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Authors' reply

We thank M Teresa Galán-Puchades for her interesting comments. In our study,[1] we considered the worms as a whole to be the relevant entity, because the cutaneous and ocular manifestations of onchocerciasis result from a combination of immune reactions against *Wolbachia* spp (mobilisation of neutrophils), and filarial antigens (mobilisation of eosinophils).[2] Consequently, it seemed artificial to consider the partners of this symbiotic relationship separately.

Galán-Puchades hypothesises that *Wolbachia* spp released during the natural death of *O volvulus* (adults or microfilariae) induce inflammatory processes that trigger epilepsy, which would indeed justify distinguishing wolbachia from the worm in our study. Should this hypothesis be true, the release of *Wolbachia* spp into the blood after treatment with diethylcarbamazine or ivermectin (a demonstrated occurrence)[3] would, as Galán-Puchades suggests, induce an epidemic of seizures after mass treatment with these drugs. However, such an event has never been reported with either drug, even in populations with extremely high microfilarial densities (eg, the Vina valley in northern Cameroon). On the contrary, a decrease in seizure frequency was reported after the first ivermectin distribution in the Kabarole focus, Uganda.[4] Furthermore, the nodding syndrome epidemic in northern Uganda, which Galán-Puchades refers to, started in 2000, whereas war in that region delayed mass ivermectin treatment until 2009. Some factors have been proposed[5] to explain the epidemic pattern of nodding syndrome in Uganda and South Sudan, but these hypotheses are difficult to test.

Galán-Puchades suggests that the inter-foci variability in prevalence and severity of onchocercal ocular manifestations is due to some parasite populations harbouring higher wolbachia burdens. A study[6] published in 2017, in different foci in four west-African countries, showed indeed that this burden can vary considerably between and within foci; however, this variability does not correlate with the ecotype of the focus, even though savanna onchocerciasis causes more blindness than forest onchocerciasis. These results certainly deserve to be complemented by analysis of parasites from areas where a strong association between onchocerciasis and epilepsy has been shown.

As mentioned by Galán-Puchades, a study is ongoing to determine whether doxycyline treatment leads to reduction in symptoms and perhaps reversal of the course of nodding syndrome in affected children. However, doxycycline mass treatment to prevent onchocerciasis-associated epilepsy or nodding syndrome, as Galán-Puchades recommends, does not appear feasible because this requires compliance with daily dosing for 5 weeks to achieve macrofilaricidal effects. Importantly, doxycycline is contra-indicated in children younger than 8 years, and the physio-pathogenic mechanisms that put children with high *O volvulus* microfilaridermia at higher risk of developing epilepsy probably appear before this age.

We declare no competing interests.

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Cefiderocol for treatment of complicated urinary tract infections

Co-trimoxazole, fluoroquinolones, and cephalosporins have been used to treat almost all kinds of complicated urinary tract infections, but this golden age has come to an end. Worldwide, an increase in resistant uropathogens, including those resistant to carbapenems, has been observed.[1,2]

Several new drugs or drug combinations are in development or have been made available, such as new or old cephalosporins or carbapenems combined with new or old β-lactamase inhibitors (ceftolozane-tazobactam, ceftazidime-avibactam, meropenem-vaborbactam, and imipenem-cilastatin-relebactam), new aminoglycosides (plazomicin), and new fluoroquinolones (finafloxacin).

Another new drug is cefiderocol, the first siderophore-antibiotic conjugate to reach late stage clinical testing, which was developed for treatment of complicated urinary tract infections.[3] Siderophore antibiotics bind to free iron and use the bacterial active iron transport channels to cross the outer membrane of Gram-negative bacteria and reach the periplasmic space. In