alessio Pollice, Nicola Tedesco and Maurizio Cotrufo
J Am Coll Cardiol Vol 33 Issue 6 May 1999

warfarin

Outcome of Pregnancies

Warfarin Dose (mg)	Healthy Fetuses	Fetal Complications			Total
≤5	28		5		33
	27 FT	4 SA	1 PR	1 GR	
>5	3 FT		22		25
		2 WE	18 SA	1 SB	1 VSD
Total	31		27		58

legend FT = full term; GR = growth retardation; PR = premature; SA = spontaneous abortion; SB = stillbirth; VSD = ventricular septal defect; WE = warfarin embryopathy.

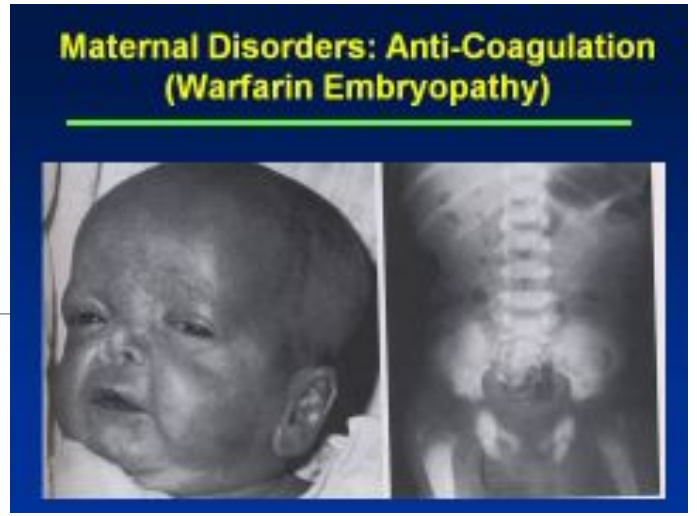
Warfarin-induced embryopathy

Also known as “foetal warfarin syndrome”; “Di Saia syndrome”

Warfarin prevents the normal formation of the vitamin K-dependent matrix gla-protein in the embryo

Howe A M Teratology Vol 46 (4) 1992 379-390
Hou JW Chang Gung Med J Vol 27 (9) 2004

Warfarin-induced embryopathy



Facial dysmorphism – reduced growth of embryonic nasal septum

Hypoplasia of nasal ridge

Laryngomalacia

Pectus carinatum

Congenital heart defects (ASD, PDA)

ventriculomegaly

Stippled epiphyses

Telebrachydactyly

Growth retardation

Agenesis of corpus callosum

Optic atrophy

Low birth weight

Seizures

Reduced muscle tone

Intellectual disability

Deafness

Feeding difficulty

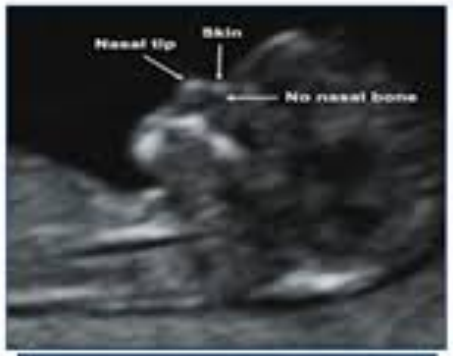


Fig. 1: ANTENATAL USG – REVEALING ABSENT NASAL BONE

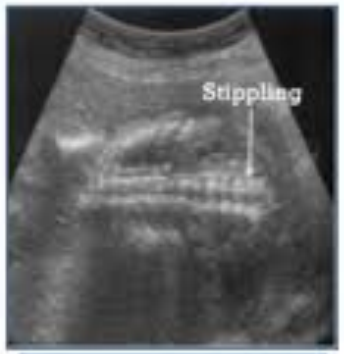
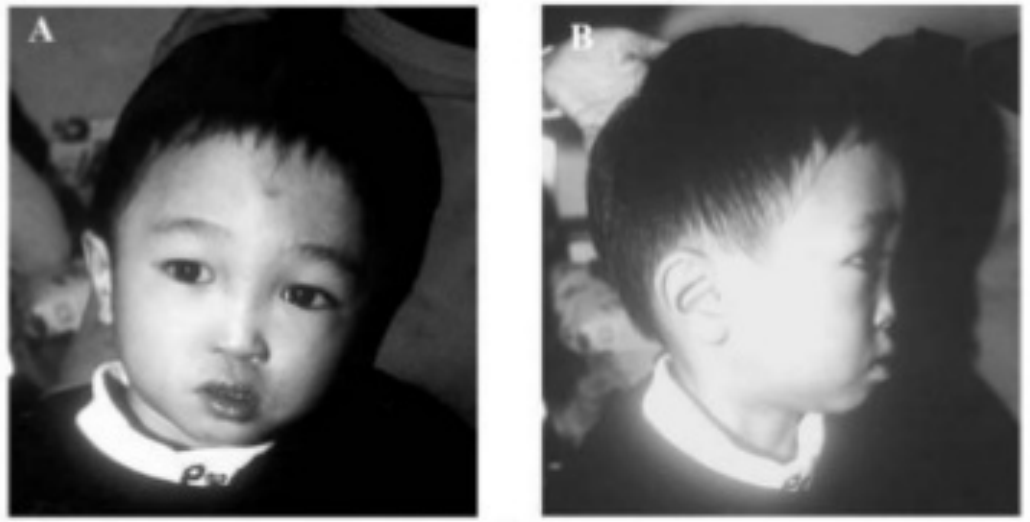


