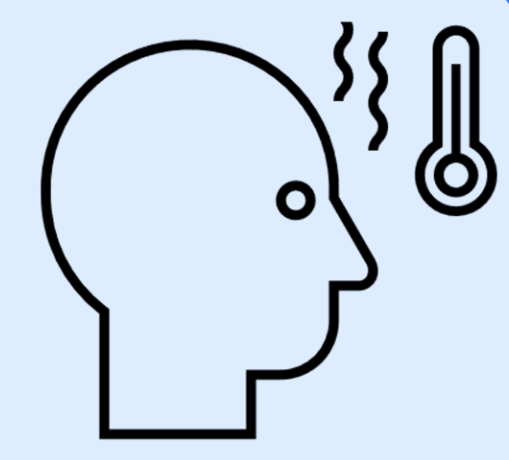


# Delayed haemolysis after IV Artesunate therapy for *P. falciparum*

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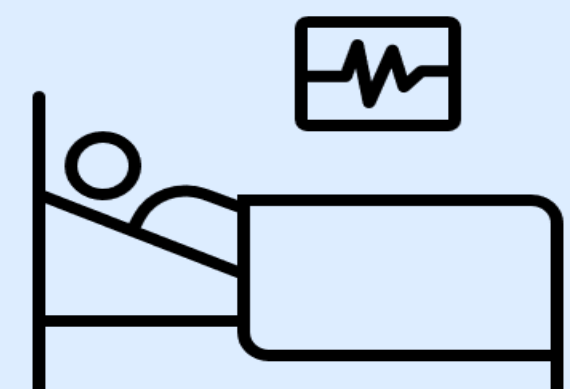
A 27-year-old male presented to the Emergency Department with high grade fever, myalgia, and headaches after returning to Ireland from Angola. Examination of a blood film showed *P. falciparum*-infected erythrocytes with a parasite count of 14%. He was diagnosed with severe *P. falciparum* infection and treated initially with IV artesunate followed by oral artemether/lumefantrine. He had complete parasite clearance within 48 hours



He was seen a week later in the Infectious Diseases outpatient clinic complaining of dizziness, shortness of breath and palpitations. His Hb of 14.8g/dL decreased to **9.8g/dL** since first admitted. He was admitted the following week with ongoing symptoms and a Hb concentration of **8.0g/dL**. A haematology consult and work-up confirmed **haemolytic anaemia [Figure 1]**

Total bilirubin 52  $\mu\text{mol/L}$   
(conjugate bilirubin 16  $\mu\text{mol/L}$ )  
reticulocyte count (11.7%)  
LDH (703IU/L)  
haptoglobins (<0.24g/L)  
He had normal G6PD levels  
Thalassaemia and sickle cell screens: negative  
weakly positive Direct Coombs Test  
Haem consult= haemolytic anaemia

Figure 1: Blood test results



During his second admission, he was started on folic acid replacement due to low levels; his B12 levels were normal in addition to his iron studies. He did not require any full blood transfusions. Figure 2 shows Hb evolution.

