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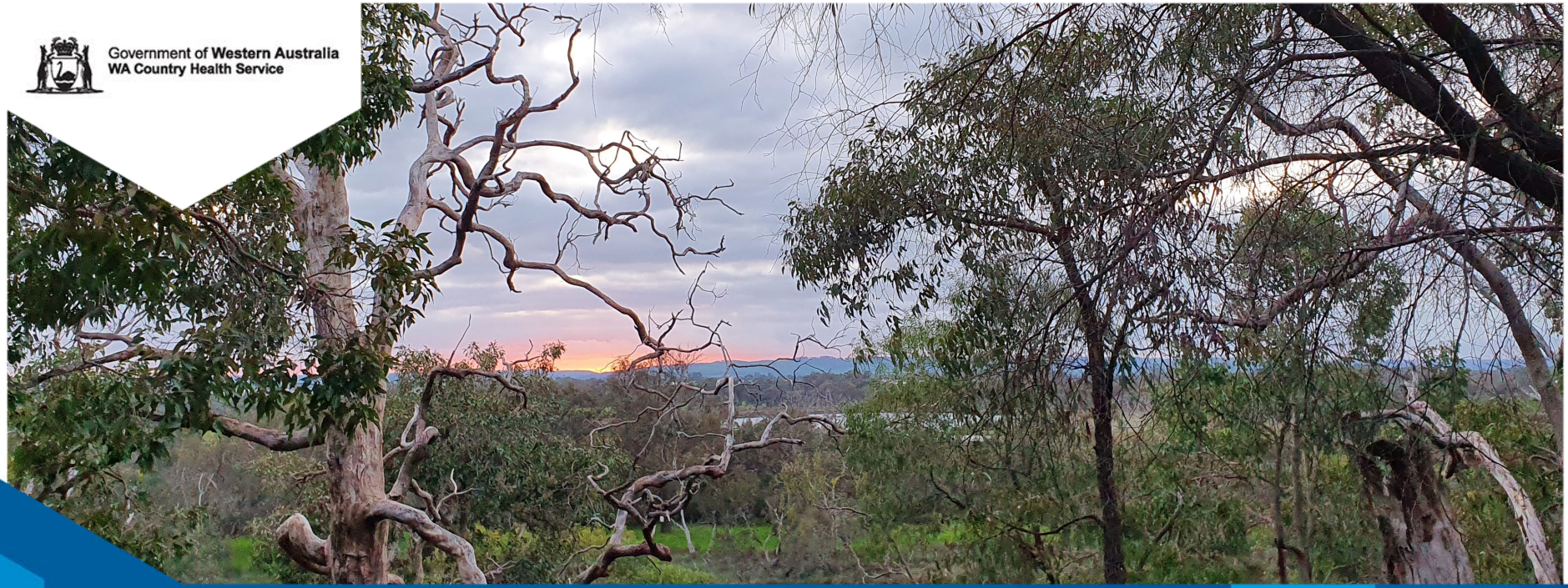
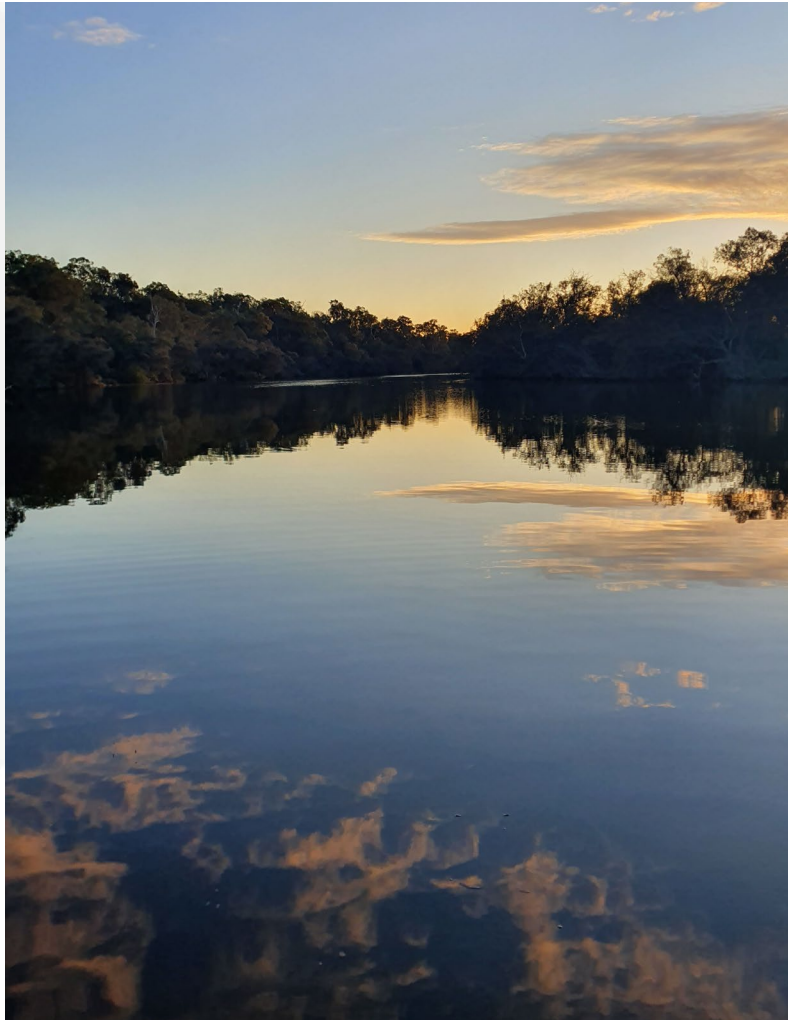


