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Department:
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SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 10: INFECTIONS AND RELATED CONDITIONS
NEMLC RECOMMENDATIONS FOR MEDICINE MANAGEMENT (2016 – 2018)

Medicine amendment recommendations, with supporting evidence and rationale are listed below. Kindly review the medicine amendments in the context of the infections and related conditions chapter.

SECTION	MEDICINE	ADDED/DELETED/AMENDED
10.2 Chickenpox	NSAIDs, oral	Caution box not amended
	Antivirals, (active against varicella zoster): e.g. aciclovir, oral	Therapeutic class recommended
10.5 Fever	Ceftriaxone	Caution box amended
10.7.2 Malaria, severe/ complicated	Quinine, IM/IV	Loading dose amended
10.7.3 Malaria, prophylaxis (self-provided care)	Malaria chemoprophylaxis agents, oral (including doxycycline, oral)	Not added
10.8 Measles	Azithromycin, oral	Paediatric dosing amended
10.12 Schistosomiasis (Bilharzia)	Praziquantel, oral	Recommendation for retreatment not added; Amendment - note added of paradoxical reaction in acute schistomiasis
	Corticosteroids, oral	Not added
10.13 Shingles (Herpes zoster)	Aciclovir, oral	Added and dosing not amended
	Antivirals, (active against herpes zoster): e.g. aciclovir, oral	Therapeutic class recommended
- Pain	Paracetamol, oral	Added
	Tramadol, oral	Added
	NSAIDs, oral	Not added
- Post herpetic neuralgia	Amitriptyline, oral	Added
10.14 Tick bite fever	Azithromycin, oral	Added
	Doxycycline, oral	Added
10.17 Viral haemorrhagic fever (VHF)	Ceftriaxone, IM	Dose not amended

10.2 CHICKENPOX

NSAIDs, oral: *caution not added*

The caution to avoid use of NSAIDS in children with chicken pox due to increased risk of severe skin and soft tissue complication was considered.

Evidence of harm: Nested case control study[1] matching for age and practice showed an association between use of NSAIDS and skin or soft tissue complications. In children (mean age 10.7 years) severe skin or soft tissue complications occurred at a rate of 2.8/1000. NSAID use was associated with an increased rate of complications: rate ratio (adjusted for age, sex, concomitant medication and comorbidities) was 4.9, 95% CI2.1 to 11.4.

Level of Evidence: II Nested case control study

NEMLC meeting, 2 November 2017:
NEMLC Recommendations:
- *Pregnant women* added to the patient groups requiring antiviral agents.

[1]Mikaeloff Y, Kezouh A, Suissa S. Nonsteroidal anti-inflammatory drug use andthe risk of severe skin and soft tissue complications in patients with varicella or zoster disease. Br J Clin Pharmacol. 2008 Feb;65(2):203-9.https://www.ncbi.nlm.nih.gov/pubmed/18251759

- *NSAID caution* not to be added, as NEMLC was of the opinion that the evidence was inadequate to caution against using NSAIDs in children with chickenpox due to possible increased risk of severe skin and soft tissue complications (i.e. nested controlled study).

Antivirals, (active against varicella zoster): *therapeutic class recommended*

Evidence for recommending therapeutic class for management of chickenpox in immunocompromised patients and in severe varicella zoster infection in adults is limited. There is no available head-to-head RCT data comparing aciclovir to either valciclovir or famciclovir. Guidelines[2] do recommend these alternative agents which are pro-drugs with enhanced bioavailability and are dosed less often than aciclovir, assisting adherence.

The following therapeutic agents are recommended for use in adults (excluding pregnancy and children[3]), with aciclovir listed as the example of class:

Medicine (INN)	Strength	Unit	ROA	Dosing interval (times per day)	DDD	Unit	Course (days)	ATC	Total price for course of therapy	MSH drug price indicator, 2015[4] (Price for course of therapy)
Aciclovir	800	mg	oral	4	3200	mg	7	J05AB01	R 39.77*	R 26.32***
Valaciclovir	1000	mg	oral	3	3000	mg	7	J05AB11	R 479.64**	R 357.80****
Famciclovir	250	mg	oral	3	750	mg	7	J05AB09	R 346.29**	n/a

* Contract circular HP02-2015AI
** SEP database, 27 May 2017 - 60% of SEP.
***SUDANMSF - CIF: Aciclovir 400 mg - $0.0310/tab-cap i.e. R0.470/tab-cap
****OECS/PPS - CIF: Valaciclovir 500 mg - $0.5625/tab-cap i.e. R8.519/tab-cap
ROA=route of administration

Level of Evidence: III Guidelines

10.5 FEVER

Ceftriaxone: *caution box amended*

The caution box relating to ceftriaxone was updated for clarity purposes, and aligned with the the most recent FDA warning.

