## Diagnosis and treatment of human sparganosis

I read with interest the Clinical Picture by Hong Li and colleagues[1] describing a human case of ocular sparganosis. Sparganosis is a human parasitation caused by the plerocercoid larvae of tapeworms belonging to the *Spirometra* genus. Humans acquire the disease either orally or by active penetration of the larvae. The oral route involves the ingestion mainly of raw or undercooked snakes and frogs infected with the plerocercoid larvae, as well as the accidental ingestion of microscopic water fleas infected by the procercoid larvae while drinking. For particular curative practices that include the use of snakes and frogs as poultices, any plerocercoid larvae infecting the animals can actively penetrate the individual through wounds or the eye.

The authors identify the species causing the case of ocular sparganosis (*Spirometra mansoni*) only by histopathological examination.[1] However, morphology does not allow specific diagnosis because plerocercoid larvae do not have specific morphological features. Histopathology can confirm only that the worm extracted from the eye is a plerocercoid-type larva. The most rapid methods for the specific diagnosis are molecular techniques—for instance, PCR restriction fragment length polymorphism.[2]

Surgical removal is the required treatment when the parasite is accessible, as in this case. According to the authors, after the worm extraction, albendazole was given to prevent dissemination of the parasites.[1] In my opinion, the pharmacological treatment would be needed only in the case that the larval scolex had remained in the patient's eye, because the worm grows (via a process known as strobilation) at the neck zone located behind the scolex.[3] Figure 2 of their supplementary material shows the removed worm with an attenuation at one end. The scolex is located in this thinner part. Assessing whether the worm had or did not have a scolex would have been easy under a microscope. If the extracted worm had a scolex, albendazole would not have been needed. Only *Sparganum proliferum* has the ability to disseminate by branching and budding.[3] Apparently, this form of dissemination was not the case as the extracted plerocercoid did not show signs of either of these two processes. Furthermore, a point to consider is that in potential endemic areas of *Taenia solium* cysticercosis such as China—the patient's country in this case—asymptomatic human neurocysticercosis can become symptomatic because of the cysticidal effect of drugs such as praziquantel and albendazole,[4] which therefore should be used under constant medical supervision and only if strictly necessary.[5]

I declare no competing interests.

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1 Li H, Hu J, Yang P. A 50-year-old woman with a recurrent eyelid swelling. *Lancet Infect Dis* 2019; **19:** 338.
2 Liu Q, Li M-W, Wang Z-D, Zhao G-H, Zhu X-Q. Human sparganosis, a neglected food borne zoonosis. *Lancet Infect Dis* 2015; **15:** 1226–35.
3 Schmidt GD, Roberts LS. Foundations of parasitology, 7th edn. New York, NY: McGraw-Hill, 2006.
4 White AC Jr, Coyle CM, Rajshekhar V, et al. Diagnosis and treatment of neurocysticercosis: 2017 Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH). *Am J Trop Med Hyg* 2018; **98:** 945–66.
5 Flisser A, Madrazo I, Plancarte A, et al. Neurological symptoms in occult neurocysticercosis after single taeniacidal dose of praziquantel. *Lancet* 1993; **342:** 748.

## Sensitivity and negative predictive value for a rapid dengue test

In 2016, WHO recommended Dengvaxia, the first-ever licensed dengue vaccine, for use in children aged 9 years or older residing in high-burden settings. The vaccine had shown efficacy against all four dengue serotypes in two large phase 3 trials.[1,2] A safety signal of an excess risk of severe dengue was detected in vaccinated children aged 2–5 years.[3] This finding prompted further analyses with a new immunological assay to assess whether the risk was associated with age per se or was due to a higher proportion of children in this age group having had no previous dengue infections. These analyses[4] showed that although the vaccine offered substantial protection among children who had been previously infected with dengue, dengue-naive vaccinees were at increased risk of dengue hospitalisation and severe dengue during the 5-year trial follow-up compared with similar children in the placebo group. This effect had been previously postulated in mathematical models.[5]

In response to this new evidence, WHO revised their previous advice and now recommends a pre-vaccination screening strategy to avoid the vaccination of dengue-naive children.[6] In the absence of a licensed rapid diagnostic test to detect previous dengue infection, discussions around a target product profile for such a test have focused on the need for high test specificity to limit the number of false-positive test results, and thus minimise the risk of vaccinating dengue-naive children. However, increasing the specificity of a test typically decreases its sensitivity, and a test with poor sensitivity would leave many unvaccinated who would have potentially benefited from vaccination.

Isabel Rodriguez-Barraquer and colleagues[7] argue for the use of the positive predictive value (PPV) of a

test as a unifying indicator for an acceptable safety profile of a pre-vaccination screening strategy. A high PPV ensures that a high proportion of individuals who test positive are not truly dengue-naive. The required sensitivity to achieve a high PPV will depend on the seroprevalence in the population on which the test is done and on the test specificity. Charts can be used to determine—for tests with different specificities and in different seroprevalence situations—the minimum sensitivity needed to ensure that, for example, less than 10% of test positives are actually dengue-naive (appendix).

