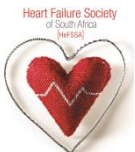


HeFSSA Practitioners Program 2015

Theme - Women and Heart Failure

08:00 - 08:20	Registration & Breakfast
08:20 - 08:25	Welcome and Thank You to Sponsors
08:25 - 08:30	HeFSSA smartphone patient app (video)
08:30 - 09:15	Implantable devices, women and heart failure
09:15 - 10:00	Peri-partum cardiomyopathy
10:00 - 10:30	Tea Break
10:30 - 11:15	Hypertension in pregnancy
11:15 - 11:45	Elderly women with Heart Failure
11:45 - 12:00	Questionnaire
12:00	Departure



CASE STUDY:

Hypertension in pregnancy

Overview

- Physiological changes in haemodynamics and cardiac function in pregnancy
- Hypertension
- Management and treatment

Normal physiological changes in pregnancy

- Increase in HR, SV, CO, decrease in SVR
- Increase in LVEDD, LV mass. “Contractility” unchanged or slightly increased
- Plasma volume increases up to 45% and plateaus at about 34 weeks
- Predominantly 2D echo / M-mode studiesKatz et al Circulation 1978. 19 women.

Robson et al AJP 1989.

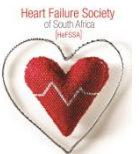
13 women

Poppas et al Circulation 1997.

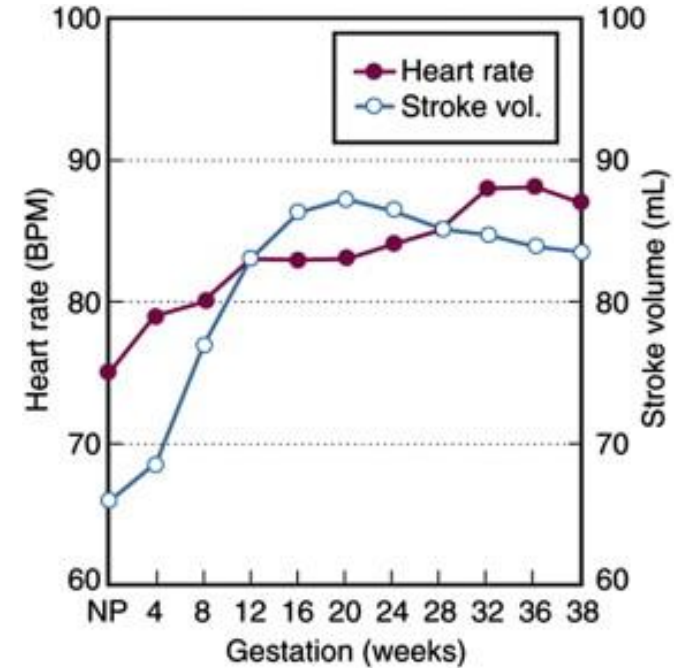
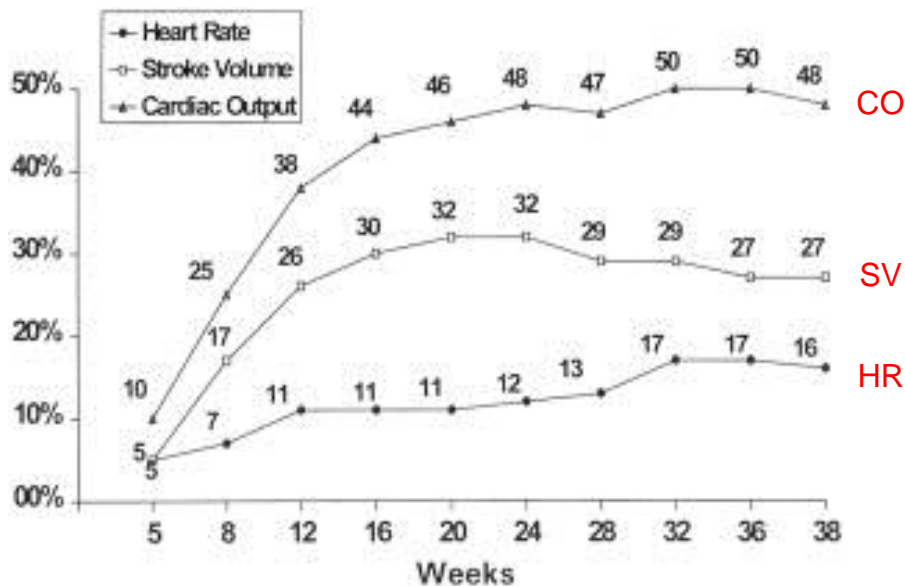
14 women.

