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Rilpivirine (RPV) in pregnancy

RPV was registered as a non-nucleoside reverse transcriptase inhibitor (NNRTI) in 2011.[1] It is in the same class as efavirenz (EFV) and has the advantage of fewer neuropsychiatric side effects. However, in comparative trials with EFV, there was more virological failure with baseline plasma HIV RNA >100,000 copies per mm^3. RPV is becoming more widely used as a within-class replacement.[2] There is both prospective and retrospective data that switching from EFV to RPV in virologically suppressed adults is safe and well tolerated, especially if EFV-related neuropsychiatric effects are problematic.[3,4]

RPV is category B for pregnancy and should only be used if advantages outweigh the risks. There was no evidence of embryonic or foetal toxicity in rat and rabbit dams treated during pregnancy and lactation at doses 15 and 70 times higher, respectively, than exposure in humans at 25 mg once daily. However, there are extremely limited data in human pregnancy and no data on transfer to human breast milk, although presence in milk from rats has been confirmed. Major depression has been linked to RPV and increased gastric pH, as may be associated in treating pregnancy-related dyspepsia, causes reduced absorption and virological failure. The antiretroviral pregnancy registry lists no human experience with RPV in pregnancy.[5]

While RPV is a very useful replacement for EFV, there is no evidence for safety in pregnancy. In contrast, EFV, category D for risk of fetal malformations, has been studied over many years and to date, meta-analyses support its safety in pregnancy.[6]

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Is there a need for 6-monthly CD4 monitoring in patients with stable virological suppression on ART?

Monitoring of the CD4+ T-lymphocyte count has been a central part of HIV management since the 1990's. The CD4 count has played an important role in guiding decisions about when to start ART and primary prophylaxis for opportunistic infections, as well as assessing the degree of immunosuppression and thus guiding investigations and treatment when patients present with opportunistic diseases.

Once patients are established on ART and their HIV viral load is suppressed < 50 copies/ml and this is maintained it can be predicted that in the majority who start with a CD4 count < 200 this will rise to and remain above 200. Also, in those who start with a CD4 count > 200 the CD4 count is very unlikely to drop below that threshold provided viral suppression is maintained.

A recent study from the Khayelitsha ART cohort addressed the question of whether it was safe to stop CD4 count monitoring in people doing well on ART. The inclusion criteria were: adults who started ART between 2001-2012; and achieved a viral load < 400 copies/ml and a CD4 cell count > 200 after 9-15 months on ART; and who subsequently remained virologically suppressed. At 2, 5 and 10 years on ART, 99.3, 95.8 and 92.9% of these patients with ongoing virologic suppression maintained CD4 cell counts continuously above 200. In the majority where the CD4 count dropped below 200 this was transient.[1] An analysis of patient data collected in the 192 week ARTEMIS trial also concluded that after 48 weeks of ART for 'responder' patients (viral load < 50 copies/ml and rises in CD4 ≥ 200 at week 48) there was little clinical benefit from continued CD4 monitoring if viral load remains suppressed < 400 copies/ml.[2]

In patients on ART the key indicator of the efficacy of therapy is sustained suppression of the HIV viral load. The CD4 count is of use initially in deciding when primary and secondary prophylaxis can be stopped in patients in whom this was initially indicated. However, once a patient has demonstrated reliable ART adherence, their HIV viral load is suppressed and the CD4 count is > 200, the role of ongoing CD4 count monitoring in clinical management has been called into question.[3] In 2013, the WHO convened a consultation meeting on the future role of CD4 testing for ART monitoring. Cohort data was reviewed and the consensus was that where HIV viral load testing is widely available the frequency of CD4 monitoring could be reduced or stopped altogether in patients stable on ART.[4] The SA HIV Clinicians Society guidelines have advised that in patients on ART who have HIV viral load monitoring routine CD4 count monitoring can be stopped when the viral load is suppressed and the CD4 count is > 200.[5] The SA Department of Health 2015 guidelines advise checking a CD4 count at 12 months on ART and thereafter if clinically indicated.