See Online for appendix

We think that an additional reasonable criterion for the selection of a diagnostic test is that individuals who are deemed ineligible for vaccination as a result of the test should be at a lower risk of hospitalised or severe dengue disease if they are left unvaccinated than if they are vaccinated.

High sensitivity ensures a low proportion of misclassifications among those who test negative, particularly in high-prevalence settings. In the Dengvaxia trials,[4] the 5-year cumulative incidence of dengue hospitalisation in vaccinees aged 9 years or older was reduced by 1·50 percentage points relative to the control group for seropositive participants (1·88% [95% CI 1·54–2·31] in seropositive controls *vs* 0·38% [0·26–0·54] in seropositive vaccinees), and increased by 0·48 percentage points relative to the control group for seronegative participants (1·09% [0·53–2·26] in seroponegative controls *vs* 1·57% [1·13–2·19] in seronegative vaccinees). Hence, if more than 25% of individuals who test negative in a pre-vaccination screening strategy are misclassified (ie, are not dengue-naive) then, on average, the individuals with a test-negative result would benefit from vaccination (appendix). In other words, a meaningful rapid diagnostic test will need a negative predictive value of at least 75%. This implies the need for high test sensitivity in highly endemic settings because of the few true seronegative individuals (appendix).

As manufactures develop rapid diagnostic dengue tests to achieve an optimal balance between sensitivity and specificity they will need to prioritise specificity to ensure the safety of vaccinees. However, we argue that it is important that test sensitivity is of the order of 90% (appendix) or more as otherwise those who test negative might be, on average, at higher risk of hospitalised or severe dengue than they would be if they were vaccinated.

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1 Capeding MR, Tran NH, Hadinegoro SRS, et al. Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial. *Lancet* 2014; **384:** 1358–65.
2 Villar L, Dayan GH, Arredondo-García JL, et al. Efficacy of a tetravalent dengue vaccine in children in Latin America. *N Engl J Med* 2015; **372:** 113–23.
3 Hadinegoro SR, Arredondo-García JL, Capeding MR, et al. Efficacy and long-term safety of a dengue vaccine in regions of endemic disease. *N Engl J Med* 2015; **373:** 1195–206.
4 Sridhar S, Luedtke A, Langevin E, et al. Effect of dengue serostatus on dengue vaccine safety and efficacy. *N Engl J Med* 2018; **379:** 327–40.
5 Ferguson NM, Rodriguez-Barraquer I, Dorigatti I, Mier-y-Teran-Romero L, Laydon DJ, Cummings DAT. Benefits and risks of the Sanofi-Pasteur Dengue vaccine: modeling optimal deployment. *Science* 2016; **353:** 1033–36.
6 Wilder-Smith A, Hombach J, Ferguson N, et al. Deliberations of the Strategic Advisory Group of Experts on Immunization on the use of CYD-TDV dengue vaccine. *Lancet Infect Dis* 2018; **19:** e31–38.
7 Rodríguez-Barraquer I, Salje H, Cummings DA. Dengue pre-vaccination screening and positive predictive values. *Lancet Infect Dis* 2019; **19:** 132–34.

## Taiwan commits to eliminating hepatitis C in 2025

I read with great interest Talha Burki's report[1] "Eliminating hepatitis C", in which he described situations in Egypt, Pakistan, Mongolia, China, Australia, and Rwanda. He reiterated that drugs alone are not enough for elimination, and that countermeasures, such as screening and accessibility of harm reduction services, are also needed. Elimination of chronic viral hepatitis is an ambitious task that needs national and international efforts, as was indicated by WHO.[2]

Because of its heavy disease burden, Taiwan has been fighting hepatitis B since the late 1970s,[3] with successful results.[4,5] Despite the fact that Taiwan is not a member of WHO and, for political reasons, WHO never helps Taiwan in the control of infectious diseases, Taiwan still took serious actions to follow the WHO guidelines on control of viral hepatitis.[3] When the World Health Assembly adopted the Global Health Sector Strategy on viral hepatitis in 2016, it immediately caught the attention of the Taiwanese people and government, and efforts towards the elimination of chronic hepatitis C were seriously considered. After 2 years, the efforts from experts, public health officers, legislators, and the government leaders have culminated in a consensus of reaching the WHO goals in 2025—ie, 5 years earlier than the 2030 deadline set by WHO. Accordingly, the Taiwan Hepatitis C Policy Guideline 2018–2025[6] was approved and published at the beginning of 2019. The government will provide US$1·7 billion in the coming 8 years for the control of hepatitis C. Actions will include lowering the barriers of