Gilson et al Obstetr Gynecol 1997.

76 women.



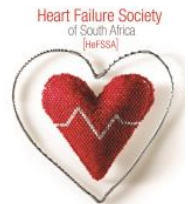
Normal physiological changes in pregnancy



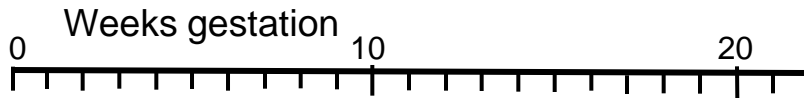
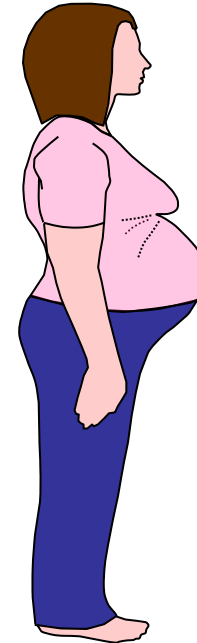
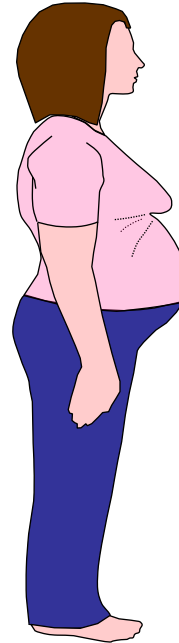
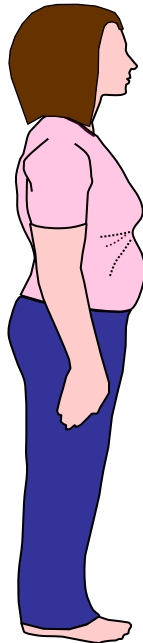
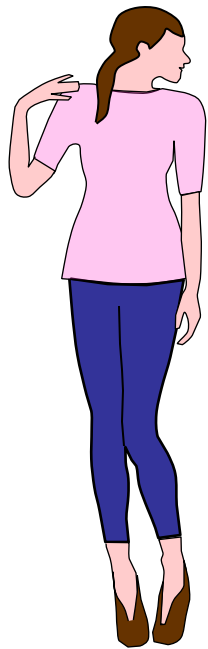
Robson et al
AJP 1989

Conditions that may cause heart failure in pregnancy

- Hypertension and pre-eclampsia
- Peripartum cardiomyopathy
- Myocardial infarction (usually due to coronary dissection)
- Undiagnosed pre existing cardiomyopathy
- Undiagnosed valve disease
- Congenital heart disease



