Clinical Education Session

https://ashm.org.au/training/SSHC-sessions/

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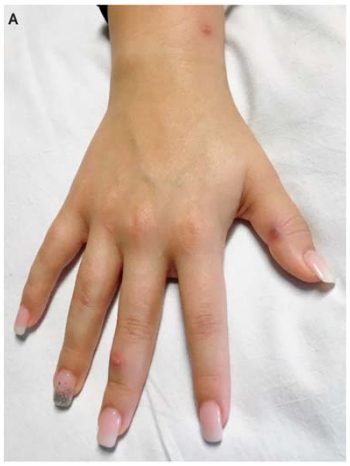
Journal Club
9th October 2019
Dr Anna McNulty

New England Journal of Medicine



March 14

A Randomized Trial of Prophylactic Antibiotics for Miscarriage Surgery, David Lissauer et al

- Randomised double blind placebo controlled trial of 3400 women in 4 low income settings
- Single dose Doxy 400mgs and Metronidazole 400mgs
- PID at 14 days (strict 2 of 4 - purulent vag d/c, pyrexia, uterine tenderness, leucocytosis or pragmatic - 1 and clinical judgement)
- PID (strict) 1.5% in the antibiotic-prophylaxis group vs 2.6% in the placebo group (risk ratio, 0.60; 95% CI, 0.37 to 0.96).
- PID (pragmatic) 4.1% in the antibiotic group vs 5.3% in the placebo group (risk ratio, 0.77; 95% confidence interval [CI], 0.56 to 1.04; P=0.09)

Editorial

- Change in study definition of PID more sensitive but less specific
- Using strict criteria benefit demonstrated in this setting

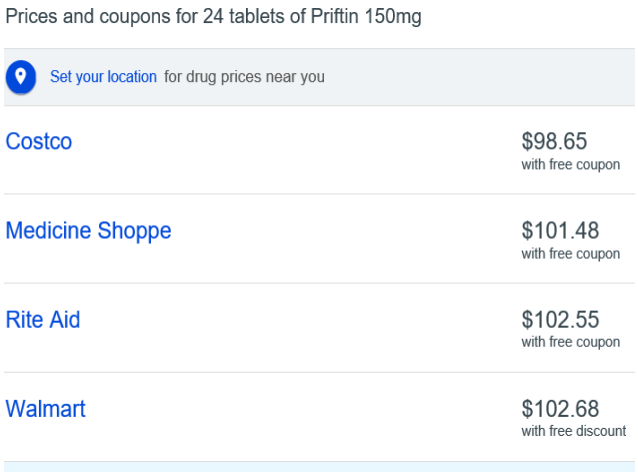
  → justifies prescribing prophylactic antibiotics

March 14
One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis
Susan Swindells et al

- Randomised open label study comparing 1m of rifapentine and isoniazid with 9m of Isoniazid in HIV positive people with evidence of latent infection or living in high prevalence setting
- Endpoint: TB or death from TB or unknown cause
- Followup median 3.3 years, median CD4 470
- n=3000, half on ARVs
- Endpoint in 2% in both groups
- SAEs no difference
- Treatment completion 97% vs 90%

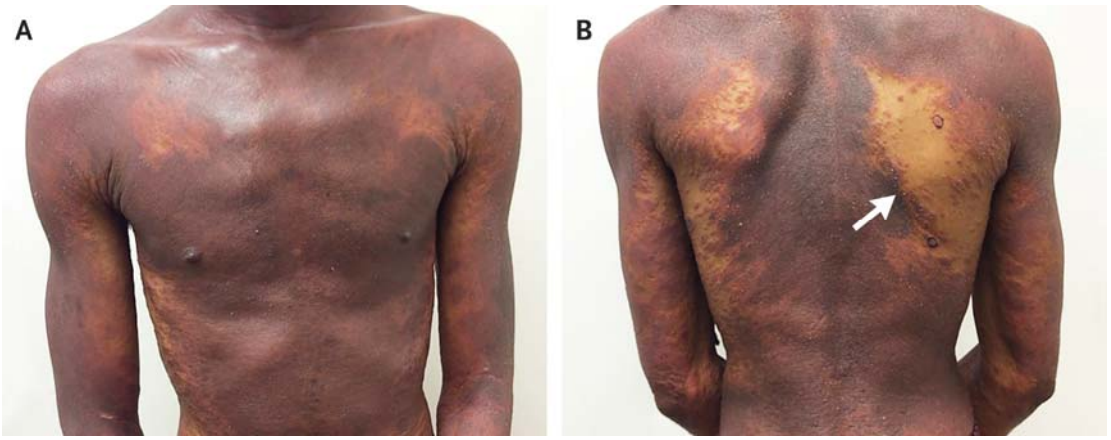
Rifapentine

- Potent, long acting rifamycin
- Not available in Australia



Editorial

- 'Tuberculosis kills more people than any other infection'. TB programs have ↓ mortality but no effect on incidence globally
- Up to 1/3 of worlds population are thought to have LTBI
- Cost effective regime for LTBI
- Evidence for
  - *Rifapentine and isoniazid administered weekly for 3 months - DOT* and self administered
  - 3m of daily isonaiazid and rifamycin
  - 4m of daily rifamycin



August 29
Neural-Tube Defects and Antiretroviral Treatment Regimens in Botswana
Rebecca Zash et al

Background and method

- Preliminary signal from routine surveillance
- Neural tube defects occur by end of 6th week of pregnancy
- Follow up study
- 8 (2014) - 18 (2018)sites, trained midwives
- Photographed abnormalities
- Determined maternal HIV and ARV status

Results

- 119,033 evaluable deliveries
- 98 (0.08%) had neural tube defects (NTD)