FEVER: ?CAUSE

Dr Xavier Cornwall

18 October 2025

Initial presentation?



Doc I've got malaria again

- 54M presenting to ED 2x in 4 days with reports of arthralgias, night sweats and subjective fevers
- Associated nausea, vomiting and diarrhea
- Feels like previous malarial infection
- Currently on PO Abs for infected ankle ORIF

Background

PMHx

- Patient reports 4-5 malarial infections between 2001 and 2015, at least one hospital admission for the same
- Ankle ORFI 2024 with recurrent infections requiring PO antibiotics, has previously been advised to remove, but has been too busy
  - Presented to ED for same 7 days prior and commenced on flucloxacillin
  - Seen in fracture clinic and changed to cotrimoxazole 5 days ago in discussion with ID services

Medications

- Nil regular

Allergies

- No known drug allergies

Social history

54M born in PNG, has visited multiple times

Lives in QLD

- recently working in far north Queensland

Runs and works in his construction business

Long term partner for 15 years

Nonsmoker

Regular THC enjoyer, nil other, never IVDU

Drinks 5-6 beers per day

Currently staying in a caravan park with his employees

- In WA for Work, arrived 2 weeks prior, here for ~6 weeks

Independent all ADLs

Drives

Was discussed with ID 4 days prior

- Clinically well and unremarkable bloods
- Requested exclusion of unlikely arbovirus and tropical virus
  - Leptospirosis, dengue, rickettsia, ross river virus, barma virus, Resp viral PCR and blood cultures
- OP follow up of above testing

Initial Exam

O/E

- CVS - HR 66, BP 133/89, JVP not elevated, no peripheral oedema oedema
- Resp - sats 100%RA, RR 16, chest clear anteriorly
- CNS – awake and oriented
- Infective – euthermic in ED, no cervical lymphadenopathy
- GIT – no obvious jaundice, dry mucosa, tender RUQ with out organomegaly
- MSK – small ulcer overlying R) ankle with out palpable fluctuant collection