Hypertension in pregnancy



Pre-eclampsia

Gestational hypertension

Chronic hypertension

Postpartum hypertension

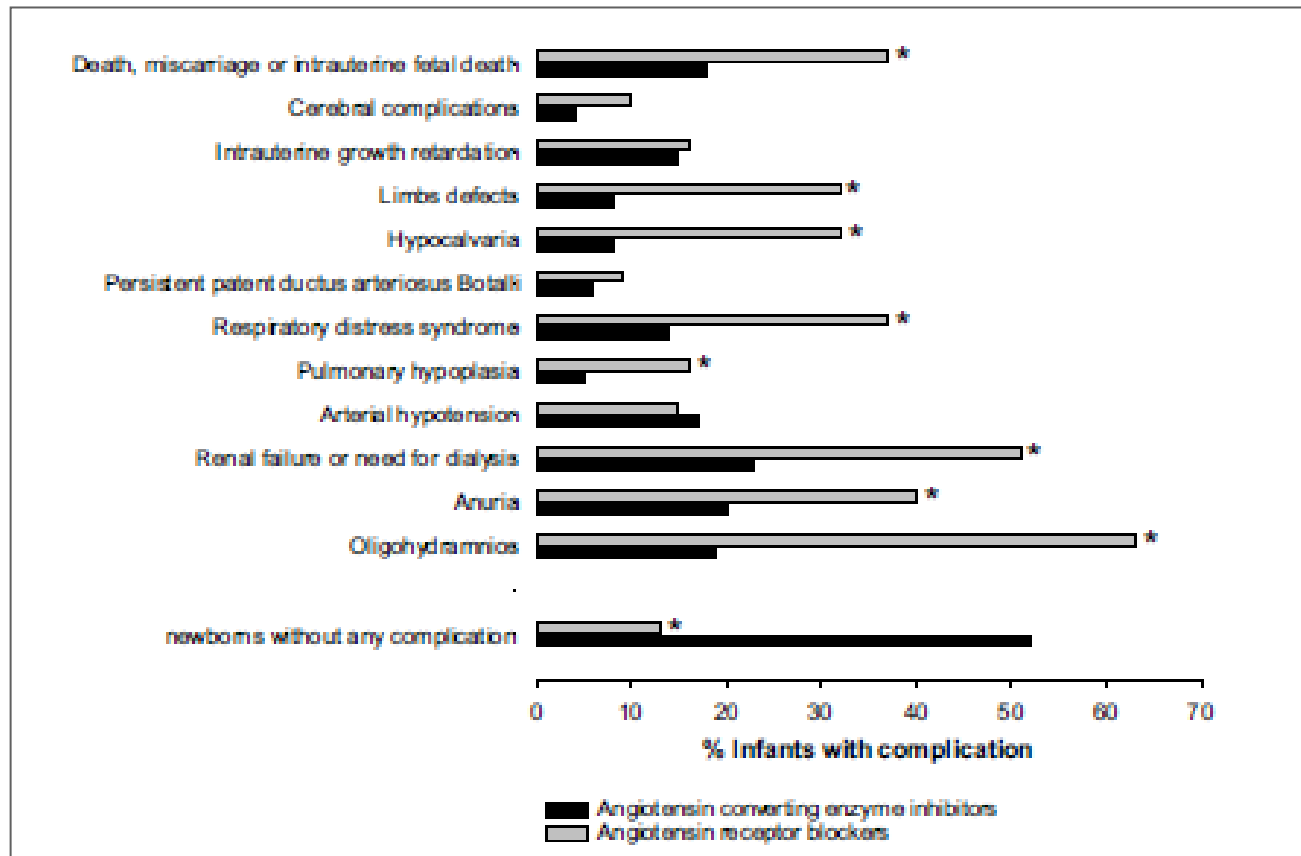
Case study

- A 38yr old lady at 18 weeks of gestation
- Essential Hypertension diagnosed 2yrs before pregnancy. Not diabetic.
- Blood pressure 155/95 mm Hg at this initial visit
- Normal cardiovascular examination
- Uterus appropriate for gestational age

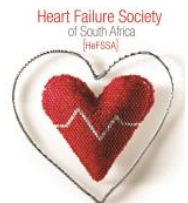
Current management

- Telmisartan 80 mg daily
- HCTZ 12,5 mg daily

ACEi and ARB in pregnancy ?



- If patient seen 1st time on no treatment repeat blood pressure on at least two occasions 6hours apart to ascertain the readings
- What are the differential diagnoses of hypertension in pregnancy?