CAUTION: USE OF CEFTRIAXONE IN NEONATES AND CHILDREN

» If *SUSPECTING SERIOUS BACTERIAL INFECTION* in neonate, give ceftriaxone, even if jaundiced.
» Avoid giving calcium-containing IV fluids (e.g. Ringer Lactate) together with ceftriaxone:
  – If ≤ 28 days old, avoid calcium-containing IV fluids for 48 hours after ceftriaxone administered.
  – If >28 days old, ceftriaxone and calcium-containing IV fluids may be given sequentially provided the giving set is flushed thoroughly with sodium chloride 0.9% before and after.
  – Preferably administer IV fluids without calcium contents
» Always include the dose and route of administration of ceftriaxone in the referral letter.

10.7 MALARIA

Malaria areas: the following hyperlinks for global and South African malaria endemic areas were included in the STG, respectively:
https://www.iamat.org/risks/malaria?gclid=CjwKEAiAjIbBBRCitNvJ1o257WESJADpoUt072u5_X4Wb0fVtkQLiEFrWye263Ef_on8eykkOwLK_hoCFtDw_wcB

[2] Tunbridge AJ, Breuer J, Jeffery KJ; British Infection Society. Chickenpox in adults - clinical management. J Infect. 2008 Aug;57(2):95-102. https://www.ncbi.nlm.nih.gov/pubmed/18555533
[3] Acyclovir versus Valacyclovir for Herpes Virus in Children and Pregnant Women: A Review of the Clinical Evidence and Guidelines [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2014 Sep 5. Available from http://www.ncbi.nlm.nih.gov/books/NBK253720/
[4] MSH International drug price indicator guide, 2015. https://www.msh.org/resources/international-drug-price-indicator-guide (Discount rate of 5% used to inflate price to 2017)

http://www.santhnet.co.za/index.php/malaria-advice-for-travellers/item/330-malaria-risk-map-for-south-africa-2013.html

10.7.2 MALARIA, SEVERE/COMPLICATED

Quinine, IV/IM: *Loading dose amended*

The loading dose of quinine at a dose of 20 mg/kg was aligned with the SAMF, 2016, the Adult Hospital level STGs and EML, 2015 and Paediatric Hospital level STGs and EML, 2017. The PHC STG recommends a single loading dose at primary level of care, prior to referral.

Level of Evidence: III Guidelines

10.7.3 MALARIA, PROPHYLAXIS (SELF-PROVIDED CARE)

NEMLC[5] had previously recommended that the PHC Committee review malaria prophylaxis with discussion with the NDoH Malaria programme.

Malaria chemoprophylaxis agents, oral (including doxycycline): *not added*

In the previous PHC review cycle (2012-2014), the PHC Committee had collaborated with technical expert(s) from the programme and recommended that:

- Malaria programme identify high risk groups (including pregnant women and children) and safe, efficacious and affordable chemoprophylaxis for these high risk groups, appropriate for the South African population.
- Malaria chemoprophylaxis not to be added in the PHC STG.

Recommendation: The current PHC Committee proposes that malaria prophylaxis not be included in the EML.

Rationale: The target population, numbers needed to treat and pragmatic implementation strategy was unknown and could not inform any decisions. In the interim, the Malaria programme will be engaged to advise of the delivery platform model for malaria chemoprophylaxis and progress on the requests previously made to identify high risk groups (including pregnant women and children) and safe, efficacious and affordable chemoprophylaxis for these high risk groups, appropriate for the South African population.

Level of Evidence: III Expert opinion

10.8 MEASLES

Children with otitis media:

Severe penicillin allergy

Azithromycin, oral: *Paediatric dosing amended*

Dosing was aligned to the Paediatric Hospital Level STGs and EML, 2017 for consistency.