Investigations

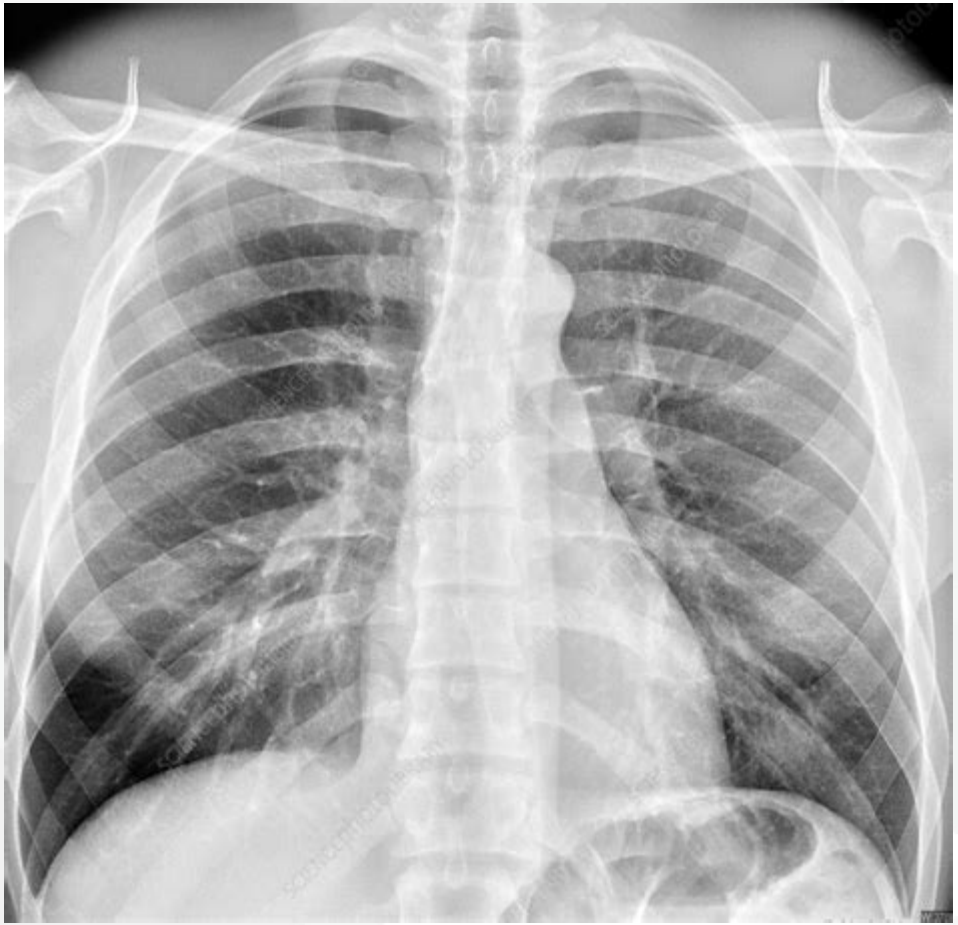
	12Aug2025 00:50	12Aug2025 02:26	15Aug2025 12:10	15Aug2025 14:45	18Aug2025 09:11	18Aug2025 12:14
COMMON LAB						
FULL BLOOD PICTURE						
Comment FBP					*See belo...	
Haemoglobin	* 144		* 144		* 174	
White Cell Count	* 8.21		* 10.69		↓ * 3.40	
Platelet Count - Blood	* 220		* 184		↓ * 107	
Red Cell Count	↓ * 4.45		↓ * 4.46		* 5.31	
Haematocrit -	* 0.41		* 0.41		* 0.47	
Mean Cell Volume - blood	* 93		* 92			
Mean Cell Haemoglobin	↑ * 32.4		↑ * 32.3			
Mean Cell Hb Conc	* 349		* 352			
Red Cell Distribution Width	* 12.6		* 12.4		* 12.1	
Mean Platelet Volume	* 9		* 9		* 12	
Neutrophils Absolute (Interim)						
Neutrophils Absolute	* 4.09		↑ * 10.25		* 2.86	
Lymphocytes Absolute	* 2.96		↓ * 0.13		↓ * 0.33	
Monocytes Absolute	* 0.54		* 0.28		↓ * 0.12	
Eosinophils Absolute	↑ * 0.56		* 0.01		* 0.07	
Basophils Absolute	* 0.06		* 0.02		* 0.02	
Reactive Lymphocytes Absolute						
INFLAMMATORY MARKERS						
C Reactive Protein - Serum	1.7		↑ 14		↑ 118	
COAGULATION PROFILE						
Prothrombin M2						
INR -						
APTT						
Fibrinogen - Plasma						
UREA AND ELECTROLYTES						
Sodium - Plasma	* 136		↓ * 133		↓ * 132	↓ * 132
Potassium - Plasma	* 4.3		* 4.3		*Haemoly:...	* 4.3
Bicarbonate - Plasma	* 23		* 22		↓ * 19	* 23
Urea - Plasma	* 5.5		* 4.0		* 3.4	* 4.3
Creatinine - Plasma	* 79		* 76		* 72	* 86
eGFR	* >90		* >90		* >90	* 88
LIVER FUNCTION						
Bilirubin Total - Plasma	7		16		Haemolys...	↑ 23
ALT - Plasma	25		23		↑ 627	↑ 610
AST - Plasma						
Alk Phos - Plasma	73		80		Haemolys...	↑ 316
GGT - Plasma	22		23		↑ 253	↑ 298
Albumin - Plasma	42		43		Haemolys...	42
Protein Total - Plasma	74		77		Haemolys...	↑ 81