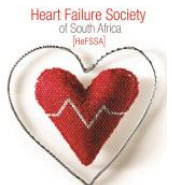


Classification of hypertension in pregnancy

- **Chronic hypertension:** Pre-existing hypertension diagnosed prior to or during pregnancy and persists beyond the 6th postpartum week
- **Gestational hypertension:** New hypertension arising after 20th week of pregnancy. BP of $\geq 140/90$ mmHg on 2 separate occasions (Korotkoff V). Resolves by the 6th postpartum week
- **Pre-eclampsia:** Hypertension with new proteinuria ($> 300\text{mg}/24\text{h}$ or ++ dipstick x2) or other systemic features of vascular dysfunction (e.g. HELLP syndrome). Oedema not required for diagnosis.
 - May be superimposed on new or chronic hypertension

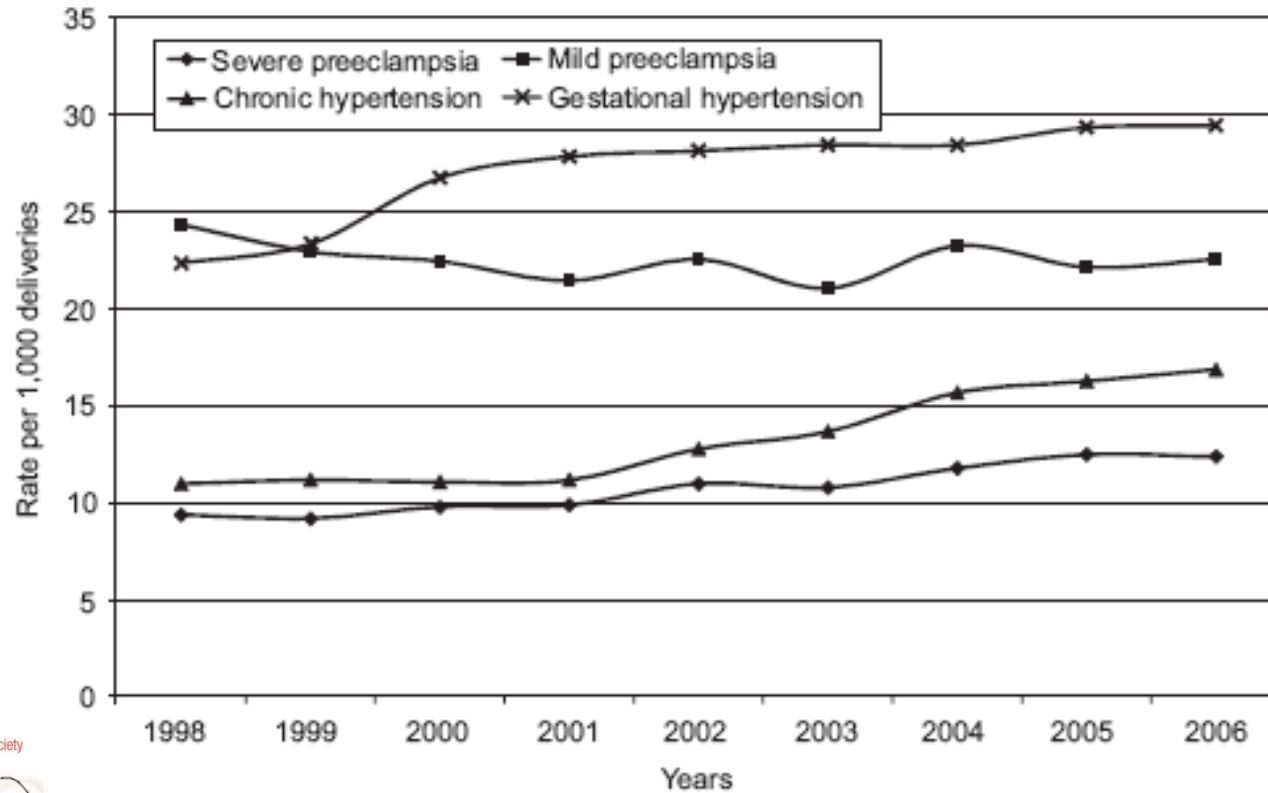
Why is detection and treatment of hypertension in pregnancy important?