Level of Evidence: III Guidelines

10.12 SCHISTOSOMIASIS (BILHARZIA)

A: Retreatment of schistosomiasis

Praziquantel, oral: *not amended (recommendation for retreatment not added)*

Cochrane review[6]: Efficacy of treatment assessed by parasitological failure and % egg reduction at 1

[5] NEMLC minutes of the meeting of 29 June 2017.

[6] Kramer CV, Zhang F, Sinclair D, Olliaro PL. Drugs for treating urinary schistosomiasis. Cochrane Database Syst Rev. 2014 Aug 6;(8):CD000053. https://www.ncbi.nlm.nih.gov/pubmed/25099517

month post treatment. Primary clinical outcomes were resolution of haematuria and proteinuria assessed as secondary outcomes. Generally, 1-2 months is when treatment effect is assessed as sooner is premature and complete excretion of eggs can take several weeks. The review showed that on average, a single 40 mg/kg dose of praziquantel reduced the proportion of people still excreting *S. haematobium* eggs in the urine by an estimated 60% vs. placebo, at 1-2 months after treatment (high quality evidence), and reduced the mean number of schistosome eggs in the urine by over 95% in five out of six trials (high quality evidence). RCTs showed that persistent haematuria resolved by 8 weeks in the majority of patients.

Retreatment: It was reported in the Cochrane review by Kramer et al that, "There are too few trials to determine the optimal frequency and timing of repeated praziquantel dosing". Two RCTs comparing single standard dose of praziquantel vs repeat doses given at 2-3 week intervals, found no statistically significant differences in parasitological failure, percentage egg reduction, or clinical resolution. However, another very small RCT that compared praziquantel every three months for two years vs single dose of praziquantel, showed that at 2 years, higher risk of treatment failure was associated with single dose vs. multiple dose regimens, RR 2.71, 95% CI 1.47 to 5.00; n=62). Egg reduction was 96% after multiple doses and 80% after a single dose of praziquantel at 2years (n=90). Effects were not apparent a year after the last praziaquantel dose.

Pragmatic implications for primary level of care: Although laboratory reports advise whether the bilharzia ova are viable or not, guiding retreatment; the PHC Expert Review Committee was of the opinion that it was not pragmatic to retreat persistent at primary level of care. Healthcare workers should preferably refer patients with persistent haematuria 60 days after being treated with standard single dose praziquantel.

Recommendation: Retreatment of cases of schistosomiasis with repeated doses of praziquantel for persistent bleeding not be included in the STG for primary level of care.

Rationale: More pragmatic for persistent haematuria (more than 8 weeks) to be referred for retreatment, verified through laboratory tests to determine if schistosome ova are viable.

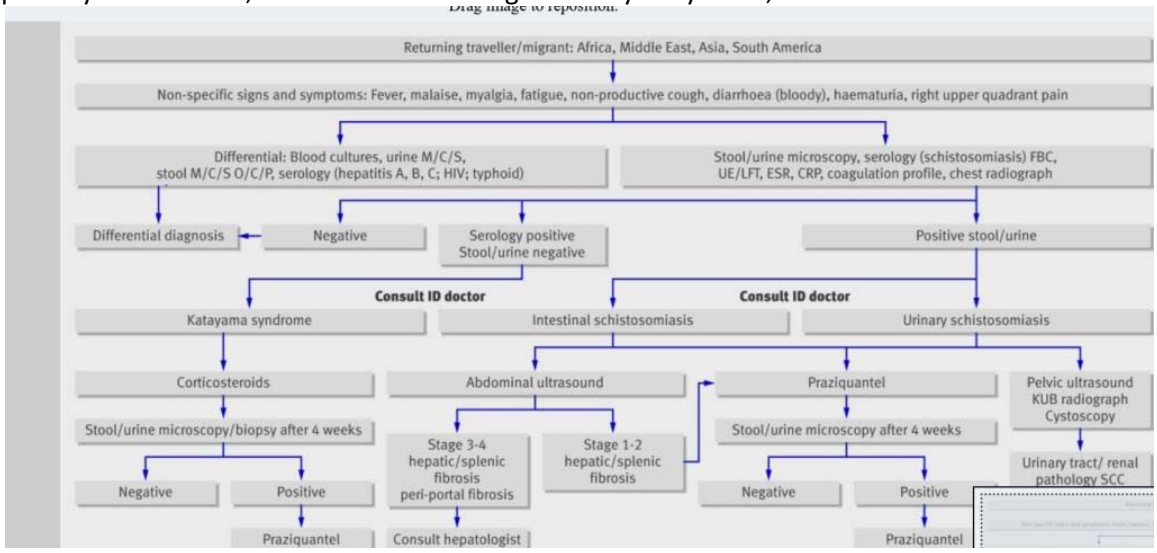
Level of Evidence: I Systematic review, Expert opinion

