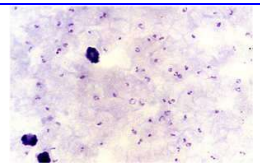
Convegno

Aggiornamenti in tema di medicina dei viaggi e delle migrazioni:

1° Evento

Palazzo Grandi Stazioni, Venezia 30 Maggio



Stato dell'arte su diagnosi e mangement della malaria

Centro Malattie Tropicali
NEGRAR - VERONA - ITALY
Centre for Tropical Diseases
Ospedale Sacro Cuore Don Calabria
FONDAZIONE DON GIOVANNI CALABRIA PER LE MALATTIE TROPICALI

WHO Collaborating Center on strongyloidiasisand other intestinal parasitic infections

Zeno Bisoffi &
Federico Gobbi

Epidemiological and research definition of severe falciparum malaria

Impaired consciousness:	Glasgow Coma Score <11 (adults) or Blantyre coma score <3 (children)
Acidosis:	A base deficit of >8 meq/l or, if unavailable, a plasma bicarbonate of <15 mM or venous plasma lactate >5 mM. Severe acidosis manifests clinically as respiratory distress – rapid, deep and laboured breathing
Hypoglycaemia:	Blood or plasma glucose <2.2 mM (<40 mg/dl)
Severe malarial anaemia:	A haemoglobin concentration <5 g/dl or a haematocrit of <15% in children <12 years of age (<7 g/dl and <20%, respectively, in adults) together with a parasite count >10 000/μl
Renal impairment:	Plasma or serum creatinine >265 μM (3 mg/dl) or blood urea >20 mM

Tropical Medicine and International Health volume 19 suppl 1 pp 7–131 september 2014

Epidemiological and research definition of severe falciparum malaria (cont.)

Jaundice:	Plasma or serum bilirubin >50 μM (3 mg/dl) together with a parasite count >100 000/μl
Pulmonary oedema:	Radiologically confirmed, or oxygen saturation <92% on room air with a respiratory rate >30/min, often with chest indrawing and crepitations on auscultation
Significant bleeding:	Including recurrent or prolonged bleeding from nose gums or venepuncture sites; haematemesis or melaena
Shock:	Compensated shock is defined as capillary refill ≥3 s or temperature gradient on leg (mid to proximal limb), but no hypotension. Decompensated shock is defined as systolic blood pressure <70 mm Hg in children or <80 mm Hg in adults with evidence of impaired perfusion (cool peripheries or prolonged capillary refill)

Hyperparasitaemia: *P. falciparum* parasitaemia >10%

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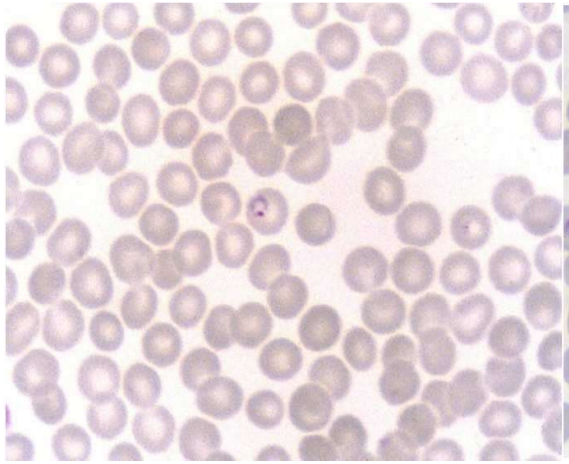
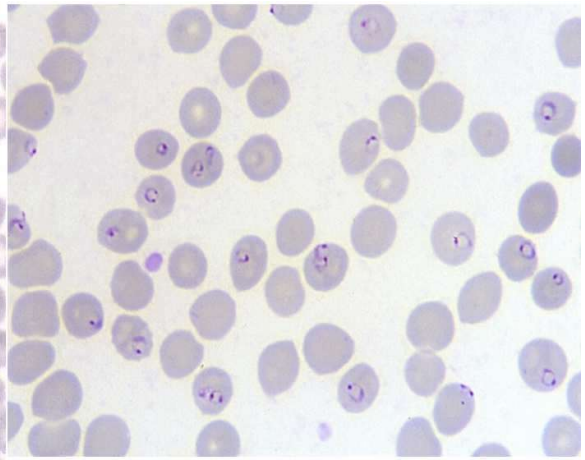
Ritardo diagnostico e carica parassitaria