- **To prevent maternal morbidity and mortality**
 - Haemorrhagic stroke
 - Other complications: Pulmonary oedema / heart failure, renal failure, ARDS
- **To reduce perinatal morbidity and mortality**
 - Placental abruption, stillbirth
 - Foetal growth retardation
 - Preterm birth
- **Not to accrue long-term benefit as in non-pregnant individuals!**



Magnitude of the problem

US Nationwide Inpatient Sample 1998-2006
>36 million hospital discharges

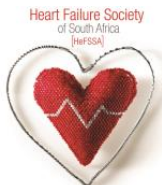


3% gestational

2.2% mild PE

1.7% chronic

1.2% severe PE



*Kuklina et al
Obstet Gynecol 2009*

Magnitude of the risk (adjusted)

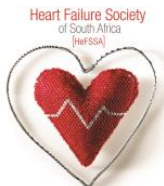
Table 3. Estimated Odds Ratios of Severe Obstetric Complications for Delivery Hospitalizations With Hypertensive Disorders Compared With Delivery Hospitalizations Without Hypertensive Disorders: The 1998–2006 Nationwide Inpatient Sample (N=36,537,061)

	Estimated Odds Ratio (95% Confidence Interval)*				
	Eclampsia/Preeclampsia		Hypertension		
	Severe	Mild	Chronic	Gestational	Any†
Acute renal failure	34.8 (30.4–39.9)	5.8 (4.8–6.9)	9.9 (8.4–11.6)	2.2 (1.7–2.9)	10.7 (9.6–11.8)
<u>Pulmonary edema</u>	9.4 (7.9–11.3)	3.7 (3.0–4.5)	3.7 (2.9–4.7)	1.5 (1.1–2.1)	4.7 (4.1–5.3)
ARDS	11.9 (10.7–13.2)	2.9 (2.5–3.4)	3.7 (3.2–4.3)	1.2 (0.9–1.4)	4.1 (3.7–4.4)
PCD cerebrovasc	16.6 (14.2–19.5)	2.5 (1.9–3.1)	4.2 (3.3–5.2)	1.4 (1.1–1.9)	5.1 (4.5–5.7)
DICS	14.8 (13.6–16.2)	3.3 (3.0–3.7)	2.3 (2.0–2.6)	1.7 (1.5–1.9)	4.5 (4.2–4.7)
Ventilation	11.0 (9.9–12.1)	2.3 (2.0–2.6)	3.4 (3.0–3.9)	1.1 (0.9–1.3)	4.0 (3.7–4.3)
Mortality	6.9 (5.2–9.2)	1.3 (0.8–2.0)	2.9 (2.0–4.0)	0.9 (0.5–1.5)	2.7 (2.3–3.3)

ARDS, adult respiratory distress syndrome; PCD, puerperal cerebrovascular disorder; DICS, disseminated intravascular coagulation syndrome.

* Adjusted for multiple birth, diabetes, preterm labor, chronic condition, year of study, maternal age, payer, hospital location, hospital teaching status, hospital region, and mode of delivery.

† Includes eclampsia and severe preeclampsia, mild preeclampsia, chronic hypertension, and gestational hypertension in hierarchical order; all groups are mutually exclusive.



Proportion of complications attributable to hypertension

US Nationwide Inpatient Sample 1998-2006

>36 million hospital discharges

36.7 % (32.6-40.8%) of AHF associated with hypertension

24.1% (20.8-27.3%) of AHF associated with severe preeclampsia

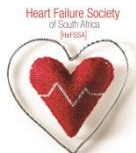
Odds ratios for development of AHF (pul oedema)

Gestational hypertension 2.2 (1.7-2.9)

Chronic hypertension 3.7 (2.9-4.7)

Mild preeclampsia 3.7 (3.0-4.5)