Other Ix available

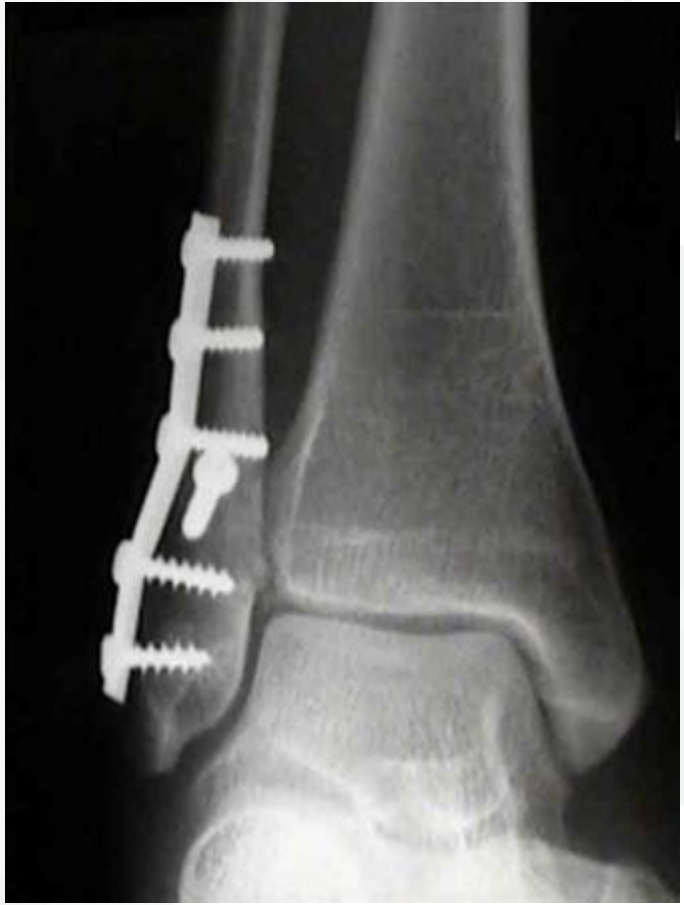
P. Falciparum screen – NAD

Previous investigation (all done 15/08):
Wound MCS – MRSA, sensitive to doxy/cotrim
Blood culture - no growth 48hrs
Ross river virus - IgG positive / IgM negative
Barmah forest virus - IgG positive / IgM negative
Dengue virus - IgG positive / IgM negative / NS1 negative
Leptospira serology - **PENDING REPORT**
Rickettsia serology - **PENDING REPORT**
resp virus PCR - NAD

Investigations



Investigations



Re-Discussion with Infections diseases

- Malaria possible but unlikely (two reported cases in recent times in FNQ)
- New hepatitis
- Recommend: HBV, HCV, HIV, EMB, CMV, Paracetamol level, USS abdomen, thick and thin film

DDX?

