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Letters to the Editor

Dear Editor,

POTENTIAL EBOLA PROPHYLAXIS

Your Editorial provides insights into Ebola and the impact of such terrible infectious diseases.[1] In addition to providing International Emergency Health Services and developing vaccines and treatments, it would be wise to consider prevention measures.

Health workers in Africa need effective Ebola prophylaxis. While waiting for effective vaccines, an epidemiological survey could show if a non-infected cohort had been prescribed chloroquine (CQ) for malaria. CQ-resistant malaria predominates, but CQ is sometimes given with proguanil. The hypothesis that CQ might afford Ebola prophylaxis comes from our own work showing hydroxychloroquine (HCQ) induces apoptosis (programmed cell death) in peripheral blood mononuclear cells.[2] HCQ also inhibits the replication of HIV *in vitro*.[3]

There is a possible clinical analogy. Prior to anti-retroviral therapy (ART), HIV-positive pregnant women in Uganda taking CQ for concurrent malaria had reduced transmission of HIV to their newborns. Also, viral loads were far lower if HIV subjects were taking CQ, and the HIV infected children on concurrent CQ were well and lived longer.[4,5]

A randomised controlled trial (RCT) in 13 ART-naïve patients found CQ was associated with decreased memory CD8 T-cell activation, CD4 and CD8 T-cell proliferation and lipopolysaccharide levels compared with baseline, but there were no changes in plasma HIV RNA.[6] However, another RCT of HCQ in ART-naïve patients demonstrated no change in T-cell activation and proliferation, an increase in HIV RNA and a decrease in CD4 T-cell counts.[7] In a small non-randomised study of 20 patients receiving suppressive ART, HCQ administration was associated with a reduction in multiple markers of immune activation but no significant increase in CD4 T-cell recovery.[8]

HCQ or CQ could possibly stop the spread of Ebola, similar to HIV. Ebola infects dendritic cells, which display signals of infection on their surfaces to activate T lymphocytes that destroy other infected cells before the virus replicates further. Defective dendritic cells fail to give the right signal to T-cells to limit infection. Ebola works in part by inhibiting interferon: an Ebola protein, VP24, binds to and blocks a transport protein on the surface of immune cells that plays an important role in the interferon pathway.[6]

Finally, the recent emergence of the coronavirus MERS, as a serious threat to life in Asia and the Middle East, has led to investigation of possible Therapeutic Agents against this virus. The team of Dr. E.J. Snijder, in Holland, has identified benefit with four agents – chloroquine, chlorpromazine, loperamide, and lopinavir – out of 348 Food and Drug Administration-approved compounds.[9] CQ could be a useful first-line treatment for Ebola and warrants further investigation.

Conflict of interest: None.

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References

1 Isaacs D. Pandemic paranoia: a heretical view of Ebola and other infectious threats. *J. Paediatr. Child Health* 2015; **51**: 129–30.
2 Meng XW, Feller JM, Ziegler JB, Pittman SM, Ireland CM. Induction of apoptosis in peripheral blood lymphocytes following treatment in vitro with hydroxychloroquine. *Arthritis Rheum.* 1997; **40**: 927–35.
3 Sperber K, Kalb TH, Stecher VJ, Banerjee R, Mayer L. Inhibition of human immunodeficiency virus type 1 replication by hydroxychloroquine in T cells and monocytes. *AIDS Res. Hum. Retroviruses* 1993; **9**: 91–8.
4 Mandalakas A, Guay L, Musoke P, Carrol-Pankhurst C, Olness K. HIV status and delayed type hypersensitivity skin testing. *Pediatrics* 1999; **103**: 1–7.
5 Neely M, Kalyesubula I, Bagenda D, Myers C, Olness K. Cord blood chloroquine levels and HIV transmission in Ugandan infants. *Afr. Health Sci.* 2003; **3**: 61–7.
6 Xu W, Edwards MR, Borek DM. Ebola virus VP24 targets a unique NLS Binding site on karyopherin alpha 5 to selectively compete with nuclear import of phosphorylated STAT1. *Cell Host Microbe.* 2014; **16**: 187–200.
7 Murray SM, Down CM, Boulware DR *et al*. Reduction of immune activation with chloroquine therapy during chronic HIV infection. *J. Virol.* 2010; **84**: 12082–6.
8 Paton NI, Goodall RL, Dunn DT *et al*. Effects of hydroxychloroquine on immune activation and disease progression among HIV-infected patients not receiving antiretroviral therapy: a randomized controlled trial. *JAMA* 2012; **308**: 353–61.
9 De Wilde AH, Jochmans D, Posthuma CC *et al*. Screening of an FDA-approved compound library identifies four small-molecule inhibitors of Middle East respiratory syndrome coronavirus replication in cell culture. *Antimicrob. Agents Chemother* 2014; **58**: 4875–84.

Dear Editor,

A UNIQUE METHOD OF ORAL ULCERATION MANAGEMENT IN A PATIENT WITH PATHOLOGICAL TONGUE THRUST

We wish to draw your attention to a novel approach our maxillofacial team adopted when recently managing a case of oral ulceration for a 9-year-old girl with cerebral palsy.

We have no conflict of Interest.