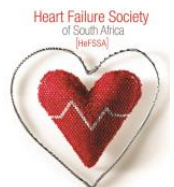
Severe preeclampsia 9.4 (7.9-11.3)



*Kuklina et al
Obstet Gynecol 2009*

Limitations

- **No data on relationship between level of hypertension and complications**
- **Gestational hypertension may include pre-eclampsia before development of proteinuria**
- **No data on ethnicity (outcomes worse in Afro-Caribbean patients)**



Multiple guidelines for antihypertensive treatment in pregnancy

- **Australasian 2000**
- **American College of Obstetricians & Gynecologists 2001**
- **Joint National Committee on Prevention, Detection, Evaluation & Treatment of Hypertension JNC7 (US) 2003**
- **Canadian 2008**
- **UK NICE guidelines 2011**
(<http://www.nice.org.uk/guidance/CG1>)
- **ESC Guidelines on management of cardiovascular diseases in pregnancy 2011**

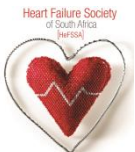


Grading of severity of hypertension

- **Mild hypertension** **140-149 sys** **OR** **90-99 dias**
- **Moderate hypertension** **150-159 sys** **OR** **100-109 dias**
- **Severe hypertension** **≥ 160 sys** **OR** **≥ 110 dias**

NB

- **Proper BP measurement:** *Cuff size, Korotkoff V, zero terminal bias*
- **Automated oscillometric devices need to be validated:**
Villar et al Int J Gynecol Obst 2004



Pre-existing chronic hypertension

- **Pre-conception evaluation**
 - end-organ damage, 24 hr urine protein
- **Optimal drug treatment**
 - Methyldopa, labetalol
 - Nifedipine, hydralazine, thiazides, clonidine (**NOT ACEi, ARB**)
- **Dose requirements may *reduce* during pregnancy (↓SVR)**
 - target levels controversial 150/100 to 140/90
- **Regular antenatal surveillance**

Monitor for pre-eclampsia. NB: Anti-hypertensives do NOT prevent pre-eclampsia (Abalos et al Cochrane 2007) Monitor foetal growth

High risk chronic hypertension

- Presence of hypertension > 4yrs
- Maternal age > 40 yrs
- Renal disease
- Cardiomyopathy
- Coarctation of the aorta
- Retinopathy
- Diabetes
- Collagen vascular disease
- Antiphospholipid syndrome
- Previous severe preeclampsia

Pre-existing chronic hypertension

- Low risk chronic(no end organ damage or proteinuria)-favourable maternal and peri natal prognosis
- High risk chronic increased complications-careful monitoring for proteinuria and renal function

Gestational hypertension

- **Thresholds for treatment vary between guidelines**
 - UK NICE: treat >150 sys OR >100 diastolic or lower if end-organ damage
 - ESC: >150 sys OR >95 dias
 - Canadian/Australasian/ACOG: >169 sys OR >109 dias
- **Higher risk features**
 - end-organ damage
 - co-morbidity (renal, diabetes, autoimmune disease)
 - high BMI, age >40 , FH, multiparity
- **Methyldopa, labetalol ,Nifedipine,hydralazine,thiazides, clonidine**
- **Monitor for pre-eclampsia / monitor foetal growth**
- **CHIPS Study NCT01192H2: Randomised tight (DBP 85) vs less tight (DBP 100) control of hypertension in pregnancy**

Antihypertensive drugs used in pregnancy

- Methyldopa-only agent where long-term safety for mother and foetus assessed and common drug used in pregnancy.
- Calcium channel blockers-nifedipine used extensively with no adverse foetal effects reported. Controlled trials lacking
Role of amlodipine not proven. CCBs in pregnancy
FDA category C.
- Beta blockers-in pregnancy associate with neonatal bradycardia, hypoglycaemia, foetal growth retardation-avoid
- Labetalol-as safe as methyldopa for short term use in 3rd trimester. Long-term use associated with small for gestational age infants

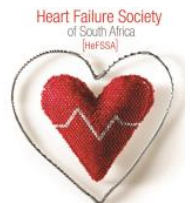
Antihypertensive drugs used in pregnancy

- Thiazide diuretics-probably not teratogenic. Although they effect plasma volume expansion, does not cause negative foetal growth
- Observe for side effects including hyperglycaemia, hyperuricaemia, hyponatremia and hypokalemia
- Hydralazine-IV or orally
- Clonidine—FDA category C in pregnancy



Labetalol / beta blockers and ACEi in pregnancy ?