B: Delineation of acute treatment with steroids from chronic management with praziquantel

Corticosteroids, oral: *not added*

Praziquantel, oral: *amended (note added regarding possible parodoxical reaction in acute schistosomiasis)*

Differential diagnosis and management of acute vs. chronic schistomiasis would be complex for primary level of care, as indicated in the algorithm by Gray et al[7], below:



[7]Gray DJ, Ross AG, Li YS, McManus DP. Diagnosis and management of schistosomiasis. BMJ. 2011 May 17;342:d2651.

Diagnostic and treatment algorithm. M/C/S=microscopy/culture/sensitivity; O/C/P=ova/cysts/parasites; FBC=full blood count; UE/LFT=urea, electrolytes, and liver function test; ESR=erythrocyte sedimentation rate; CRP=C-reactive protein; ID doctor=infectious diseases doctor; KUB=kidney, ureter, and bladder; SCC=squamous cell carcinoma.

Praziqiantel is the recommended treatment for acute and chronic cases, with corticosteroids used as an initial adjuvant to treat Katayama syndrome (which is acute schistosomiasis) within 2 months of water contact and in the treatment of sequelae of neuroschistosomiasis. Paradoxical reaction occurs in approximately 50% of patients with acute schistosomiasis treated with praziquantel[8 9 10]; in some cases this worsening of symptoms can be life-threatening by causing encephalitis related to vasculitis[11], myocarditis[12] or pulmonary events[13].

Recommendations:

- Possible syndromic diagnosis and referral of suspected acute schistosomiasis, with a note that if praziquantel worsens treatment, consult a specialist for possible acute schistosomiasis.

Level of Evidence: III Expert opinion

10.13 SHINGLES (HERPES)

Management of shingles (herpes zoster) was added to the chapter, as the condition commonly presents at primary level of care. Guidance was aligned to the Paediatric Hospital Level STGs and EML, 2017 and the Adult Hospital Level STGs and EML, 2015.

Description

Dermatomal eruption of vesicles on an erythematous base due to varicella zoster virus (lies dormant in nerve ganglia following chickenpox).

General measures

» Isolate patient from immunocompromised or pregnant non-immune individuals (who may develop severe chickenpox).
» Offer HIV test, especially to patients < 50 years of age.

Medicine treatment

Antiviral therapy, indicated for herpes zoster:

» in immunocompetent individuals - only of benefit within 72 hours of onset, and
» in immunocompromised patients - beyond 72 hours, provided that there are active lesions.

- Aciclovir, oral, 800 mg five times daily for 7 days (4 hourly missing the middle of the night dose).

For pain:

Pain is often very severe and requires active control. A combination of different classes of analgesics is often necessary.

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

AND/OR

If pain is not adequately controlled:

- Tramadol, oral 50 mg 6 hourly
  - If response not adequate. Increase dose to 100mg 6 hourly

Post-herpetic neuralgia (doctor initiated):

Initiate treatment with adjuvant therapy early.

- Amitriptyline, oral 25mg at night

[8]Bottieau E, Clerinx J, de Vega MR et al. Imported Katayama fever: clinical and biological features at presentation and during treatment. J Infect 2006; 52: 339–345. (Abstract) https://www.ncbi.nlm.nih.gov/pubmed/16169593

[9]Grandiere-Perez L, Ansart S, Paris L et al. Efficacy of praziquantel during the incubation and invasive phase of Schistosoma haematobi-um schistosomiasis in 18 travellers. Am J Trop Med Hyg 2006; 74: 814–818. (Abstract) https://www.ncbi.nlm.nih.gov/pubmed/16687686