Clinicians and patients have become very accustomed to routine 6-monthly CD4 count testing and reducing the frequency of monitoring will require specific education of patients about the fact that the HIV viral load is the key indicator of sustained ART efficacy, and that their CD4 count is very unlikely to drop provided their viral load remains suppressed. If CD4 count monitoring is stopped in asymptomatic patients who have CD4 counts > 200 and are virally suppressed, a repeat test should be considered if the patient develops virological failure or has any new opportunistic condition suspected or diagnosed.

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AfA is pleased to announce that the highly regarded **Clinical Guidelines booklet** is now available as a **free App*** from the Apple iStore and Android play store, just search for **HIV Management Guidelines:**

Developed in 1998 by local infectious disease experts, the aim was to provide an evidence-based, **comprehensive guide to HIV management** in Southern Africa; available to all healthcare professionals responsible for the care of people living with HIV and AIDS. The Guidelines also form the basis of the **Aid for AIDS Disease Management Programme**.

Already in its **10th edition**, they remain a fundamental, up-to-date source of information that reflects current best practice in the **treatment of HIV infection**, including the **use of antiretrovirals** and **the management of common opportunistic infections** in both adults and children.

The **App provides** a convenient and practical way of accessing and searching through the most up to date version of the guidelines.
To further improve these Guidelines, AfA welcomes feedback from users.

* Compatible with any Apple or Android device.

SAASP
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The South African Antibiotic Stewardship Programme (SAASP) prescribing guideline is a freely available app downloadable on Apple and Android platforms. It offers users an algorithmic approach to the management of common bacterial infections. It's aim is to guide you towards an appropriate choice of antibiotic, to limit optimise treatment whilst limiting the development of bacterial resistance to antibiotics.

Twitter for the busy Clinician – Opening up a world of HIV-related information

If you are reading this and over the age of 30 years, then more likely than not, your view of twitter is that it is used by the young to inform friends of what they had for breakfast that morning. And that may in part be true, but it is also a growing resource for professionals from all spheres including the health sector, who use it as a means of accessing work-related information and communicating with like-minded professionals.

Unlike Facebook, which is predominantly a social chat forum for friends and family, twitter is aimed at concise communications (tweets) of a maximum 140 characters, which may just involve text, or include an image(s) or link to a web-based document (unlike email, you cannot 'attach' documents that are not on the web). The brevity of the text forces the user to focus on the key information to be imparted.

A full explanation of how to set up and use twitter is beyond the scope of this article, but a useful guide compiled by University of Durham is already out there,
https://www.dur.ac.uk/resources/public.health/leadingtransformation/event2/Twitter-For-HealthCare-Professionals.pdf

You choose whom to 'Follow' on twitter i.e., whom you will receive tweets from, and likewise, people can choose to follow you and see your tweets. Once a tweet from a follower is received on your home page, you can either just read it and take no further action, reply to the tweet directly, or 'retweet' it so that the people that follow you (followers) see it on their home page. You only receive tweets from people you follow and can 'unfollow' people without offense, and can easily block tweets from any company that may have paid to boost circulation of their tweet.

There are a number of ways of identifying whom to follow on twitter:

- By clicking the twitter symbol on websites of people or organizations that you are interested in, you can automatically add them to the list of people who you are following.

- The hash tag symbol (#) can be used in front of a search term and typed into the search function on your twitter page. To find people who are tweeting about HIV/AIDS, #HIV, #AIDS, #antiretroviral #ART #PMTCT etc. may be a useful place to start. If you include these #-related terms in your tweets, then anyone searching for that # will see your tweet and will then be able to view your profile and decide whether to follow you. For example, in the following tweet I wanted people attending the Congress of the International Society of Travel Medicine (CISTM) that I was at to see my tweet, and therefore used #cistm14, (the # associated with that conference) in my tweet. In addition, I wanted the South African Department of Health (@HealthZA) and a colleague (@idpharmd) specifically to see the tweet and therefore included them in my tweet, using their name or 'twitter handle', which is their tweeting name prefaced by the @ symbol. Lastly, the blue-coloured link ('niaid.nih.gov…..) attached a document announcing the cessation of the antiretroviral START study to my tweet, so that anyone reading the tweet could also read the article.