- Malaria
- Other viral hepatitis
- Other tropical infection
- Drug reaction
- Diarrhoeal illness
- Worsening MRSA infection of R) ankle with systemic features

Management

- General medical admission
- Cotrimoxazole to doxycycline
- Not for antipyretics
- Ix as previously suggested

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Inpatient Events

Further History and Exam

History

- No new history
- Has had ongoing fevers over night

O/E

- Documented fevers over night >38 degrees
- GI - liver edge palpable 1cm below costal margin, tender RUQ, rest of abdomen soft, non distended
- Skin - No rash or bites present over skin, unable to palpate any lymph nodes in axilla, submandibular or inguinal areas
- GU - nil visible boils, nil testicular tenderness
- MSK - R ankle non tender to palpation, evidence of healed ulcer over lateral malleolus, no evidence of effusion, no warmth

Infectious diseased consultation

New history

- Malaria: reports diagnosis in 2000 by QLD ID team after extensive investigations and then again in 2005 after returning to PNG. Has not travelled internationally for at least 2 years, the last been to the Maldives
- Ankle ORIF: operation 2 years ago in QLD, slow to resolved with multiple courses of POABs. Feels as though his work and work boots aggravated the screw
- Was commenced on cefalexin, changed to cotrimoxazole on the 1 day prior to representation based on sensitivities. With in 24 hours developed systemic symptoms
- Pt vague but wife, a nurse, thinks no previous cotrimoxazole as she is allergic and thinks she would recall

Investigations

- 2x thick and thin films are prelim neg, malaria PCR pending
- EBV past infection, CMV past infection
- HBV/HCV/HIV serologies are negative
- Urine <100 leuks10-100 RBC

Management

- Continue doxycycline 100mg BD (will cover rickettsia, MRSA)
- Repeat rickettsia serology in 10 days in case of acute illness.
- Needs follow up with ortho re: Removal of ORIF in QLD.

OP Follow up

Systemic features resolved

Ongoing discharge from ankle wound

Plans to return to QLD and follow up with local orthopaedic team

Conclusion

Serum sickness, SSLR, Drug fever and DILI

Serum sickness is a type III hypersensitivity reaction, with antibody-antigen complex formation, normally cleared by phagocytes, these complexes are unprocessed due to deficiency or over saturation and then deposit in tissues.

SSLR may mimic serum sickness, although is caused by an alternate poorly understood mechanism, and does not seem to rely on high antibody titres

DILI relates to drug hepatoxicity and can be be classified by presentation, mechanism or histology. Toxicity can be direct or idiosyncratic.

Drug fever can be the sole manifestation of 3-4 percent of drug reactions, through poorly understood mechanisms but can be divided into hypersensitivity, idiosyncratic pharmacological mechanisms, altered thermoregulation and direct relation to administration

Cotrimoxazole has been linked with all of these processes

Serum sickness, SSLR, Drug fever and DILI

Serum sickness includes: 1-2 weeks after exposure unless previous exposure, almost always includes a fever, almost all patients have a pruritic rash, arthralgias are common but inconsistently present and GI symptoms can be present. Urine MCS can show protein or bloods.

SSLR generally less severe with fever variably present, which is usually low grade, includes arthralgia and commonly has a puritic rash. Organ involvement very uncommon

DILI RUQ pain, hepatomegaly, GI upset, LFT derangement. Fever is usually low grade. Arthralgias not a feature. Also immunologic in cotrimoxazole, occurs after 3 weeks unless primed

Drug fever accounts for no other features of this patient

Other key learning from this case

Diagnostic priming

- Many clinicians were thrown off by the patients stated history and surety of his malarial symptoms which directed his investigations toward malaria and other tropical disease. While this was an appropriate and necessary activity of exclusion, it possibly delayed the cessation of cotrimoxazole (at second presentation).
- Hopefully, by bringing you in halfway through the case, as we were, you have experienced similar diagnostic priming in your own thought processes!!

Other key learning from this case

Communication and documentation

- The commencement of cotrimoxazole was miscommunicated and mis documented multiple times by multiple clinicians, and who the responsible prescriber was and in what setting
- On exploration it was found that at the third presentation cotrimoxazole drug reaction was felt to be the most likely explanation for the patients' symptoms by the specialty team
- However, this was not documented and not communicated to the general medical team until subsequent review
- This later created strain between clinicians and ultimately led to confusion and miscommunication to the patient, fortunately it did not effect patient treatment or patient outcome!

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Thank you for Listening any questions