CLINICAL GUIDELINE TITLE

TITLE: *Strongyloides stercoralis* : Protocol for treatment in patients with Human T-lymphotropic virus type 1 (HTLV-1)

1) SUMMARY

Positive serology for Strongyloides

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Assess clinical status of patient

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Dose as below

Clinical Status	1 Dose on each of the following days				
	1	2	15	16	Notes
Normal Immunity	✓		✓		
Immunocompromised, but asymptomatic	✓	✓	✓	✓	
Immunocompromised and symptomatic	✓	✓	✓	✓	Consider further doses.*
Hyperinfection	Daily dosage, minimum 2 weeks.*				
Pregnancy	✓		✓		In second or third trimester. Repeat after delivery.

1 Dose: Approximately 200 micrograms Ivermectin per kilogram body weight p.o. See Table 1.

* Liaise with Professor Chiodini's Team at the Hospital for Tropical Diseases, London

2) INTRODUCTION

This is an update on treatment due to new available evidence.

3) DEFINITIONS

Strongyloides stercoralis : A human parasitic roundworm infection common in tropical and subtropical regions, which is unique for its ability to cause autoinfection of the human host, and therefore persists for many years, and can act as an opportunistic infection in immunosuppressed patients.

Strongyloides Hyperinfection syndrome : In HTLV-1 infection, or in immunosuppressed patients, accelerated autoinfection results in pulmonary or gastrointestinal disease.

Disseminated strongyloidiasis : Larvae migrate away from pulmonary and gastrointestinal systems to other organs. This is usually associated with bacterial sepsis and multiorgan failure.

4) SCOPE
(Identify which staff, department and patient this relates to)
This guidelines relates to the National Centre for Human Retrovirology (NCHR)where patients with HTLV infection are managed.

5) FULL GUIDELINE

National Centre for Human Retrovirology (NCHR)

Protocol for treatment of *Strongyloides stercoralis* in patients with HTLV infection

Based on advice from Professor Chiodini, Hospital for Tropical Diseases, London.

Scope

This provides guidance to those working within the NCHR on the treatment of *Strongyloides stercoralis* in patients with HTLV-1infection.

Background

Strongyloides stercoralis is an intestinal nematode that is more common in tropical and subtropical regions of the world. In North America, Latin America, Africa and Southeast Asia, the infection is endemic. Non-infectious larvae are found in humid soil in hot regions. In an unfavourable environment, infectious larvae develop which can penetrate human skin, and spread via blood to the alveoli, migrate to the epiglottis and are swallowed into the intestines. Here, they are unique in being able to transform into infectious larvae which can penetrate the gut and re-enter the circulation to reinfect the host and thus persist for many years. Enhanced autoinfection occurs in HTLV-1 infection and immunosuppression and can lead to hyper-infection syndrome which carries a high mortality. Acute infection is usually asymptomatic, but may result in urticarial tracks with severe pruritus, known as ground itch. Chronic infection is also usually asymptomatic. However, migration of larvae intradermally can also present as larva currens (‘running larvae’) which is characterised by migrating short linear erythematous papules, usually in the anal margin, buttocks or upper thighs. Other symptoms include recurrent dry cough, wheeze and dyspnoea or abdominal pain and non-bloody diarrhoea due to pulmonary and gastrointestinal involvement respectively. Investigations may show a mild leucocytosis and a moderate eosinophilia. Disseminated strongyloidiasis, which involves migration of the organism outside the pulmonary and gastrointestinal tract, results in oedematous duodenitis and colitis causing vomiting and diarrhoea which may be bloody and contain mucus. Malabsorptionoccurs leading to fluid and electrolyte disturbance. In later stages, paralytic ileus appears with abdominal distension. Presence of larvae in the lungs may cause pulmonary haemorrhage and respiratory failure. Bacteraemia, septicaemia,andmeningitis may also occur due to bacterial dissemination. Investigations may not show an eosinophilia. The mortality rate may be up to 90%.

There is conflicting data on whether Strongyloides infection is more common in those with HTLV-1 infection. This is due in part to it being present endemically in the same regions where HTLV-1 is found, and also to differences in methods of diagnosing infection. However, in those with disseminated infection, HTLV-1 co-infection has been found in 85%. (1,2)

All patients at the NCHR with HTLV-1 are screened for co- infection with S*trongyloides stercoralis* at their initial assessment, and if positive, require treatment.

This is an update on treatment due to new available evidence.

Diagnosis

Stool microscopy for ova, cysts and parasites has low sensitivity for detecting *S stercoralis* (around 50%) because of intermittent larval excretion and low infectious burden(3). Serological testing for IgG to larval antigen is a more sensitive tool, and is used at the NCHR. However, in the presence of other helminthic infections there is a risk of a false positive result owing to cross reactivity.

Treatment

Ivermectin (STROMECTOL) Approximately 200 micrograms per kilogram body weight p.o. on days 1 and 15. See Table 1. Take on an empty stomach with water.

There is a named patient formulation for intravenous use. This is not licensed for human use and takes at least 2 working days to order. All requests should be directed to one of the specialist pharmacists.

Table 1. Dosage Guidelines for ivermectin for Strongyloidiasis (4)

Body Weight (kg)	Number of 3mg tablets required for single oral dose
15-24	1 tablet
25-35	2
36-50	3
51-65	4
66-79	5
≥ 80	200mcg/kg. Round up or down to the nearest 3 mg tablet.

Normal immunity: Dose on day 1 and 15

Immunocompromised but asymptomatic: Dose on day 1, 2, 15, 16

Immunocompromised and symptomatic: Dose on day 1, 2, 15, 16. Consider further doses depending on clinical and laboratory response after discussion with Professor Chiodini's team.