- Get someone else to advise you. The table below gives some examples of HIV-related twitter sites that may be of interest to those in the field.

Twitter Handle	Description
Information	
@aidsmap	NAM works to change lives by sharing information about HIV and AIDS
@UNAIDS	Inspiring the world in Getting to zero
@AIDSgov	U.S. HIV/AIDS and news media information
@CDC_HIVAIDS	CDC's Division of HIV/AIDS prevention
@GlobalFund	The Global Fund to fight AIDS, Tuberculosis and Malaria
@mothers2mothers	Innovative HIV prevention & treatment support program that uses education & empowerment to PMTCT
@HIVSA	Developing and implementing innovative programmes related to HIV work in South Africa
@HIV_AIDSNews	News updates and developments
@info_TGHN	Global Health Network sharing research knowledge
Societies	
@SAHIVSoc	SA HIV Clinicians Society
@BritishHIVAssoc	British HIV Association
@iasociety	The International AIDS Society
Research	
@CAPRISAOfficial	Centre for the AIDS Programme of Research in SA
@HIVpxresearch	A global source of updates, advocacy & information on biomedical HIV prevention
@HelpEndHIV	International organization working towards safe and effective vaccine against HIV/AIDS
@journalaids	Journal of Acquired Immune Deficiency Syndrome
@nejm	The New England Journal of Medicine
General Interest	
@WHO	World Health Organization
@Gatesfoundation	The Bill and Melinda Gates Foundation
@TEDMED	TED talks on medical issues
@HealthZA	South African Department of Health
@ZackieAchmat	South African HIV activist

Twitter will not change your life, but it could open up a world of HIV knowledge. Hope to see you on the other side.

@southafricanasp

The role of micronutrient supplementation in adults

Numerous cross-sectional studies have shown that concentrations of many micronutrients are lower in HIV-infected patients with advanced disease. A number of micronutrients (notably vitamin A, vitamin D, zinc and selenium) are important for normal immune function. It is well established that malnutrition causes clinically significant immune suppression. Therefore micronutrient deficiencies could exacerbate HIV induced immune deficiency, and supplementation with micronutrients might reduce morbidity and mortality. A number of randomised controlled trials (RCTs), using single or multiple micronutrients, have been conducted to test this hypothesis. However, it is difficult to compare studies as the combination and/or doses of micronutrients differ so much. In addition, a number of small RCTs assessed only surrogate markers (e.g. change in CD4 counts) rather than clinical endpoints, and most studies were done in populations who were not on combination ART. This overview will concentrate on clinical endpoints.

A systematic review[1] of micronutrient supplementation in pregnant and lactating women found that multivitamins at the recommended dietary allowance (RDA) reduced premature delivery, increased infant birth weight, and slowed HIV disease progression in the mothers. Multivitamin doses above RDA did not confer additional benefit. Single micronutrients in pregnancy have also been evaluated:[1] zinc had no clinical benefit, while selenium and vitamin A[3] increased infant birth weight but had no other benefits. The limitations of the RCTs included in the systematic reviews are that most were done by one research group in Tanzania and none of the participants were on ART.[1]

The evidence of benefit of micronutrient supplementation is unclear in non-pregnant adults. Single micronutrient RCTs of vitamin A, beta carotene, vitamin D and zinc failed to show clinical benefit,[2] but selenium reduced hospitalisations.[6] A small Tanzanian RCT[4] of HIV-infected participants with tuberculosis showed a mortality benefit in participants randomised to multivitamin-zinc supplements, but a subsequent larger Malawian RCT[5] and a meta-analysis[2] showed no mortality benefit. Finally a Thai study reported a mortality benefit for a multivitamin-mineral supplement only in the sub-group with CD4 counts <200 cells/µL.[6]

AfA have revised guidelines for micronutrient supplementation. Multivitamin supplementation at RDA is recommended for all pregnant and lactating women, preferably with added selenium. In non-pregnant adults micronutrient supplementation is recommended only for patients with CD4 counts <200 cells/µL or an active opportunistic infection.

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