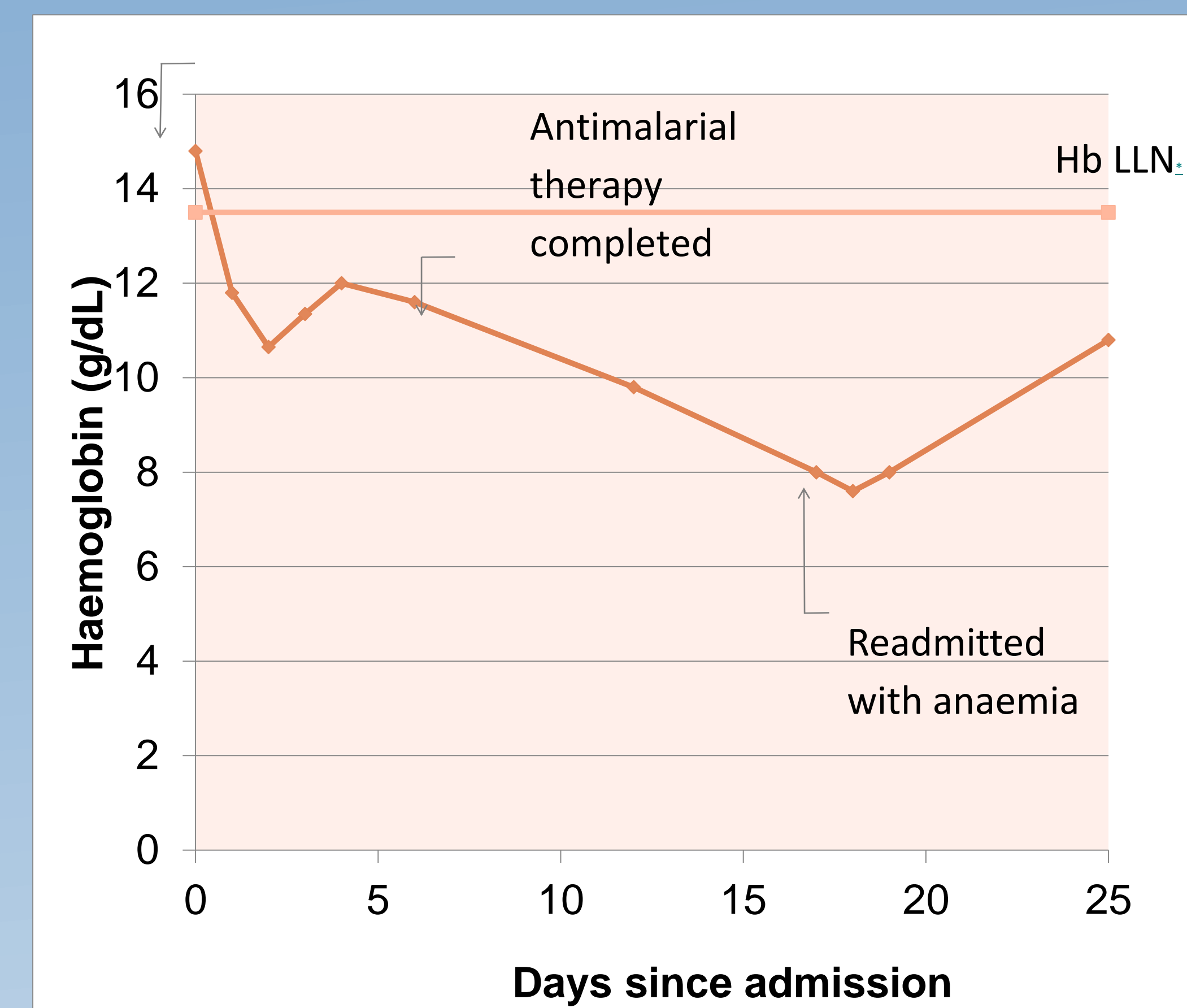


Figure 2: Hb evolution since first admission



This presumed adverse drug event was reported to the Health Products Regulation Authority (HPRA).



**Delayed haemolysis post artesunate** also known as post-artemisinin or artesunate delayed hemolysis (PADH) is a side effect of artemisinin-based therapy (both IV & PO). It is associated with >10% decrease in Hb or >10% rise in LDH more than 8 days after treatment. The pathophysiology is not fully understood, but hyperparasitaemia appears to be a risk factor. Up to 60% may require blood transfusion but it is self-limiting; no deaths associated with this phenomenon have been reported. Our patient recovered well with no long term sequelae. All patients infected with malaria are followed up in the ID clinic with a specific focus on haematological surveillance for those who received artemisinin derivatives. This adverse effect should not deter clinicians from using this effective antimalarial.



Figure 3: Anopheles Mosquito (image from orkin.com)

## References:

- Lahoud J S, Lahoud O B et al. Artesunate-related fever and delayed hemolysis in a returning traveler. ID Cases. 2015; 2(2):63-65
- Aldámiz-Echevarría L T, López-Polín A, et al. Delayed haemolysis secondary to treatment of severe malaria with intravenous artesunate: report on the experience of a referral centre for tropical infections in Spain. Travel Med Infect Dis. 2017; 15:52-56.
- Roussel C, Caumes E, et al. Artesunate to treat severe malaria in travelers: review of efficacy and safety and practical implications. J Travel Med. 2017;24(2)
- Gómez-Junyent J, Ruiz-Panales P, et al. Delayed haemolysis after artesunate therapy in a cohort of patients with severe imported malaria due to Plasmodium falciparum. Enferm Infecc Microbiol Clin. 2017; 35(8):516-519.
- Jauréguiberry S, Ndour P A, et al. Postartesunate delayed hemolysis is a predictable event related to the lifesaving effect of artemisinins. Blood. 2014

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