[10] Harries AD, Cook GC. Acute schistosomiasis (Katayama fever): clini-cal deterioration after chemotherapy. J Infect 1987; 14: 159–161. (Abstract) https://www.ncbi.nlm.nih.gov/pubmed/3106506

[11]Jaureguiberry S, Ansart S, Perez L, Danis M, Bricaire F, Caumes E. Acute neuroschistosomiasis: two cases associated with cerebral vas-culitis. Am J Trop Med Hyg 2007; 76: 964–966. (Abstract)

[12]Epelboin L, Jaureguiberry S, Esteve J et al. Myocarditis during acute schistosomiasis in 2 travelers. Am J Trop Med Hyg 2010. in press (Abstract)

[13] Schwartz E, Rozenman J, Perelman M. Pulmonary manifestations of early schistosome infection among nonimmune travelers. Am J Med 2000; 109: 718–722. (Abstract)

- Titrate as necessary to a maximum of 75mg

Referral

» Herpes zoster with secondary dissemination or neurological involvement.
» Ocular involvement (if the tip of the nose is involved then ocular involvement is more likely).

Level of Evidence: III Guidelines

Aciclovir, oral: *dosing not amended*

NEMLC had previously recommended[14] that 6 hourly dosing for aciclovir be considered. The PHC Committee reviewed the evidence, and recommended that aciclovir dosing in herpes zoster be retained as 5 times a day.

Rationale: The evidence for 6 hourly dosing is all for the treatment of chicken pox in healthy children[15] [16] [17] [18]. The PHC committee did not feel that this evidence could be extrapolated to the treatment of herpes zoster in immunocompromised patients.

Level of Evidence: III Expert opinion

Antivirals, (active against varicella zoster): *therapeutic class recommended*

Therapeutic class recommended for management of herpes, with aciclovir, the cheapest medicine, listed as an example of class.

Indication	Medicine	ROA	DDD	Regimen	Evidence
Shingles (Herpes zoster)	Aciclovir	Oral	4000 mg	800 mg 5 times daily for 7 days	**Level of Evidence: I Systematic review[19]**
	Valaciclovir	Oral	3000 mg	1000 mg 8 hourly x 7 days	
	Famciclovir	Oral	750 mg	250 mg 8 hourly x7 days	

Price (per course of therapy): Aciclovir 400 mg (Contract circular HP09-2016SD[20]), 70 tab-cap; R49.72
Valaciclovir 500 mg (60% of SEP- weighted average price[21]), 42 tab-cap: R 479.64
Famciclovir 250 mg (60% of SEP- weighted average price[22]), 21 tab-cap: R 346.29

Pain

Tramadol, oral: *added as doctor initiated*

Pain management aligned with Adult STG, 2015 which recommends the use of tramadol if paracetamol is insufficient.

Level of Evidence: III Guidelines

NSAIDs, oral: *not added*

Guidelines recommend[23] that NSAIDS can be used to treat pain in herpes zoster, in combination with opioids and paracetamol. However, similar to children, NSAID use was associated with an increased rate of skin and soft tissue complications: rate ratio (adjusted for age, sex, concomitant medication and comorbidities) was 1.6, 95% CI 1.1 to 2.4.

