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#### Our Issues, Our Drugs, Our Patients

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# Tuberculosis and pregnancy

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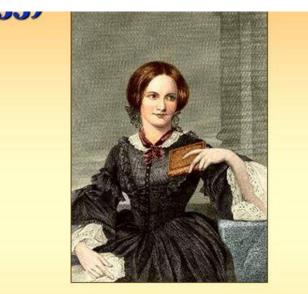
**Clinical Microbiology and Infectious Diseases** 

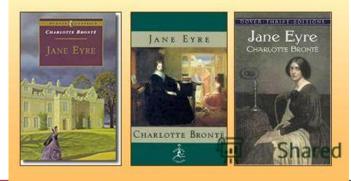
National Health Laboratory Service

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# Charlotte Brontë (1816-1855)







# Consequences of TB in pregnancy

- Low birth weight
- Prematurity
- Congenital TB
- Increased neonatal and maternal mortality
- Increased pregnancy complications
- Abortion
- Post partum haemorrhage
- Pre-eclampsia



#### Consequences of TB in pregnancy

Pregnant women with pulmonary TB who access early appropriate TB treatment do not have an increase in maternal or neonatal complications.



# Incidence of TB in pregnancy in pregnancy



• Therefor it is important to:

Prevent TB in pregnancy

Diagnose and treat TB in pregnancy

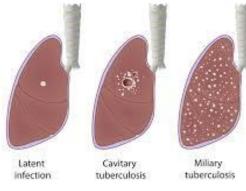




#### Prevention

Improve immunity among HIV infected people Expansion of ART is associated in a reduction in TB associated maternal mortality

Treat latent TB



Tuberculosis





# Treating latent TB – non pregnant populations

- Absence of HIV, INH has a 62% reduction in TB in people with a positive TST (Smieja MJ et al 2000, Cochrane database)
- South African adult HIV positive largely on ART. RCT of 1635. INH+ ART reduced incidence of TB > ART alone. TST not important. No difference in mortality. (Rangaka MX et al 2015, Lancet)



# Treating latent TB – non pregnant populations

- SA paediatric population; advanced HIV with no ART 263 children randomised to INH/placebo. Study stopped survival benefits in IPT compared to control arm (72% reduction) (Zar H et al, 2007 BMJ)
- SA paediatric population; HIV positive, ART and HIV exposed, RCT IPT compared to a control group. No difference in outcomes. (Madi S et al, 2011 NEJM)



# Lessons learned from nonpregnant populations

• Need information on the population of interest, extrapolation may not be accurate

• Effective screening reduces the 'incidence' of TB more effectively than INH prophylaxis

• INH does not reduce mortality



Wood R, Bekker L-G. 2014 SAMJ

#### Prevention

Limited data in pregnancy (3 studies – 2 in US)

Higher risk of INH hepatitis in pregnant than non pregnant women – although this was not significant.

Low adherence to INH therapy in all three studies



# Prevention INH prophylaxis in pregnancy

- ART more beneficial overall than INH
- Added/common toxicity between ART, INH and pregnancy
- Risk benefit is different in pregnancy than general population





#### Prevention

- Screen women effectively
- Initiate ART and stabilise women on treatment
- Wait until post partum period unless high risk – for TB such as household exposure
- Research in pregnant women
- DoH advocates INH for all HIV positive pregnant women



# Diagnosis

- Studies have shown delays in diagnosis
- Clinical symptoms overlap with pregnancy symptoms
- Need a low threshold to send specimens





## Treatment of TB in pregnancy

- Fourteen studies have been conducted with treatment outcomes, including 375 pregnant women treated for TB
- Good treatment outcomes with 88.5% cure rate.
- The mortality was 6.6% most due to meningitis or MDR TB



# Treatment of TB in pregnancy

- Streptomycin was not used in a single pregnant women among these studies
- All other first line agents can be used (INH, Rif, ETB, PZA) and appear not to be associated with congenital abnormalities
- Remember pyridoxine (50mg daily) supplementation
- No dose adjustments in pregnancy required

Loto OM et al. 2012 Journal of pregnancy Denti P et al. 2015. AAC



# Treatment of MDR TB in pregnancy

- 55 pregnant women with MDR were treated
  - 11 women died
  - 6 women opted for TOP
  - 1 still birth
  - 1 early infant death d/t pneumonia
  - 1 loss to follow up
- The remaining women were successfully treated
- MDR TB in pregnancy can be cured



### Treatment of MDR TB in pregnancy

- Kanamycin, Amikacin, Capreomycin and fluoroquinolones are all CI in pregnancy
- However, they should be used with MDR TB in pregnancy as per sensitivity profile
- Pregnant women with MDR TB have been treated with: aminoglycosides, fluoroquinolones, thiomides, cycleserines and terizidone

TB elimination, 2012, CDC Loto OM et al. 2012 Journal of pregnancy



### Treatment of MDR TB in pregnancy

- Curing TB is the more important objective
- Where a number of treatment options exist: Fluoroquinolones seem to be ok
- Avoid aminoglycosides (if needed amikacin is preferred to streptomycin)
- Replace prothinomide and ethionamide (toxic in animal studies) with PAS
- Reduce fetal levels of capreomycin by only using it 3 times a week



#### Conclusion

Important to diagnose and treat TB in pregnancy early to ensure favourable outcomes

- TB is difficult to diagnose in pregnancy
- Treat primary TB as per non pregnant women
- Tailor treatment in MDR TB where possible
- Benefit:risk of treating latent TB in pregnancy still needs to be determined

