

We urge WHO to act on cytomegalovirus retinitis

On Nov 11, 2013, *The Lancet Global Health* published an analysis of the causes of vision loss 1990–2010.¹ This analysis does not mention the risk of vision loss as a result of untreated cytomegalovirus retinitis in people with HIV, despite the infection's continued prevalence in low-income and middle-income countries. Cytomegalovirus disease was one of three unusual infections in the report by the US Centers for Disease Control and Prevention² that marked the official start of the AIDS epidemic on June 5, 1981. Before the availability of antiretroviral therapy, cytomegalovirus retinitis, the most common manifestation of AIDS-related cytomegalovirus infection, affected a third of patients with AIDS and accounted for more than 90% of AIDS-related blindness.

Sadly, cytomegalovirus retinitis remains the neglected disease of the AIDS pandemic,³ and there is an increasing group of young patients in low-income and middle-income countries made healthy by successful treatment of underlying HIV, yet left permanently blind from undiagnosed or inadequately treated cytomegalovirus retinitis. Cytomegalovirus retinitis was second only to cataract as a cause of bilateral blindness in the Chiang Mai region of Thailand,⁴ and findings of a recent systematic review confirmed a substantial burden of disease, particularly in southeast Asia, with no apparent reduction in prevalence noted in the past decade.⁵

On Oct 12, 2013, *The Lancet* editors⁶ cited the “bold but attainable goal” of reducing the global prevalence of avoidable blindness. Cytomegalovirus retinitis is covered in every set of guidelines from the US Centers for Disease Control and Prevention, and now there is a unique opportunity for

both the WHO Department of Blindness and WHO Department of AIDS to give full attention to this problem. Roche and the Geneva-based UNITAID-supported Medicines Patent Pool have signed an agreement that provides a unique opportunity to reduce blindness and mortality in patients who present with late-stage HIV infection and cytomegalovirus retinitis or extraocular cytomegalovirus disease.⁷ The agreement immediately makes valganciclovir available to treatment programmes at a price reduction of up to 90% in 138 low-income and middle-income countries. Additionally, increased use of valganciclovir might incentivise generic drug entry into the market, promising even deeper and more sustainable price reductions than at present.

Treatment with a simple pill, valganciclovir, is realistic in every setting, whereas the standard of care in low-income and middle-income countries—a weekly intraocular injection of ganciclovir⁸—is inadequate for several reasons and even intraocular injection is unavailable in most settings.³ However, a simple pill will not entirely solve the problem, and appropriate measures for crucial early detection of cytomegalovirus retinitis in the well-defined vulnerable group of newly diagnosed patients with AIDS (those with CD4 cell counts below 100 cells per μL), are urgently needed. Unfortunately, with no mention of cytomegalovirus retinitis by WHO and no WHO guidelines on cytomegalovirus treatment, there has been little attention to treatment in national programmes, and systematic early screening is done in only one country, Myanmar (Burma), by enterprising non-governmental organisations.⁹ Strong action by WHO and others now offers opportunity to break the vicious cycle of underdiagnosis of cytomegalovirus retinitis and a lack of available, affordable treatment.

Valganciclovir and systemic (rather than local) treatment

are the standard of care in high-income countries.¹⁰ Furthermore, there is compelling evidence that cytomegalovirus retinitis¹¹ and systemic cytomegalovirus infection¹² are linked to mortality rates, and reasonable evidence that systemic treatment of cytomegalovirus retinitis will reduce mortality.¹³ How should valganciclovir be given to newly diagnosed patients with AIDS and cytomegalovirus retinitis? A common-sense starting point (based on both standards of care in high-income countries and extensive direct personal clinical experience) would be to provide valganciclovir 900 mg twice a day for 2 weeks and then valganciclovir 900 mg once a day until three conditions are met: a minimum of 3 months has elapsed, active cytomegalovirus retinitis has completely resolved, and a good response to antiretroviral therapy has been achieved. The current practice of intraocular ganciclovir injection should be continued for the first 2 weeks to provide local induction. The blood cell count should be monitored for leucopenia. It is important to preserve techniques of intraocular injection for patients who become cytopenic and for patients who might not be able to take oral drugs (comatose state, severe dysphagia, etc), or in whom the retinitis does not seem to respond promptly (including because of the development of resistant strains).

Well designed operational research is needed to refine this starting point. Research is also needed to find out whether prophylactic valganciclovir treatment in high-risk patients might reduce AIDS mortality as well as blindness, as substantial data suggest.^{14,15} WHO leadership is needed to provide cytomegalovirus diagnosis and treatment guidelines, support countries' efforts to scale up diagnosis, and explore the possibility of integration of routine eye screening with indirect ophthalmoscopy into routine care for all patients first



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presenting with advanced HIV, as has been done in Myanmar.⁹

WHO needs to take action against cytomegalovirus retinitis for treatment programmes to move towards elimination of preventable blindness and meet their targets for universal eye health.

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