

Tuberculose en Schistosomiasis

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09-09-2019

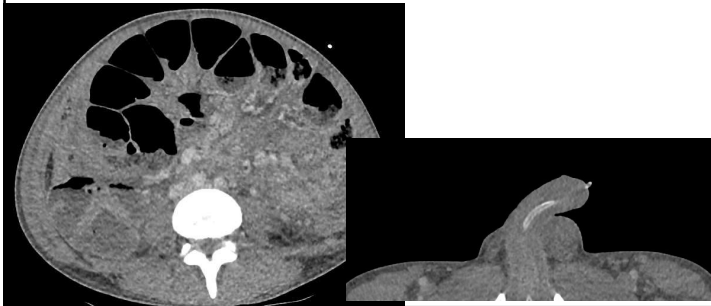
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Casus

- 7-2: Overname 22-jarige patiënt
- Uit Eritrea, 5 jaar in NL
 - Verdenking peritonitis tuberculosa en orchitis obv TBC.
 - Per 26-01-2019 pyrazinamide+ethambutol+rifampicine+isoniazide
- PCR TBC positief 23-01-2019
- Sputumweek 15-2: m. tuberculosis

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- 16-2 ontstaan buikpijn, hypotensief, koorts.
 - Ceftriaxon + metronidazol bijgestart en naar IC t/m 20-2
 - Ontwikkeld ileus met verdenking op (micro-)perforatie



- 1-3: screening feces

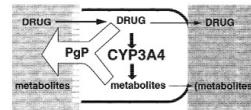
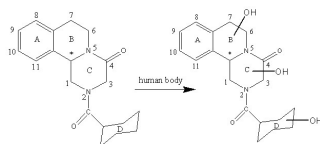


- Wat nu?

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Interactie

- Rifampicine CYP3A4-inducer
- Maximaal <10 dagen
- Houdt >2 weken aan na staken, hoe lang precies?
- Anti-epileptica zoals carbamazepine, Sint-Janskruid, nevirapine



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Interactie

- Rifampicine verlaagt spiegel praziquantel
- Spiegel praziquantel 40mg/kg is 80-85% lager

Rifampin markedly decreases plasma concentrations of praziquantel in healthy volunteers

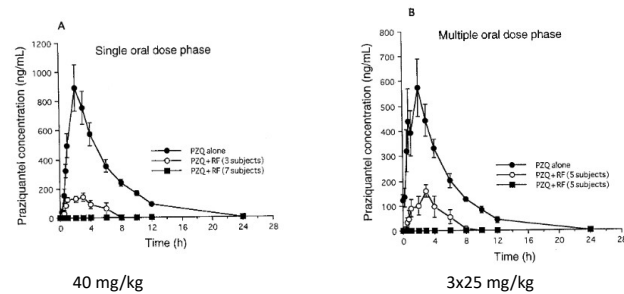
Conclusion: Rifampin greatly decreased plasma concentrations of single and multiple oral doses of praziquantel to levels lower than that of the minimum therapeutic concentration. Because praziquantel and rifampin are widely used in the treatment of liver flukes (*Opisthorchis viverrini*) and *Mycobacterium tuberculosis*, respectively, in Thailand and in some other countries in southeast Asia, the possibility of one drug influencing the pharmacokinetics of the other must be considered. Therefore simultaneous use of rifampin and praziquantel must be avoided in medical practice to optimize the therapeutic efficacy of praziquantel. (Clin Pharmacol Ther 2002;72:505-13.)

- Threshold plasma concentration praziquantel ~300 ng/mL about 6 hours to affect schistosomes lethally.

Riditid et al. 2002

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Interactie



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Interactie

Parameters	Single-dose study		Multiple-dose study	
	Praziquantel alone (n = 3)	Praziquantel plus rifampin (n = 3)	Praziquantel alone (n = 5)	Praziquantel plus rifampin (n = 5)
C				

Wat nu?

- Geen goed alternatief voor Praziquantel

Drugs for treating *Schistosoma mansoni* infection (Review)

Danso-Appiah A, Olliaro PL, Donegan S, Sinclair D, Utzinger J

Authors' conclusions

Praziquantel 40 mg/kg as the standard treatment for *S. mansoni* infection is consistent with the evidence. Oxamniquine, a largely discarded alternative, also appears effective.

Further research will help find the optimal dosing regimen of both these drugs in children.

Combination therapy ideally with drugs with unrelated mechanisms of action and targeting the different developmental stages of the schistosomes in the human host should be pursued as an area for future research.

- Mefloquine kent ook CYP3A4 en PGP-metabolisatie en oxamniquine niet in NL
- Behandeling uitstellen?
- Toch geven? Hogere dosis?

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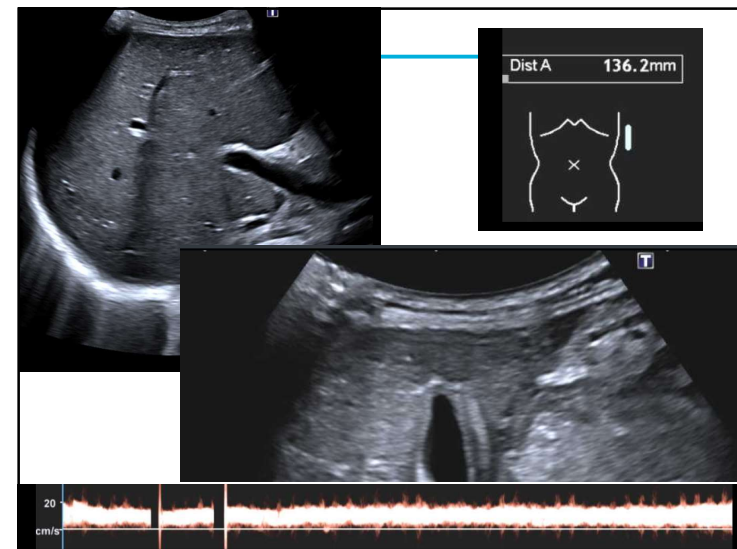
Kunnen we niet gewoon afwachten?

