Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

empirically, because of its activity against most of the causative filamentous fungi and its time-tested experience.[7,8,10] Newer agents may be useful when microbiological diagnosis is established (eg, voriconazole for *Aspergillus* spp, posaconazole for zygomycetes), although further studies are required.

Lastly, Van Damme and Hartman refer to noma (chancrum oris), a devastating necrotising destructive process of the face typically affecting young malnourished children in Africa. This condition has been presented in a recent excellent review by Baratti-Mayer and colleagues.[14]

We thank Van Damme and Hartman for their interest in our paper, and their comments which allowed us to elaborate upon the most important topic of rapidly progressive SSTIs.

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New insights into the antiviral effects of chloroquine

In a paper published 2 years ago in this journal, some of us described the potentially therapeutic benefits of the quinoline antimalarial chloroquine in viral diseases such as HIV-1/AIDS and severe acute respiratory syndrome (SARS).[1] Chloroquine/hydroxychloroquine has since been adopted to treat HIV-1-infected patients in clinical trials, and new insights into its antiviral activity have been obtained from in-vitro studies.

On the HIV/AIDS front, chloroquine (250 mg twice daily) has been administered to HIV-1-infected patients with baseline viral loads over 50 000 copies per mL, in combination with lamivudine (150 mg twice daily) and hydroxyurea (500 mg twice daily) in an ongoing clinical trial in India.[2] Ten out of 18 volunteers had an undetectable viral load at week 24.[2] The median drop in viral load was more than 2·0 log,[2] more than the median 1·5 log drop seen with a nucleoside reverse transcriptase inhibitor (NRTI) and hydroxyurea alone.[3]

These results are different from those of another trial in Singapore using didanosine (125–250 mg twice daily), hydroxyurea (500 mg twice daily), and hydroxychloroquine (200 mg twice daily, corresponding to 125 mg of chloroquine).[1] The median drop in viral load was 1·3 log, similar to that induced by a NRTI plus hydroxyurea. Follow-up of these patients at week 144 suggests that the value of hydroxychloroquine may lie in the maintenance of the effects of didanosine/hydroxyurea.[4]

The discrepancy between the two studies, besides differences in the design and patients enrolled, probably reflects the different dosages of chloroquine/hydroxychloroquine. Drops in viral load are reported to occur using daily doses of 800 mg of hydroxychloroquine,[1] corresponding to 500 mg of chloroquine (as used in the Indian study), but not using 250 mg of chloroquine daily,[5] corresponding to 400 mg of hydroxychloroquine (as adopted in the Singapore study). Chloroquine/hydroxychloroquine might thus be a valuable option to be tested in low-cost antiretroviral combinations, but correct dosages should be used, considering that the study

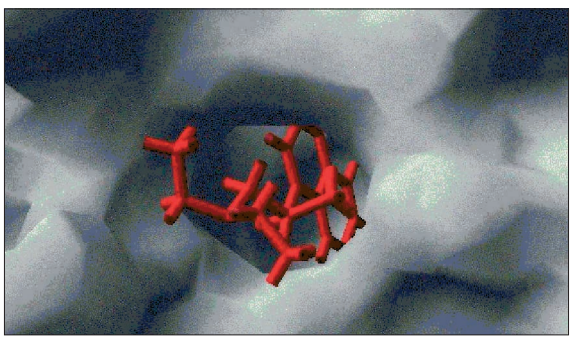

Figure: **Can chloroquine interact with sugar-modifying enzymes?**
This computer-assisted simulation of ligand/protein docking by use of the program GOLD[12] indicates that chloroquine (red) fits to the active site of UDP-N-acetylglucosamine 2-epimerase (grey). This evidence suggests that chloroquine could inhibit the enzyme that catalyses the rate-determining step in the sialic acid biosynthetic pathway.

participants should be regularly monitored to prevent retinopathy. Prospective randomised double-blind placebo studies are also needed to assess the contribution of chloroquine/hydroxychloroquine as part of an antiretroviral regimen. According to new in-vitro results, the antiretroviral effects of chloroquine are attributable to the inhibition of viral particle glycosylation.[6] These effects appeared to be specific, since the chloroquine concentrations effective in vitro neither affected any other step in HIV-1 replication nor were cytotoxic.[6]

Our hypothesis that chloroquine might inhibit replication of the SARS coronavirus[1] has been confirmed in two independent in-vitro studies.[7,8] Researchers at the Belgian Catholic University of Leuven found that chloroquine inhibited SARS coronavirus replication with a 50% effective concentration of 8·8 (SE 1·2) μmol/L, within the range of blood concentrations achievable during antimalarial treatment.[7] The dose inducing 50% cytostatic activity was much higher (261·3 [14·5] μmol/L). Time-of-addition experiments indicated that chloroquine affected an early stage of SARS coronavirus replication.[7] Researchers at the Centers for Disease Control and Prevention (Atlanta, GA, USA) reported potent anti-SARS coronavirus effects of chloroquine in vitro, attributable to a deficit in the glycosylation of the SARS coronavirus receptor ACE2.[8] Again, the antiviral drug concentrations were not cytotoxic. If animal models confirm these results, chloroquine might represent a valuable therapeutic option if SARS re-emerges.

