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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Correspondence

Risk of Strongyloides Hyperinfection Syndrome when prescribing dexamethasone in severe COVID-19

Dear Editor,

Dexamethasone reduces mortality in patients hospitalized with moderate and severe COVID-19 infection [1]. In this context there is a need to consider asymptomatic Strongyloides infection in patients undergoing immunosuppression with dexamethasone, to avoid precipitating Strongyloides Hyperinfection Syndrome (SHS). There are now two published case reports of SHS in COVID-19 patients immunosuppressed with dexamethasone and tocilizumab [2,3] but this is likely to underestimate the incidence of this event.

Strongyloides stercoralis, a parasitic nematode infection endemic in tropical and subtropical regions, is estimated to infect 30 to 100 million people worldwide. There are also foci of Strongyloides endemicity in temperate regions including Japan, Italy, Australia and the USA. In high income countries, high risk populations include migrants, refugees, travellers and ex-prisoners of war. Strongyloides infection occurs when soil-dwelling filariform larvae penetrate the skin and migrate to the small intestine. There they mature to adulthood, embed in the submucosa, and produce eggs by parthenogenesis. Rhabditiform larvae, released from eggs, are passed in the stool, but can also develop into infective filariform larvae whilst still within the gut, resulting in autoinfection. It is this unusual property that allows infection to persist for decades and cause overwhelming infection if people become immunosuppressed later in life.

Strongyloidiasis is often asymptomatic in immunocompetent adults, but may present with mild gastrointestinal or respiratory symptoms, or with larva currens, a rapidly moving pruritic linear skin eruption. In patients proven to have strongyloidiasis by microscopy or culture, 77% of patients have eosinophilia and 81% have positive serology [4]. However, microscopy and culture are frequently negative in asymptomatic infection. If these patients become immunosuppressed, most commonly with corticosteroids, chemotherapy or HTLV1 infection, hyperinfection may occur. Uncontrolled proliferation and dissemination of the parasite presents with fever, respiratory and gastrointestinal symptoms as well as episodes of Gram-negative sepsis or meningitis. At this stage, eosinophilia is often absent, serology may be negative, but respiratory secretions and stools demonstrate larvae. SHS case fatality rate is reportedly 100% if untreated, reduced to 47% in those treated with ivermectin. Fatal hyper infection has been reported following short courses of low dose glucocorticoid treatment and with single high doses of dexamethasone.

In the UK, admission to critical care with COVID-19 is most common in south Asian, Black and other ethnic minority groups. Severe Strongyloides infection is commonest in migrants from Asia and sub-Saharan Africa or other tropical regions. Clinically, it is difficult to distinguish between these conditions:

Severe COVID-19 produces cough (68.9%), fever (71.6%), dyspnoea (71.2%) and diarrhoea (20%), whilst SHS results in cough, fever (80.8%), dyspnoea or wheeze (88.6%) gastrointestinal symptoms (71.2%) and disseminated larva currens (rash). They also share some important complications: Respiratory failure, secondary bacterial infection, renal failure and venothrombotic events in severe COVID-19 infection; shock, respiratory failure and Gram negative sepsis in SHS. Bilateral lung infiltrates are seen in both conditions.

Furthermore, post mortems are not routinely performed in COVID-19 patients; it is therefore quite possible that SHS has already been overlooked in fatal cases of COVID-19 infection.

To prevent this, we propose a risk assessment and screening algorithm for Strongyloides, in COVID-19 patients with risk exposures (Fig. 1). Patients deemed at high risk (migrants with high risk exposure) may need empirical treatment with ivermectin, which has an efficacy of 85% as a single dose [5]. Those at potential, but not high risk, should be monitored and if deteriorating on immunosuppression, urgent screening with microscopy of stool, respiratory secretions, and charcoal culture for Strongyloides larvae should be undertaken. Serology should also be performed, but results are not usually available within 24 hours.

