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Hence, testing remdesivir earlier in the disease course could be more relevant, and unpublished results from the PINETREE trial reported an 87% risk reduction for hospitalisation or death with a 3-day course of remdesivir compared with placebo.⁵ However, with the encouraging preliminary results of oral molnupiravir from the MOVE-OUT trial (NCT04575597), oral antivirals might be the preferred treatment option for outpatients, making intravenous alternatives less attractive.

Remdesivir could also be a candidate drug for carefully selected hospitalised patients, since the RECOVERY trial showed a survival benefit of the monoclonal antibody cocktail REGN-COV2 in seronegative patients.⁵ In seronegative individuals and immunocompromised patients in general, head-to-head comparisons between remdesivir and antiviral monoclonal antibodies could be an option. However, with emerging variants, testing combinations of monoclonal antibodies and other antivirals, including remdesivir, could be even more relevant, given the demonstrated effect of each compound.

Before moving ahead with new trials, it should be noted that the final report from the Solidarity trial is yet to be published. In our view, there is now an urgent need for an individual-level meta-analysis based on existing trials, including consolidated data from the Solidarity trial. Such a meta-analysis is planned and will hopefully clarify the role of remdesivir in hospitalised patients and help identify the potential need for additional trials.

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Clindamycin-resistant *Streptococcus pyogenes* in Chinese children

The Correspondence by Bryan White and Emily Siegrist¹ about clindamycin-resistant group A streptococcal infection attracted much attention in the USA. White and Siegrist argued that although the findings from some studies suggest a decrease in mortality from group A streptococcal infections

in the USA, serious infections caused by clindamycin non-susceptible invasive group A streptococcus are increasing due to expansion of several *emm* types.² Therefore, we hope to provide some information about clindamycin-resistant group A streptococcus in China to compare its prevalence in different areas.

First, unlike in the USA and other countries and regions, the resurgence of group A streptococcal infection in China is mainly manifested in non-invasive group A streptococcal infections. Rheumatic fever rarely occurs. Next, in China, the resistance rate of group A streptococcus against clindamycin and macrolides in both adults and children has been very high since the 1990s but has varied by geographical location and time period (appendix). Chinese isolates mainly harbour the *ermB* resistance gene, with the constitutive macrolide, lincosamide, and streptogramin B (cMLS_B) resistance phenotypes. In China, clindamycin was not thought to be an appropriate medical intervention.

Finally, the high rate of resistance to clindamycin cannot be attributed to its clinical use because clindamycin was rarely used in paediatric patients in Western Pacific countries (including China).³ Previous studies also suggested cross-resistance between clindamycin and erythromycin.⁴ Cross-resistance to cMLS_B antibiotics is mainly mediated by the *erm* genes, and various mechanisms are involved in streptogramin B resistance.⁵

In view of the existing data, there is high resistance to clindamycin and macrolides such as erythromycin; therefore, these treatments should not be recommended as an adjuvant treatment for children with β -lactam antibiotic allergy and group A streptococcal infection in China.

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Chloroquine-resistant *Plasmodium falciparum* in Pakistan

In October, 2021, *The Lancet Infectious Diseases* published an Editorial¹ that presented the new strategies for combating malaria in endemic regions. However, over the past three decades in Pakistan unwavering efforts from the national Malaria Control Program have been unable to eliminate malaria, and it is still a major public health

concern. Around 205 million people (98% of Pakistan's population) live in malaria-endemic areas, with 1 million new cases and 50000 deaths reported annually.² *Plasmodium falciparum* cases in Pakistan are proliferating, posing a severe conundrum to the resource-constrained health sector and an alarming threat to the country's malaria eradication programme. Chloroquine, a formerly highly efficacious and cost-effective drug against *P falciparum*, has been banned for the treatment of *P falciparum* malaria in Pakistan because of the high incidence of chloroquine resistance.³

Reduced drug pressure resulted in substantial restoration of chloroquine susceptibility in malaria-endemic regions, particularly in Africa.⁴ Nevertheless, since 1990, Pakistan has seen a continuous plateau phase of chloroquine resistance (appendix p 1). This plateau can be attributed to four factors. First, malaria caused by *P falciparum* has the same clinical presentation as malaria caused by the widespread species *Plasmodium vivax*, leading to false treatment regimens. Second, poor or presumptive diagnosis by untrained laboratory personnel, who can misdiagnose *P falciparum* and mixed infection, lead to improper medication. Third, the migration of Afghan refugees and other internal displacement of people from war zones and highly endemic malaria areas to other parts of the nation present challenges for surveillance. Finally, in malaria-endemic regions, the massive amount of agricultural land available for mosquito breeding sites, the scarcity of insecticides and bednets and people's reluctance to use them, and poor sanitation and stagnant water impede elimination.

Pakistan seems to be entering an age of advanced drug resistance in which monotherapies are essential preventive measures that are ineffective for confronting the mutant malaria species.⁵ After 15 years of chloroquine withdrawal for the treatment of *P falciparum*, there is no substantial reversal of chloroquine susceptibility observed in Pakistan. Policy makers should consider this overlooked pattern of malaria when reformulating *P falciparum* control strategies and initiating research projects to gain detailed insight into drug-resistant genes through random sampling of endemic areas; otherwise, malaria in Pakistan will become more deadly.

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