Turista (Kenya), 50 a, febbre da 3 h



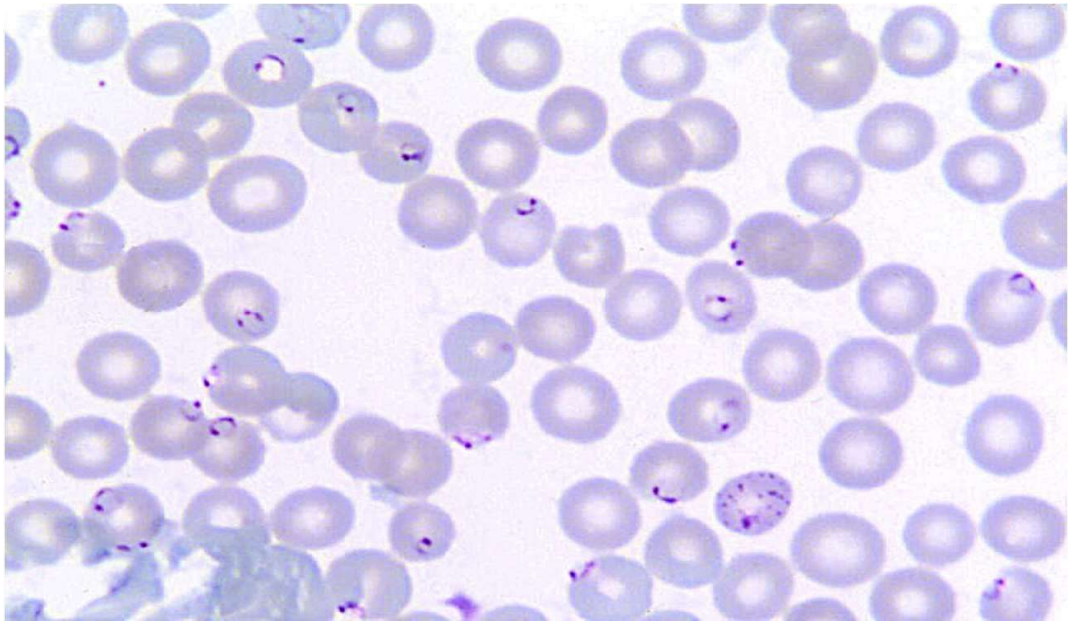
Turista (G. Bissau), 36 a, febbre da 8 gg



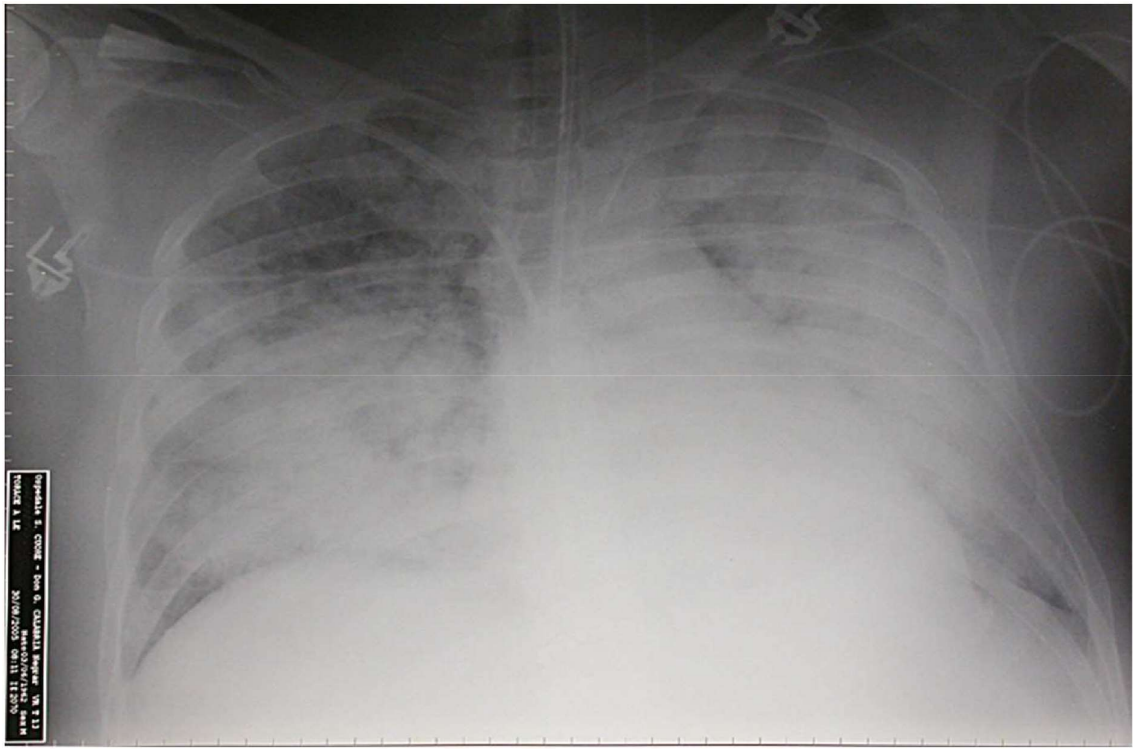
Caso clinico

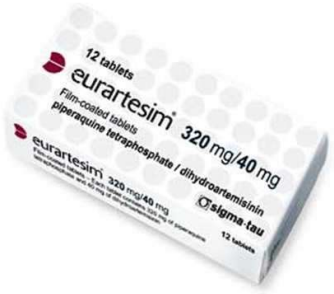
- S.A.B., femmina, 49 anni, 80kg, ghanese, immigrata dal 1985 • In Ghana 07/10-16/11/04 • No profilassi, febbre dal 16/11 • In PS il 24/11: diagnosi di malaria da *P.falciparum,* ricovero in med. tropicale (parassitemia 0,25%)