Stauffer et al. recently proposed a screening and treatment protocol for Strongyloides in COVID-19 patients [6]. We welcome their proposal but suggest more focused screening and treatment for those at the highest risk of Strongyloides infection and SHS. The proposed broad screening of all SARS-CoV PCR positive patients including outpatients with mild infection; those not requiring immunosuppression; and even patients without SARS-CoV-2 infection would require significant resource and may overburden services and supplies of anti-parasitic agents.

In summary, Strongyloides infection is common, in particular in tropical and subtropical regions and in travellers, migrants and prisoners of war who have spent time in these areas. Infection is often asymptomatic. COVID-19 patients with undiagnosed Strongyloides infection undergoing immunosuppression are at risk of developing SHS.

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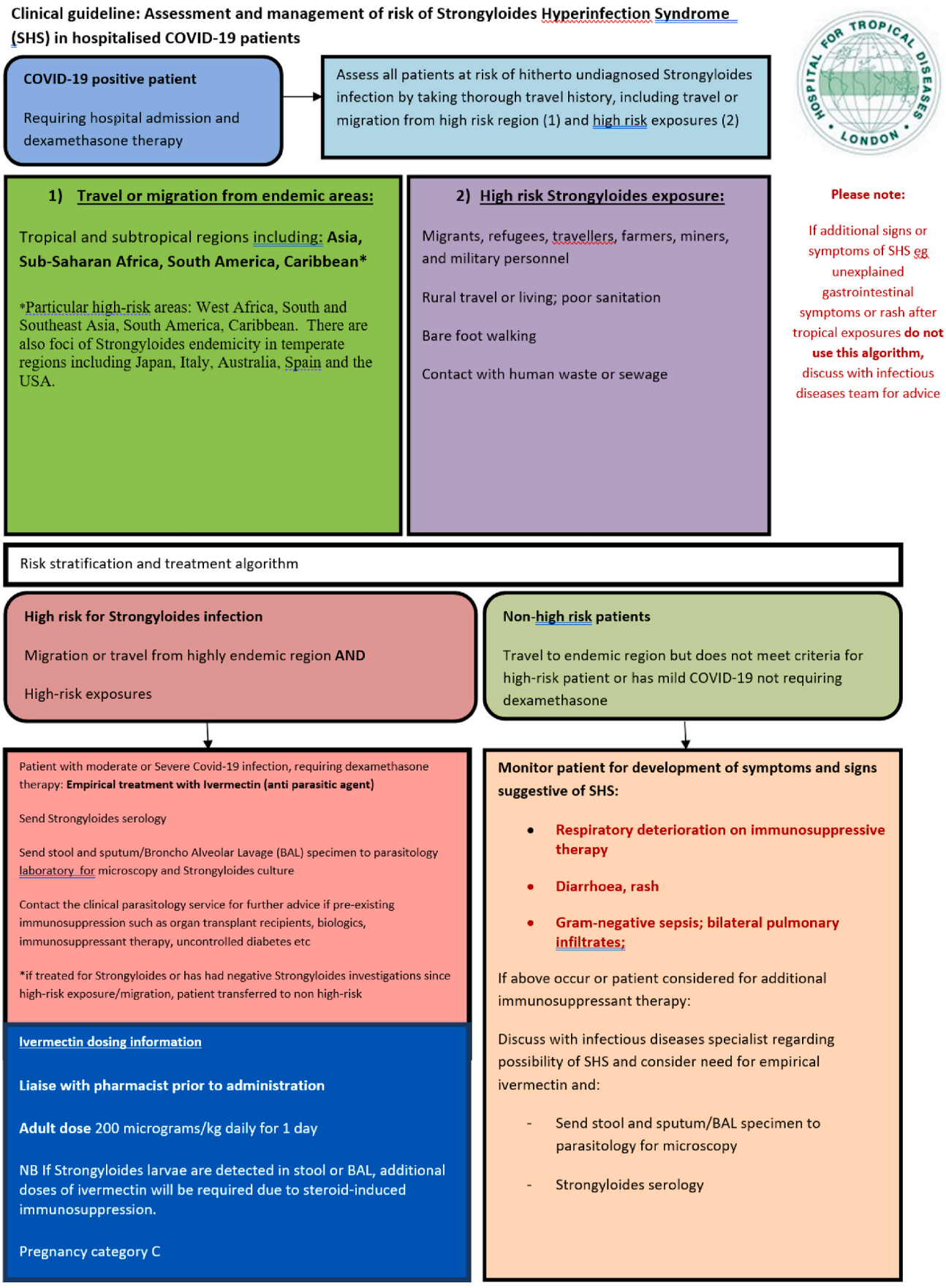

