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.

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I declare that I have no conflicts of interest.

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Use of chloroquine in viral diseases

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In *The Lancet Infectious Diseases*, Paton and colleagues[1] report results of a clinical trial investigating chloroquine for prevention of influenza, which show that this antimalarial drug had no effect on disease acquisition and clinical course. Chloroquine, and its hydroxyl analogue hydroxychloroquine, became plausible candidates for treatment of several viral diseases after many reports of their in-vitro inhibitory effects on different viruses.[2] Although these effects proved highly reproducible,[2] the antiviral effects of chloroquine in vivo have been shown only in a mouse model for coronavirus infection.[3] The antiviral effect of hydroxychloroquine was shown in two clinical trials of individuals infected with HIV-1;[4,5] the results, however, could not be reproduced with an equivalent dose of chloroquine.[6]

Several possible reasons exist for the failure of translation of the in-vitro effects to in-vivo settings: narrow therapeutic indexes (ie, the ratio between the 50% cytotoxic concentration [CC_{50}] and the 50% antivirally effective concentration [EC_{50}]); EC_{50} in the micromolar range (about three orders of magnitude greater than that necessary to inhibit chloroquine-sensitive malaria parasites—the microorganisms against which the drug was originally prescribed); poor penetration in specific tissues; and high interstrain variability of the effects of chloroquine on influenza A viruses.[7] Maybe, in the future, chloroquine derivatives with improved pharmacokinetics will be able to bridge the gap between the in-vitro and in-vivo effects.

For treatment of RNA-virus infections, I think that monotherapy should be avoided because of the potential for rapid development of drug resistance. Therefore, chloroquine and hydroxychloroquine could still be considered for treatment in combination with other antiviral drugs. An effect that merits consideration is inhibition, by chloroquine, of some cellular proteins, including the P-glycoprotein and multidrug-resistance-associated proteins, which extrude drugs from the cells and other anatomic compartments.[8] Although current anti-influenza drugs act on extracellular or transmembrane targets, new intracytosolic drug targets in the viral life cycle are being explored.[9]

My colleagues and I proposed the use of chloroquine as a therapeutic agent for some viral infections (eg, SARS and AIDS; the pathogenesis of which is characterised by deleteriously strong or persistent immune activation).[2] Chloroquine is a well known immunomodulatory agent, as shown by its continued use for treatment of rheumatoid arthritis and other immune-mediated diseases.[2] In this context, poor efficacy of this drug against pandemic influenza disease severity shown by Paton and colleagues[1] can be explained not only by absence of an antiviral effect in vivo, but also by the fact that pandemic influenza shows, in most patients, a benign clinical course and is generally uncomplicated by immune-mediated damage.

In individuals with HIV/AIDS, chloroquine was repeatedly reported to be effective in counteracting

the deleterious immune activation associated with the disease.[2,4,6] A recent study by Murray and colleagues[6] showed that chloroquine significantly decreased expression of CD38 (a marker of treatment failure and progression to AIDS, which is associated with immune activation induced by viral replication) on CD8 T cells[10] and induced downmodulation of Ki67 (a marker associated with immune-activation-induced lymphocyte mitosis) on memory T cells;[11] in-vitro and in-vivo anti-inflammatory effects were in good agreement. One reason behind this agreement is suggested by a recent study of hydroxychloroquine,[12] which showed that the drug accumulates at high concentrations in lymphoid tissues of patients infected with HIV. These reproducible in-vivo effects of quionoline antimalarials could be used as, or added to, new strategies for restricting the HIV reservoir, which are aimed at counteracting the residual immune activation during antiretroviral therapy (favouring sustained viral replication in anatomic sanctuaries), and targeting activation or proliferation of central and transitional memory T cells harbouring silent copies of the HIV proviral DNA (contributing to maintenance of the virus's genome during treatment).[11] Notwithstanding the poor efficacy of chloroquine for influenza prevention, the results reported by Paton and colleagues[1] will help to address the process of drug repositioning for treatment of infectious diseases.

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I declare that I have no conflicts of interest.

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Syphilis, still a major cause of infant mortality

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In *The Lancet Infectious Diseases* today, Sarah Hawkes and colleagues[1] review the effect of interventions to increase the coverage of screening and treatment for syphilis in pregnancy on the uptake of testing and treatment, and on adverse pregnancy outcomes averted. This study is a timely reminder that syphilis has not disappeared, and remains a major, although entirely preventable, cause of death in newborn babies.

Syphilis is estimated to be responsible for almost 500 000 perinatal deaths per year in sub-Saharan Africa alone.[2] Many of these are stillbirths, which have been largely ignored by the global-health community. They are rarely counted, are not included in national statistics, or in estimates of the global burden of disease, and are not mentioned in the Millennium Development Goals (MDGs). *The Lancet*'s Stillbirths Series is a welcome attempt to redress the balance. Lawn and colleagues[3] estimated that 2·65 million stillbirths occur annually, 98% of them in developing countries. In northern Tanzania, 51% of stillbirths in women who had not been screened for syphilis during pregnancy could be attributed to syphilis after adjustment for other possible causes.[4]

In live born infants, most deaths from syphilis occur in the first weeks of life. As many countries make progress towards achieving MDG 4—to reduce mortality by two thirds in children younger than 5 years—neonatal mortality (in the first 4 weeks of life) remains high, now accounting for some 40% of the total mortality. Early neonatal mortality (in the first week of life) has been a