Fig. 2: ANTENATAL USG – REVEALINGSTIPPLING OF THE FETAL VERTEBRAE

Warfarin Embryopathy Syndrome

- Fetal bone and cartilage formation abnormalities
- Facial abnormalities, optic atrophy, digital abnormalities, epithelial changes, and mental impairment.
- Incidence: 4% to 10%
- The risk is highest when warfarin is administered during the 6th - 12th week of gestation.
- The risks are dose-dependent, a dose of < 5 mg daily have the lowest risks (3%).



Figs. 1 (A) The patient at age 3 years. (B) Hypoplasia of the midface and nose.[19]

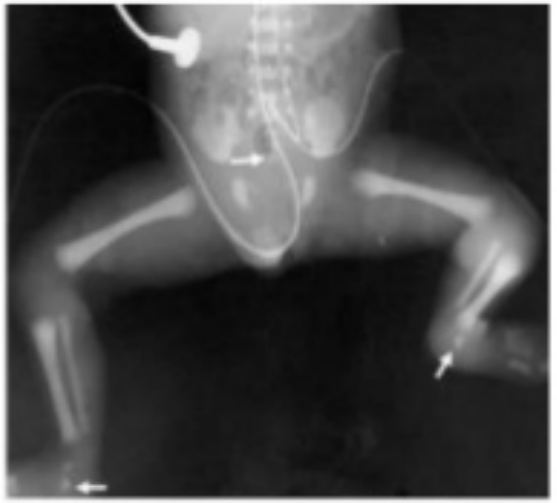


Fig. 2 X-ray at 1 day of age shows stippling in the sacral area and tarsal bones (arrow).

DOACs

Direct oral anticoagulants (or new oral anticoagulants) include :

DABIGATRAN – direct thrombin inhibitor

APIXABAN, RIVAROXABAN, EDOXABAN, BATRIXABAN – direct factor Xa inhibitor

Should NOT be considered as alternatives for use in mechanical heart valves during or outwith pregnancy

Safety data in pregnant and breast-feeding women are lacking

How to manage:
Options: first trimester

Mechanical heart valve, no associated risk factors

Warfarin maintenance dose <5mg daily

1. Continue warfarin with close INR monitoring during the first trimester

OR

1. Dose-adjusted SC LMWH from weeks 5-12 ; twice daily dosing advised

Options: first trimester

If warfarin maintenance dose is >5mg daily

Switch to SC LMWH throughout the first trimester

Target peak LMWH-anti-Xa level: 1.0-1.2 iu/ml for mitral valve; 0.8-1.0iu/ml for aortic valve

Suggested checking of trough levels aiming for a minimum level of 0.6iu/ml (safety and efficacy of this approach uncertain)

Second trimester, and up to 36 weeks

Least maternal risk:

VKA, adjusted to target INR, + aspirin 75-100mg/d until 36 weeks

(timing of anticoagulant switch may depend on risk of pre-term delivery)

OR,

Least foetal risk:

Therapeutic LMWH SC twice daily, with monitoring of trough and peak levels, + aspirin 75-100mg/d

In countries where LMWH is unavailable/low resource settings, VKA is preferred anticoagulant. Dose-adjusted SC UFH is a “last resort” option when LMWH is unavailable; regular monitoring to ensure 6 hour post dose APTT is at least twice baseline

Peripartum management

Planned delivery best

Multidisciplinary approach

Preference for vaginal delivery; reserve Caesarian section for obstetric indications