Fig. 1. Risk Assessment and Screening Algorithm.

Declaration of competing interest

The authors have no competing interests to declare.

References

[1] Patel SK, Saikumar G, Rana J, Dhama J, Yatoo MI, Tiwari R, Rodríguez-Morales AJ, Dhama K. Dexamethasone: a boon for critically ill COVID-19 patients? Trav Med Infect Dis 2020 Sep-Oct;37:101844. https://doi.org/10.1016/j.tmaid.2020.101844.

[2] Lier AJ, Tuan JJ, Davis MW, Paulson N, McManus D, Campbell S, Peaper DR, Topal JE. Case report: disseminated strongyloidiasis in a patient with COVID-19. Am J Trop Med Hyg 2020 Oct;103(4):1590–2. https://doi.org/10.4269/ajtmh.20-0699.

[3] Marchese V, Crosato V, Gulletta M, Castelnuovo F, Cristini G, Matteelli A, Castelli F. Strongyloides infection manifested during immunosuppressive therapy for SARS-CoV-2 pneumonia. Infection 2020 Sep 10:1–4. https://doi.org/10.1007/s15010-020-01522-4.

[4] Ming DK, Armstrong M, Lowe P, Chiodini PL, Doherty JF, Whitty CJM, McGregor AC. Clinical and diagnostic features of 413 patients treated for imported strongyloidiasis at the hospital for tropical Diseases, London. Am J Trop Med Hyg 2019 Aug;101(2):428–31. https://doi.org/10.4269/ajtmh.19-0087.

[5] Buonfrate D, Salas-Coronas J, Muñoz J, Maruri BT, Rodari P, Castelli F, Zammarchi L, Bianchi L, Gobbi F, Cabezas-Fernández T, Requena-Mendez A, Godbole G, Silva R, Romero M, Chiodini PL, Bisoffi Z. Multiple-dose versus single-dose ivermectin for Strongyloides stercoralis infection (Strong Treat 1 to 4): a multicentre, open-label, phase 3, randomised controlled superiority trial. Lancet Infect Dis 2019 Nov;19(11):1181–90. https://doi.org/10.1016/S1473-3099(19)30289-0. Epub 2019 Sep. 23.

[6] Stauffer WM, Alpern JD, Walker PF. COVID-19 and Dexamethasone: a potential strategy to avoid steroid-related Strongyloides hyperinfection. J Am Med Assoc 2020;324(7):623–4.

Angus De Wilton, Laura E. Nabarro, Gauri S. Godbole, Peter L. Chiodini*
Hospital for Tropical Diseases, University College Hospitals London NHS Foundation Trust, London, United Kingdom

Aileen Boyd, Katherine Woods
Homerton University Hospital NHS Foundation Trust, London, United Kingdom
E-mail addresses: aileen.boyd@nhs.net (A. Boyd), katherine.woods3@nhs.net (K. Woods).

* Corresponding author. Department of Clinical Parasitology, Hospital for Tropical Diseases, University College Hospitals London NHS Foundation Trust, London, United Kingdom.
E-mail addresses: angus.dewilton@nhs.net (A. De Wilton), laura.nabarro@nhs.net (L.E. Nabarro), gauri.godbole@nhs.net (G.S. Godbole), p.chiodini@nhs.net (P.L. Chiodini).