Optimism and concern at IAS 2017

The International AIDS Society Conference on HIV Science (IAS 2017), July 23–26, assembled more than 6000 delegates in Paris, France, to focus on the HIV pandemic, which has infected more than 70 million people and killed almost half to date.[1] For the first time, more than half of all people living with HIV (19·5 million) have initiated highly active antiretroviral therapy (ART),[1] which decreases morbidity, mortality, and infectiousness. National programmes, such as those of Lesotho and Botswana, have shown that ART scale-up is feasible and can have population-level benefits.[1] However, daunting challenges remain. Current treatment is lifelong in the absence of a cure and, although the rate of new infections has significantly decreased, last year there were still more than 1·8 million incident HIV infections worldwide, disproportionately in sub-Saharan Africa. Moreover, in some countries, notably in Russia and central Asia, the epidemic is increasing among injection drug users without recourse to evidence-based harm reduction, as well as in men who have sex with men (MSM) and transgender women.[1]

Nonetheless, substantial progress was reported. In recent years, the identification of HIV reservoirs after initial infection has helped to focus attention on what may be needed to achieve a sterilising or functional cure (ie, HIV persisting in reservoirs, but chronic medication would not be needed to keep it in check).[2] New immunological insights support consideration of the use of cytokines and monoclonal antibodies (mAbs) directed against HIV binding sites as part of a new cocktail that might be used to achieve cure or remission, or may inform preventive vaccine regimen.[3] ART has become simpler: two studies found that a single daily combined tablet containing bictegravir, a new integrase strand transfer inhibitor that does not require metabolic boosting (and associated drug interactions), coformulated with two reverse transcriptase inhibitors, was comparable to the most effective contemporary regimens and[4,5] the non-nucleoside reverse transcriptase inhibitor, doravirine, is highly effective as part of an ART regimen.[6] At the same time, new surveillance data documented an increasing level of reverse transcriptase inhibitor resistance among newly infected people in Africa, raising concerns that some cheap and effective daily single pill regimens could be compromised, requiring newer combination regimens that could be more expensive for some.[7]

Because of declining HIV mortality the global pandemic continues to grow, albeit more slowly than previously, but continue to require wider implementation of evidence-based prevention modalities. In recent years, the use of coformulated tenofovir disoproxil fumarate and emtricitabine for pre-exposure prophylaxis (PrEP) has proven highly efficacious in preventing HIV acquisition in diverse at risk populations.[8] At IAS 2017, the experience of PrEP implementation in multiple settings, from Thai, Brazilian, and Australian MSM to African heterosexuals was reported, and uptake and adherence seemed acceptable.[9] Moreover, the use of on-demand PrEP is robust for MSM, even those who had sex less frequently.[10] However, in addition to several studies suggesting that suboptimal adherence partly explained PrEP failure in African women, pharmacological studies suggest that vaginal exposure to HIV is less forgiving of missed PrEP doses than is anal exposure. Microbiological studies found that vaginal dysbiosis could attenuate the preventive benefit of topical PrEP.[11] Interventions to improve daily adherence might provide one solution to concerns about the robustness of oral daily PrEP for some populations, but data presented at IAS 2017 also suggested the contours of PrEP 2.0. An intravaginal ring containing dapivirine inserted monthly was protective against HIV in African adult women[12,13] and was reported to be safe and acceptable in adolescent American girls.[14] Two studies are underway in Africa to assess the long-term effectiveness of the ring. If they are successful, the approach could be adapted to less frequent insertion and protection against other pathogens or pregnancy could be added.

Other preventive approaches discussed at IAS 2017 involved the parenteral administration of antiretrovirals, as well as immunoprophylaxis with mAbs. Data on two injectable antiretrovirals, cabotegravir[15] and rilpivirine,[16] suggested safety and acceptability, and two large efficacy trials of cabotegravir have begun to determine if parenteral administration every 8 weeks is comparable to that of daily oral PrEP. The use of bioengineered mAbs for immunoprophylaxis protects simians against retroviral challenges, and two preventive efficacy trials

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of one candidate VRC01 are underway. Analogous to antiretroviral PrEP, VRC01 is the first of a growing group of mAb candidates that might be used for prevention, treatment, or cure, alone or in combination. The use of mAbs in prevention trials might facilitate new immunological insights regarding the correlates of protective immunity. Vaccinologists have continued to interrogate the reasons for the modest efficacy of a Thai study of a combination vaccine strategy to inform new field trials. At IAS 2017, promising findings from animal studies, in addition to progress reports from clinical trials of promising vaccine approaches, were also discussed.

Despite scientific progress and optimism about new approaches, an underlying anxiety pervaded the proceedings. In the near term, epidemic control requires that all who are infected are aware of their status, and have access to treatment, and that those who are at risk are able to use evidence-based prevention, including PrEP. The costs for an adequate global response are enormous, and although some countries (eg, South Africa) have taken increasing ownership of their epidemic, many rely on international donors. The increasingly internalised perspectives of resource-rich democracies and regressive policies of autocratic states reinforce concerns that despite scientific advances, political support might not be sufficient to sustain promising momentum, leading to the recognition that renewed advocacy and activism are needed to arrest this intractable pandemic.

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