	DTG at Conception	Any Non-DTG ART at Conception	EFV at Conception	DTG Started during Pregnancy	HIV-Negative
No. of Neural-Tube Defects	5	15	3	1	70
No. of Exposures	1683	14,792	7959	3840	89,372
Percent with Defect (95% CI)	0.30 (0.13–0.69)	0.10 (0.06–0.17)	0.04 (0.01–0.11)	0.03 (0.00–0.15)	0.08 (0.06–0.10)
Difference in Prevalence (95% CI) — Percentage Points	Reference	0.20 (0.01–0.59)	0.26 (0.07–0.66)	0.27 (0.06–0.67)	0.22 (0.05–0.62)

- No difference in other structural abnormalities

Conclusion

- Prevalence of 3/1000 births (DOL) vs 1/1000 for other ART
- Unexpected (not in animal studies)
- ? Due to folate antagonism (in-vitro studies)
- no data on other regimens (apart from Efavirenz)

Letter

Dolutegravir Use at Conception — Additional Surveillance Data from Botswana

Table 1. Prevalence of Neural-Tube Defects According to Maternal ART Exposure at Conception.*

Finding	Dolutegravir at Conception (N=152)	Non-Dolutegravir ART at Conception (N=381)	Efavirenz at Conception (N=261)	HIV-Negative (N=2328)
No. of neural-tube defects	1	0	0	2
Percent of deliveries with neural-tube defect (95% CI)†	0.66 (0.02 to 3.69)	0 (0 to 0.79)	0 (0 to 1.15)	0.09 (0.1 to 0.31)
Difference in prevalence (95% CI) — percentage points‡	Reference	0.66 (−0.48 to 3.63)	0.66 (−0.89 to 3.63)	0.57 (−0.02 to 3.55)

* Information on the type of antiretroviral treatment (ART) was unavailable for 11 women. HIV denotes human immunodeficiency virus.
† Exact confidence intervals (CIs) are shown.
‡ Newcombe–Wilson hybrid score confidence intervals are shown. The difference in prevalence between deliveries among HIV-negative mothers and deliveries among mothers who had been taking dolutegravir at conception from our sensitivity analysis, which included the "possible" neural-tube defect, was 0.53 percentage points (95% CI, −0.07 to 3.50).

Dolutegravir-Based or Low-Dose Efavirenz–Based Regimen for the Treatment of HIV-1
The NAMSAL ANRS 12313 Study Group

- N= 613 ART naive, VL <50 in 74.5% of DOL group and 69% of EFV400 at 48 weeks
- In those VL>100,000, 66.2% in DOL group and 61.5% EFV400
- More weight gain in DOL group than EFV 5 vs 3 kgs with obesity 12.3% vs 5.4%
- DOL regime non inferior
- Relevance: limited in our setting, accumulating evidence re obesity and DOL

Weight gain and integrase inhibitors (II) and TAF

Are new antiretroviral treatments increasing the risks of clinical obesity?
J Virus Erad 2019 Jan

- Weight gain noted in pre- integrase inhibitor trials 'return to health'
- Weight gain noted in 5 RCTs of II
- 3 other studies suggest TAF → greater weight gain than TDF (1.8 kgs vs 0.8 kgs in one study)
- to date, women and black people more likely to have weight gain
- Most phase 1 trials white and male participants (weight / BMI not measured in many phase 3 II trials)

Table 1.

Effects of raltegravir, dolutegravir and bictegravir on body weight in randomised trials

Study [ref]	Design	Results
Raltegravir		
NEAT 001 [12] (naïve, *n*=126)	DRV/r+RAL DRV/r + TDF/FTC	DEXA sub-study: trunk fat 7.3% higher DRV/r/RAL *vs* TDF/FTC/RAL at week 96 (*P*=0.021)
ACTG 5260s [10,11] (naïve, *n*=126)	TDF/FTC/RAL TDF/FTC/DRV/r TDF/FTC/ATV/r	Higher risk of severe weight gain for RAL vs ATV/r
Dolutegravir		
NEAT 022 [13] (switch, *n*=415)	NRTIs + DTG NRTIs + PI/r	+1 kg increase in body weight to week 48 (*P*=0.002)
SPRING-1 [13] (naïve, *n*=204)	TDF/FTC/EFV TDF/FTC/DTG	Increases in body weight higher in DTG arms
Gilead 1490 [15] (naïve, *n*=645)	TAF/FTC/DTG TAF/FTC/BIC	+3.9 kg increase in body weight to week 96 +3.5 kg increase in body weight to week 96
MONODO [9] (naïve, *n*=8)	DTG monotherapy	+4.1 kg increase in body weight to week 24

ATV/r; atazanavir/ritonavir; BIC: bictegravir; DRV/r: darunavir/ritonavir; DTG: dolutegravir; FTC: emtricitabine; NRTI: nucleoside reverse transcriptase inhibitors; PI/r: ritonavir-boosted protease inhibitor; RAL: raltegravir; TAF: tenofovir AF; TDF: tenofovir DF.

Letter

Oocyte Cryopreservation in a Transgender Male Adolescent

- Natal female initiated GnRH agonist therapy (puberty blockers) aged 14
- Age 16 advised to stop this therapy to allow maturation of oocytes, however he elected to continue
- Refused TV ultrasound so abdo ultrasound and serum E levels monitored response to hormone therapy and oocytes were retrieved
- side effects – vaginal bleeding and oocyte retrieval, breast development spontaneously regressed, depressed mood
- T therapy then initiated
- Only 4 oocytes cryopreserved

Other articles

- Neurosyphilis (review)
- Intimate Partner Violence (review)
- Global Elimination of Chronic Hepatitis (review)
- Bacterial Vaginosis and Desquamative Inflammatory Vaginitis (review)