Level of Evidence: II Nested case control study

[14] NEMLC minutes of the meeting of 29 June 2017.
[15] Dunkle LM, Arvin AM, et al. A controlled trial of acyclovir for chickenpox in normal children. N Engl J Med. 1991 Nov 28;325(22):1539-44.https://www.ncbi.nlm.nih.gov/pubmed/1944438
[16] Balfour HH Jr, Kelly JM.,et al. Acyclovir treatment of varicella in otherwise healthy children. J Pediatr. 1990 Apr;116(4):633-9. https://www.ncbi.nlm.nih.gov/pubmed/2156984
[17] Balfour HH Jr, RotbartHA, et al. Acyclovir treatment ofvaricella in otherwise healthy adolescents. The Collaborative Acyclovir Varicella Study Group. J Pediatr. 1992 Apr;120(4 Pt 1):627-33. https://www.ncbi.nlm.nih.gov/pubmed/1313098
[18] Balfour HH Jr, Edelman CK, et al. Controlled trial of acyclovir for chickenpox evaluatingtime of initiation and duration of therapy and viral resistance. Pediatr Infect Dis J. 2001 Oct;20(10):919-26. https://www.ncbi.nlm.nih.gov/pubmed/11642624
[19] McDonald EM, De Kock J, Ram FS. Antivirals for management of herpes zoster including ophthalmicus: a systematic review of high-quality randomized controlled trials. Antiviral Therapy 2012; 17(2): 255-264. https://www.ncbi.nlm.nih.gov/pubmed/22300753
[20] MSH drug price indicator, 2015: SUDANMSF - CIF: Aciclovir 400 mg - $0.0310/tab-cap i.e. R0.470/tab-cap; Contract circular HP09-2016SD - R 0.710/tab-cap
[21] MSH drug price indicator, 2015: OECS/PPS - CIF: Valaciclovir 500 mg - $0.5625/tab-cap i.e. R8.519/tab-cap; 60% SEP database 27 May 2017 - R 11.42/tab-cap, average weighted price
[22] MSH drug price indicator, 2015 - n/a: Famciclovir 250 mg - 60% SEP database 27 May 2017 - R 16.49/tab-cap, average weighted price
[23] Dworkin RH, Schmader KE. Treatment and prevention of postherpetic neuralgia. Clin Infect Dis 2003; 36:877–82

To treat post-herpetic neuralgia:

Amitriptyline, oral: *added*

- Aligned with Adult Hospital Level STGs and EML, 2015, where early initiation of amitriptyline is recommended.
- *Cochrane review*[24]showed that "Combining the classic neuropathic pain conditions of painful diabetic neuropathy, post-herpetic neuralgia and post-stroke pain with fibromyalgia for second-tier evidence, in eight studies and 687 participants, there was a statistically significant benefit (RR 2.3, 95% CI 1.8 to 3.1) with a NNT of 4.6 (3.6 to 6.6)".

Level of Evidence: I Systematic review, Guidelines

10.14 TICK BITE FEVER

STG for tick bite fever was added to the chapter, aligned with the Paediatric Hospital Level STGs and EML, 2017 and the Adult Hospital Level STGs and EML, 2015. Tick bite fever is a common condition. Management was restricted to mild to moderate cases, with referral to secondary level of care for severe cases of tick bite fever.

However, dosing of doxycycline at 4mg/kg/day for children at primary level of care would be problematic as doxycycline is only available on the South African market as a 50 mg and 100 mg capsule. The scope of practice of nurse prescribers at primary level of care does not include formulating extemporaneous preparations. Medicine review (*azithromycin for tick bite fever*) was undertaken to determine efficacy of azithromycin for mild to moderate tick bite fever compared to docycycline. Refer to the medicine review for detailed information.

Azithromycin_TickBiteFever_PHC_Medici

Recommendation: Azithromycin, oral 10 mg/kg daily for 3 days be recommended for children < 45 kg for treatment of tick-bite fever; and for children ≥ 45 kg and adults: doxycycline 100 mg daily for 3 days.

Rationale: Recommendation was aligned with guidelines and subject to availability of MCC registered formulations in South Africa that do not require extemporaneous preparation at primary level of care. Limited evidence suggests that azithromycin is effective against spotted fever group infections and can be safely dosed in paediatric patients with mild to moderate tick bite fever. From a pragmatic perspective, it was further recommended that the cut-off of 45 kg be used. This recommendation is aligned with USA Centers for Disease and Control and Prevention Guidelines.[25]

Level of Evidence: II Disease oriented RCT[26], Guidelines[27, 28, 29], Expert opinion

Description
Tick-borne infection due to *Rickettsia conorii*, acquired from dogs, or *Rickettsia africae*, acquired from cattle and game. The hallmark of tick bite fever is the eschar,

[24] Moore RA, Derry S, Aldington D, Cole P, Wiffen PJ. Amitriptyline for neuropathic pain and fibromyalgia in adults. Cochrane Database Syst Rev. 2012 Dec 12;12:CD008242. https://www.ncbi.nlm.nih.gov/pubmed/23235657