Hyperinfection Syndrome: Daily dosage and follow clinical and laboratory response. Regular stool microscopy is required. Daily dosing should continue until 2 weeks after the last positive stool sample to cover an autoinfection cycle. Management will also involve antibiotic treatment for systemic Gram negative bacterial sepsis, multiple organ support, and reduction of immunosuppression where possible. Liaise with Professor Chiodini's team.

Pregnancy: Dose on day 1 and 15 in the second or third trimester. Repeat this regimen after delivery.

Pregnancy category C. There are no adequate and well-controlled studies in pregnant women. Animal reproduction studies have shown an adverse effect on the fetus. Its use is off license in pregnancy.

Ivermectin is excreted in human milk in low concentrations. Treatment of mothers who intend to breast-feed should only be undertaken when the risk of delayed treatment to the mother outweighs the possible risk to the newborn.

Side Effects of Ivermectin

Ivermectin is generally well tolerated with few adverse side effects.

Uncommon (≥ 1/1,000 to < 1/100) dizziness, pruritus, diarrhoea, nausea.

Rare (≥ 1/10,000 to < 1/1,000) fatigue, abdominal pain, anorexia, constipation, vomiting, vertigo, tremor, rash, urticarial

Alternative regimen

In patients who are unable to tolerate ivermectin, albendazole is a reasonable alternative, although cure rates in clinical trials were inferior. In one recent study a course of albendazole 400 mg twice daily for seven days produced a cure rate of 63.3% (5).

Drug Interactions

In vitro studies have shown that ivermectin is primarily metabolised by CYP3A4. Drugs that affect these enzymes may affect concentrations of ivermectin, but there is no data on these interactions, and any clinical significance of this is unknown.

Follow up serology: Re-test 1 year after treatment in all patients.

This protocol replaces the previous regimen of:

Ivermectin 200microg/kg daily for 2 days followed by albendazole 400mg bd for 3 days

References

1. Gotuzzo E, Terashima A, Alvarez H et al. *Strongyloides stercoralis* hyperinfection associated with human T cell lymphotropic virus type-1 infection in Peru. *Am J Trop Med Hyg*, 60(1), 1999 146-149.

2. Carvalho E, Porto D. Epidemiological and clinical interaction between HTLV-1 and *Strongyloides stercoralis*. *Parasite Immunology*;2004,26,487-497.

3. Greaves D, Coggle S, Pollard C et al. *Strongyloides stercoralis* infection. BMJ 2013;347;doi:10.1136/bmj.f4610

4. Stromectol Merck & Co. Accessed at https://www.merck.com/product/usa/pi_circulars/s/stromectol/stromectol_pi.pdf on 2nd July 2014.

5. Suputtamongkol Y, Premasathian N, Bhumimuang K, Waywa D, Nilganuwong S, Karuphong E, et al. Efficacy and safety of single and double doses of ivermectin versus 7-day high dose albendazole for chronic strongyloidiasis. *PLoS Negl Trop Dis* 2011;5:e1044.

Summary

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1 Dose: Approximately 200 micrograms ivermectin per kilogram body weight p.o. See Table 1.

* Liaise with Professor Chiodini's Team at the Hospital for Tropical Diseases, London

6) IMPLEMENTATION

Training required for staff	**Yes** ☒ **No** ☐
If yes, who will provide training	Dr Dhasmana – Consultant
When will training be provided?	**Please give date(s)??** In Service Development Meeting
Date for implementation of guideline (after the process of ratification)	**10/08/2015**

7) MONITORING / AUDIT

When will this guideline be audited?	**01/09/2016**
Who will be responsible for auditing this guideline?	**Please give name/post** Dr Dhasmana, Consultant
Are there any other specific recommendations for audit?	**No**

8) REVIEW

Please indicate frequency of review: •	**Frequency of review:** 2 years **Person and post responsible for the review:** Dr Dhasmana

9) REFERENCES

List all references using the Harvard style. However, if references are included within the main body of the document, they do not then need to be reproduced here.

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10) GUIDELINE DETAIL

Start Date:	15th August 2015	
Dates approved by:	**Divisional Groupenter nameDivision of Medicine Guidelines Group and Division of Meidcine quality and safety committee.** **Date of ratification:** 30 July 2015 and 12th August 2015	
	Directorate Group enter name HIV, Sexual Health & Infection Committee **Date of ratifcation:** 22nd June 2015	
Have all relevant stakeholders (Trust sites, Divisions and Directorates) been included in the development of this guideline?	**Please list all (name and role)** Infectious Diseases – Graham Cooke Microbiology Pharmacy – Rosy Weston, Senior Lead Pharmacist for Sexual Health and HIV Trust Antimicrobial Review Group reviewed 28th April 2015	
Who will you be notifying of the existence of this guidance?	**Please give names/depts** Infectious Diseases Microbiology Pharmacy	
Related documents:	**If applicable** Click here to enter text.	
Author/further information:	Name: Dhasmana Title: Dr Division: Medicine Site: SMH Telephone/Bleep: via switch Trust email address: divya.dhasmana@imperial.nhs.uk	
Document review history:	**If applicable – version number; dates of previous reviews** **Version 1**	
Next review due:	**16/06/2017**	
THIS GUIDELINE REPLACES:	**List the title of the replaced guideline, its archive location and previous versions where known** Click here to enter text.	

11) INTRANET HOUSEKEEPING

Key words	Strongyloides, HTLV-1, treatment
Which Division/Directorate category does this belong to?	**Medicine**
Which specialty should this belong to when appearing on The Source?	Infectious diseases

12) EQUALITY IMPACT OF GUIDELINE

Is this guideline anticipated to have any significant equality-related impact on patients,

carers or staff? Yes □No☒