- Uitstellen behandeling?
- Gezien buikpijn/ileus mogelijk intestinale schistosomiasis
- Lab: eosinofilie $0,79 \times 10^9/L$
- Moet nog maanden rifampicine

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- *Schistosoma peritonitis* en darmobstructie zijn beschreven
 - Echter ook septisch, pleit tegen
- Wel splenomegalie en eosinofilie
- Advies: echo
 - Echo 11-3: Versterkte echoreflecties in de wanden van de galwegen intrahepatisch en extrahepatisch. Dit beeld wordt inderdaad gezien bij *S. Mansoni* infecties. Hobbelige levercontour, cave cirrose.

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- Toch wel behandelen?
- Rifampicine stoppen?
- Meer geven?

High-Dose Praziquantel for Neurocysticercosis: Efficacy and Tolerability

P.R.M. Bittencourt^a, C.M. Gracia^a, A.M. Gorz^a, S. Mazer^b, T.V. Oliveira^a

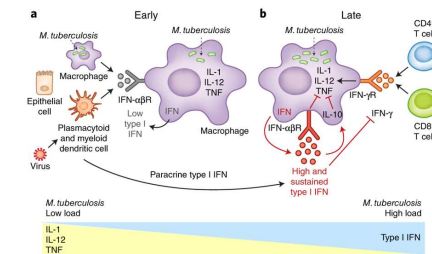
Bittencourt et al. 1986

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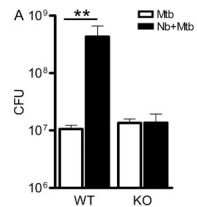
Beinvloeding Schistosomiasis -> TB

TB: Th1 -> IFN- γ , TNF- α , IL-17, IL-22

Parasieten: Th2 -> IL-4, IL-5, IL-13



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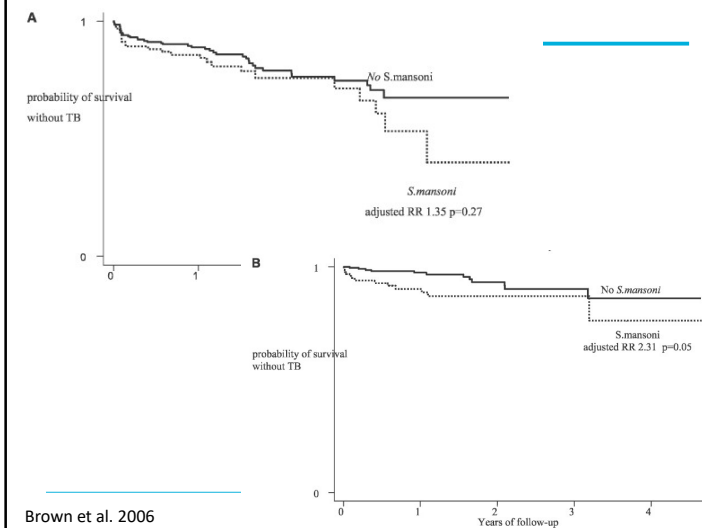
Sustained Th2 response leads to exacerbation of TB disease in co-infected animals

Hookworm infection is associated with altered systemic levels of Th1 and Th2 cytokines in latent TB

Hookworm infection is associated with constitutively decreased frequencies of mono- and dual-functional CD4⁺ Th1 and Th17 cells and increased frequencies of Th2 cells

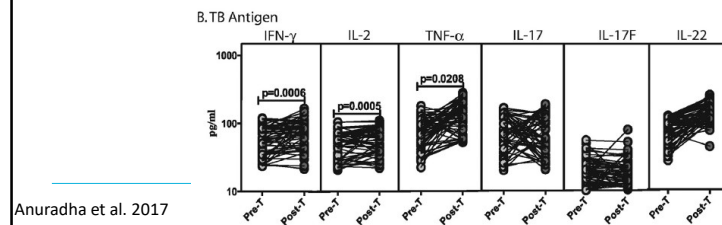
Potian et al. 2011, George et al. 2013

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Brown et al. 2006

Anthelmintic Therapy Modifies the Systemic and Mycobacterial Antigen-Stimulated Cytokine Profile in Helminth-Latent *Mycobacterium tuberculosis* Coinfection



Beloop

- 12-4 stop rifampicine
- Moxifloxacin+ethambutol gestart
- 4 weken daarna praziquantel
- 13-05 praziquantel 40 mg/kg
- 14-05 herstart rifampicine en staken ethambutol en moxifloxacin

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Conclusie

- Wees alert op interactie praziquantel en rifampicine, waardoor behandeling gecompliceerd is.
- Geen goede alternatieven voor praziquantel
 - Toch noodzaak voor oxamniquine in NL?
- Behandelen lijkt wel voorkeur te hebben boven afwachten ivm immunomodulatie

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