If on warfarin, switch to LMWH at 36 weeks

Low-dose aspirin continued up until delivery – must discuss with anaesthetist

Last dose of LMWH: 24 hours before induction if renal function normal

Planned Labour - options

1. 12 hours after cessation of LMWH, commence iv heparin at 1000-1200 units/hour, no loading dose and infusion rate adjusted to aim for APTT ratio of 2.0 -3.0 (or 1.5-2.5 dependent on lab range)

- iv heparin should be stopped when in second stage of labour

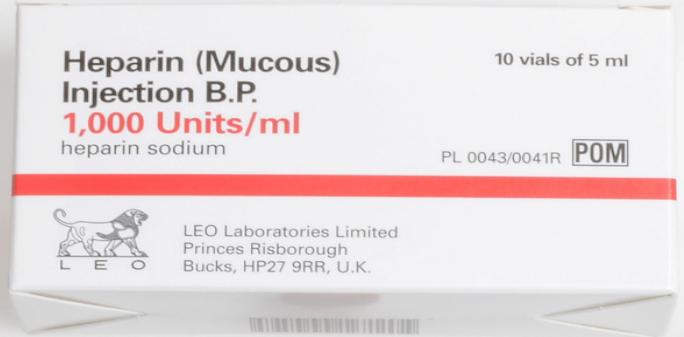
-iv heparin should be stopped 4-6 hours prior to neuraxial anaesthesia/analgesia, and catheter can be sited if APTT has returned to normal

2. use of intermittent prophylactic doses of LMWH e.g. Enoxaparin 40mg SC OD, Dalteparin 5000 units SC OD

- 12-hour rule for siting of neuraxial anaesthesia/analgesia

3. induction of labour 24 hours after last dose of LMWH, and then an early epidural catheter can be sited; 6-8 hours after non-traumatic siting a prophylactic dose of LMWH can be given if not yet in active labour and repeated every 24 hours until cervix dilated to >6cm

Which vial of heparin would you choose to make up a heparin infusion?



Safe prescribing
Use of heparin infusion nomogram

NHS Lothian
Adult Heparin Infusion Chart
(for standard bleeding risk)

Consultant		Name of Patient	
Hospital / Ward		CHI Number	
Weight (kg)		DOB	

Medicine (Approved Name)	Final Concentration	Total Dose	Volume	Route	Prescribed / Transcribed By Sign & print name
Heparin	1000 units/ml	40,000 units	40 mls	IV	

*Please note that in NHS Lothian heparin sodium solution for infusion is available in a ready concentration of 1000units/ml so further dilution is not required. If in doubt, contact pharmacy for advice.

Initiation of therapy

- Check baseline FBC, INR, APTT, urea, creatinine
- Prescribe loading dose and infusion on the patient Main Prescription Chart.
- Loading dose: 5000 units iv bolus. For patients with a high risk of bleeding eg. elderly >70yrs, creatinine clearance <30ml/min or low body mass index, a loading dose may not be required.
- Immediately start continuous infusion of heparin (1000 units/ml) set at initial rate of 1,200 units (1.2 ml)/hr. If actual body weight over 120kg seek advice from haematologist.
- For patients with a high risk of bleeding, a lower starting rate may be required, such as 1,000 units (1.0ml)/hr.

Infusion Rate Instructions

	Date	Time	Rate ml/hr	Prescribed by	Adjusted by	APTT ratio	Reason for Change/Comment
Initial Rate							
Change 1							
Change 2							
Change 3							

Emergency delivery

Differing opinions regarding when and how aggressively to reverse the anticoagulation

If on LMWH: protamine can be considered, but only gives partial reversal

- baby not at risk of bleeding

If on warfarin: “give vitamin K 2mg (oral/iv) to give partial correction of INR (note will not reverse fetal INR): and stop warfarin, and give 4-factor PCC to a target INR of 2.0” (!)

- baby will be at risk of bleeding

- must receive vitamin K at birth

Emergency delivery

For all above situations, a 24-hour rule applies for the siting of neuraxial anaesthesia/analgesia

Post-delivery neuraxial catheters may be removed no earlier than 10-12 hours after the last dose of prophylactic LMWH and before anticoagulant therapy is resumed

Postpartum

-timing of restarting anticoagulation depends on haemostasis

- one option is to restart iv heparin at usual dose, no loading dose and increase **gently** to therapeutic dose over 24-48-72 hours

- or restart prophylactic LMWH and then an intermediate dose of LMWH twice daily, incrementing to usual dose after 48-72 hours

- warfarin should not be introduced for 5-7 days

- *patient should be aware that she will be an in-patient for over a week post-delivery*

- increased risk of wound haematoma, postpartum haemorrhage

- this can be most tricky to manage!

Acknowledgements

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