- **Petersen et al BMJ Open 2012**
 - Danish study, nearly 1 million births
 - Small for gestational age: adjusted OR 1.97 (CI 1.75-2.23)
 - Preterm birth: adjusted OR 2.26 (CI 2.03-2.52)
 - Perinatal mortality: OR 1.89 (CI 1.25-2.84)
 - **Labetalol no safer than other beta blockers**
- **Bullo et al Hypertension 2012 Systematic review**
 - High rate of neonatal complications after exposure to ACEi or ARB during pregnancy



Case study

- Antihypertensive medication changed to methyldopa 500 mg bd
- Patient then developed significant proteinuria at 30 weeks and blood pressure remained elevated at 160/100-
Pre-eclampsia
- Nifedipine XL 30 mg added with good effect on blood pressure 138/85 but proteinuria persisted

Case study

- At 34 weeks patient again hypertensive, blood pressure 155/95 with proteinuria
- Small for gestational age foetus
- ? Next step

Pre-eclampsia

- **Prevention**

- Aspirin may slightly reduce risk of pre-eclampsia based on meta-analyses but has no effect on foetal outcome

- **Duley et al Cochrane Database Syst Rev. 2007. Antiplatelet agents for preventing pre-eclampsia and its complications**

- 17% reduction in the risk of pre-eclampsia (46 trials, 32,891 women)

- Relative risk 0.83 (CI 0.77 to 0.89)

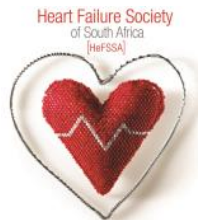
- Number needed to treat 72 (52, 119)

Pre-eclampsia

- **No specific treatment apart from delivery**
 - usually abates fully
- **Antihypertensive treatment does not improve foetal outcome**
 - Methyldopa, Labetalol, nifedipine, hydralazine, thiazide
- **Mg SO₄**
 - probably has anti-convulsant effects
- **Duley et al Cochrane Database Syst Rev. 2003. Mg SO₄**
 - Relative risk of eclampsia 0.41 (CI 0.29 to 0.58)
 - Number needed to treat 100 (CI 50 to 100)
 - Relative risk of death 0.54 (CI 0.26 to 1.10)

Case study

- Blood pressure still rising, now 160/100 with increased dose of adalat XL 60 mg daily at 36 weeks
- Next step?



Case study

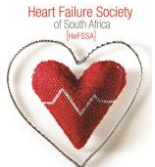
- Elective caesarean section at 37 weeks
- Blood pressure returned to normal on methyldopa 500 mg bd and adalat XL 60 mg daily
- Normal but small birth weight infant
- Post partum management-ACEi and nifedipine. Methyldopa stopped.

Post-partum management

- **Breast feeding**
 - Most antihypertensives (incl. ACEi) usually compatible. Avoid ARBs and diuretics
- **Avoid methyldopa** because of risk of worsening postnatal depression
- **Pre-eclampsia**
 - Increased future risk of gestational hypertension and pre-eclampsia

Conclusions

- Hypertension is relatively common in pregnancy and preeclampsia is the commonest cause of acute heart failure
- Treatment thresholds remain uncertain and drug dose requirements may decrease during pregnancy
- Most drugs used in pregnancy FDA category C
- Methyldopa is the first line agent; Ca channel blockers, thiazides, ?labetalol
- Do not use ACEi or ARBs.
- Anti-hypertensive Rx does not prevent pre-eclampsia



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