The broad spectrum antiviral effects of chloroquine deserve particular attention in a time in which the world is threatened by the possibility of a new influenza pandemic, and the availability of effective drugs would be fundamental during evaluation of an effective vaccine. The effect of chloroquine against replication of Orthomyxoviridae has long been known.[9,10] Inhibitory effects of chloroquine on both type A and B influenza viruses have been described.[9,10] We are currently investigating the inhibitory effect of chloroquine on the H5N9/A/chicken/Italy/9097/97 avian influenza virus, recently isolated from poultry in Italy.[11] Depending on the viral challenging doses and the methods adopted to detect the antiviral effects, the inhibitory concentrations fell within the 0·5–10 μmol/L range—ie, clinically achievable in plasma during malaria treatment (LDT, AS, ID, RC, and AC, unpublished data). If these effects are confirmed, chloroquine would deserve to be tested against the H5N1 type A avian influenza virus, currently a matter of serious concern for public health.

As discussed above, glycosylation inhibition might represent a major mechanism for the antiviral effects of chloroquine, suggesting that specific interactions of chloroquine with sugar-modifying enzymes or glycosyltransferases may occur within human cells (figure). Chloroquine was recently shown to inhibit quinone reductase 2,[13] a structural neighbour of UDP-N-acetylglucosamine 2-epimerases,[14] which are involved in sialic acid biosynthesis. If chloroquine should indeed inhibit the biosynthesis of sialic acid, this effect could explain not only the effects of chloroquine on HIV and SARS coronavirus (sialic acid moieties are present in HIV-1 glycoproteins and SARS coronavirus receptor ACE2), but also the in-vitro effects on orthomyxoviruses (which use sialic acid moieties as receptors[15]). These effects deserve further investigation, in that they may lead to new strategies controlling the replication of several viruses.

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Postgraduate training in infectious diseases

I write in response to the article by Fiona Cooke and colleagues[1] on training in infectious diseases around the world. I would like to bring our efforts to initiate such a programme at the Infectious Diseases Institute (IDI) at Makerere Faculty of Medicine, Kampala, Uganda to the readers' attention. The IDI was built to carry out the programmes of the Academic Alliance for AIDS Care and Prevention in Africa, aimed at developing human capacity to fight HIV/AIDS and other infectious diseases in Africa. The alliance is made up of professors of medicine, paediatrics, and public health from Makerere (including Nelson Sewankambo, the medical school dean, Harriet Mayanja, Moses Kamya, Edward Mbidde, Roy Mugerwa, David Serwadda, Fred Wabire-Mangen, Philippa Musoke, and Elly Katabira) together with infectious diseases academic physicians from North America (Allan Ronald, Tom Quinn, Mike Scheld, Jerry Ellner, and myself). In 2004, Bob Colebunders from Antwerp joined the alliance, and Keith McAdam was recruited as the first IDI director. We have now trained more than 350 African physician trainers (from 15 African countries) in advanced HIV/AIDS care and prevention in a 1-month course in partnership with trainers from the Infectious Diseases Society of America. The programmes of the alliance were initially funded by a generous grant from Pfizer Inc and the Pfizer Foundation, under the leadership of Hank McKinnell.

We started our infectious diseases fellowship programme 4 years ago and our first trainee, Andrew Kambugu, completed his training last September and was recruited as a faculty member at IDI. We have three others currently in the programme. We have primarily used the American model which includes emphasis on developing clinical and investigational expertise that is currently mainly focused on HIV/AIDS. The trainees have completed their training in internal medicine or paediatrics and are mentored by members of the alliance and the director. We have also made experiences available in North America for training in microbiology (in Manitoba, Canada) and western clinical infectious diseases (in Salt Lake City, UT, USA). One of our current trainees is doing a paediatric infectious diseases rotation at Baylor (Houston, TX, USA) and another a tuberculosis epidemiology rotation in Atlanta, GA, USA. Our objective for this programme is to train the African infectious diseases academic leaders of tomorrow as part of our commitment to build human resources.

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