[25] Chapman AS, Bakken JS, Folk SM, Paddock CD, Bloch KC, Krusell A, Sexton DJ, Buckingham SC, Marshall GS, Storch GA, Dasch GA, McQuiston JH, Swerdlow DL, Dumler SJ, Nicholson WL, Walker DH, Eremeeva ME, Ohl CA; TickborneRickettsial Diseases Working Group.; CDC.. Diagnosis and management of tickbornerickettsial diseases: Rocky Mountain spotted fever, ehrlichioses, and anaplasmosis--United States: a practical guide for physicians and other health-care and public health professionals. MMWR Recomm Rep. 2006 Mar 31;55(RR-4):1-27. https://www.ncbi.nlm.nih.gov/pubmed/16572105

[26] Meloni G, Meloni T. Azithromycin vs. doxycycline for Mediterranean spotted fever. Pediatr Infect Dis J. 1996;15(11):1042-4. https://www.ncbi.nlm.nih.gov/pubmed/8933556

[27] Chapman AS, Bakken JS, Folk SM, Paddock CD, Bloch KC, Krusell A, Sexton DJ, Buckingham SC, Marshall GS, Storch GA, Dasch GA, McQuiston JH, Swerdlow DL, Dumler SJ, Nicholson WL, Walker DH, Eremeeva ME, Ohl CA; TickborneRickettsial Diseases Working Group.; CDC.. Diagnosis and management of tickbornerickettsial diseases: Rocky Mountain spotted fever, ehrlichioses, and anaplasmosis--United States: a practical guide for physicians and other health-care and public health professionals. MMWR Recomm Rep. 2006 Mar 31;55(RR-4):1-27. https://www.ncbi.nlm.nih.gov/pubmed/16572105

[28] Paediatric Hospital level STGs and EML, 2017.

[29] Adult Hospital level STGs and EML, 2015.

i.e. a round black lesion ± 5 mm in diameter with an inflammatory halo, which occurs in about two thirds of patients with *R. conorii* and in most cases of *Rickettsia africae* infection, where multiple eschars are common. A rash develops on about the third day of illness in about two thirds of patients with *R. conorii* and in fewer cases of *Ricketsia africae* infection. In *Rickettsia. conorii* infection the rash is maculopapular and involves the palms and soles. In *Rickettsia africae* infection the rash is sparse and may be vesicular. The classic triad of fever, eschar and rash occursin 50-75% of patients. Signs of severe tick bite fever include severe headache, hypotension, shortness of breath and neurological manifestations.

General measures

» Application of insect repellent to exposed skin and clothing.
» Wearing long sleeves, long trousers and socks, if outside.
» Inspect clothing for presence of ticks after suspected exposure.

Complications include:

» vasculitis
» encephalitis
» thrombosis
» renal failure
» myocarditis
» pneumonitis
» thrombocytopaenia

Medicine treatment

Antibiotic therapy:

Treatment must be started before confirmation of diagnosis by serology.
Although not recommended for children <8 years of age, doxycycline is still regarded as the medicine of choice for children with tick-bite fever. However, due to the unavailability of lower dosage forms of doxycycline alternative medicines are considered in children <8 years of age or those weighing < 45 kg with mild infection.

Mild to moderate infection:

Children < 45 kg

- Azithromycin, oral, 10 mg/kg/dose daily for 3 days. See dosing table page xxx

Children ≥ 45 kg and adults

- Doxycycline, oral, 100 mg 12 hourly for 7 days.

In pregnancy:

- Azithromycin, oral, 500 mg 12 hourly for 3 days.
  - In severe cases, initiate therapy with 1–2 days of doxycycline.

For headache and fever:

Children

- Paracetamol, oral, 15mg/kg/dose, 6 hourly as required. See dosing table, pg 22.6.

Adults

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours

Referral

» Patients unable to take oral therapy.
» Patients not responding to adequate therapy.
» Patients with complications.
» Patients with severe tick bite fever.

10.17 VIRAL HAEMORRHAGIC FEVER (VHF)

Ceftriaxone, IM: *not amended*

NEMLC had previously recommended[30] that the PHC ERC align management of VHF with National Guidelines. The PHC STG is aligned with the current NDoH VHF Guidelines (2015), and the pre-referral dose of ceftriaxone would be retained.

Level of Evidence: III Guidelines

Brucellosis and hydatid disease: STGs for brucellosis and hydatid disease were not considered for inclusion to the chapter. These conditions are diagnosed at secondary level of care and should be managed through the down referral system.

[30] NEMLC minutes of the meeting of 29 June 2017.