Caso clinico: aumento “drammatico” della parassitemia in g. 2



Caso clinico - Evoluzione





Dosaggio (adulti):

<75 kg **3** compresse
>75 kg **4** compresse

-QTc lungo >440
- il dosaggio

Indicazioni WHO:

60-80 kg **4** compresse
80-100 kg **5** compresse

Gobbi et al. Malar J (2016) 15:525
DOI 10.1186/s12936-016-1572-3

Malaria Journal

CASE REPORT Open Access

Failure of dihydroartemisinin-piperaquine treatment of uncomplicated *Plasmodium falciparum* malaria in a traveller coming from Ethiopia

Federico Gobbi[1*], Dora Buonfrate[1], Michela Menegon[2], Gianluigi Lunardi[1], Andrea Angheben[1], Carlo Severini[2], Stefania Gori[1] and Zeno Bisoffi[1]

Roseau et al. Malar J (2016) 15:479
DOI 10.1186/s12936-016-1535-8

Malaria Journal

CASE REPORT Open Access

Failure of dihydroartemisinin plus piperaquine treatment of falciparum malaria by under-dosing in an overweight patient

Jean Baptiste Roseau[1,2], Bruno Pradines[3,4,5*], Nicolas Paleiron[2,6], Serge Vedy[2], Marylin Madamet[4,5,7], Fabrice Simon[8,9] and Emilie Javelle[8*]

Efficacia degli interventi medici per malaria grave

Intervention	Result
Urea	No benefit
Aspirin	Harm
Heparin	Harm
Mannitol	Harm
Prostacyclin	No benefit
Corticosteroids	Harm
Plasmapheresis	No benefit
Pentoxyphylline	No benefit (? ↑ mortality)
Desferrioxamine	Harm
Low-dose quinine	Harm
Anti-TNF antibody	Harm
Hyperimmune globulin	No benefit

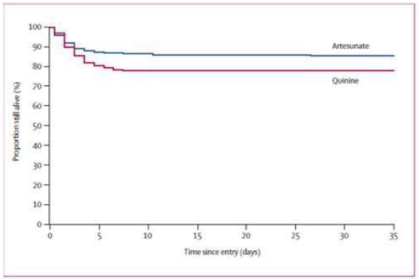
Intervention	Result
High-dose phenobarbitone	Harm
Exchange blood transfusion	No benefit
Fluid loading	Harm
Albumin	Harm
Erythropoetin	Ongoing
Activated charcoal	Ongoing
L-arginine	Ongoing
Sevuparin	Ongoing
Levamisole	Ongoing
Artesunate	*Reduced mortality by 35%*

The Journal of Infectious Diseases 2013;208:192–8

Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial

South East Asian Quinine Artesunate Malaria Trial (SEAQUAMAT) group*

Lancet 2005; 366: 717–25



o Multi-centre, open-label, randomised controlled trial
Comparing parenteral artesunate and parenteral quinine in (mostly) adults and children from Bangladesh, Myanmar, India andIndonesia.
Absolute reduction in mortality with artesunate of 34.7% (95% CI 18.5–47.6; P = 0·0002)

Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial

Arjen M Dondorp, Caterina I Fanello, Ilse C E Hendriksen, Ermelinda Gomes, Amir Seni, Kajal D Chhaganlal, Kalifa Bojang, Rasaq Olaosebikan, Nkechinyere Anunobi, Kathryn Maitland, Esther Kivaya, Tsiri Agbenyega, Samuel Blay Nguah, Jennifer Evans, Sa
Catherine Kahabuka, George Mtove, Behzad Nadjm, Jacqueline Deen, Juliet Mwanga-Amumpaire, Margaret Nansumba, Corine Karema, Noella Umulisa, Aline Uwimana, Olugbenga A Mokuolu, Olanrewaju T Adedoyin, Wahab B R Johnson, Antoinette K Tshefu, Marie A Onyamboko, Tharisara Sakulthaew, Wirichada Pan Ngum, Kamolrat Silamut, Kasia Stepniewska, Charles J Woodrow, Delia Bethell, Bridget Wills, Martina Oneko, Tim E Peto, Lorenz von Seidlein, Nicholas P J Day, Nicholas J White, for the AQUAMAT group*

Lancet 2010; 376: 1647–57

o An open-label, randomised trial comparing parenteral artesunate and parenteral quinine in children (<15 years) from 11 centres in nine African countries.
Relative reduction in mortality with artesunate of 22.5% (95% CI 8.1–36.9; P = 0.0022).
Artesunate also reduced the incidence of convulsions and coma. These are often associated with subsequent neurological sequelae.

Travel Medicine and Infectious Disease (2015) 13, 143–149

REVIEW

Delayed haemolysis after artesunate treatment of severe malaria – Review of the literature and perspective

Thierry Rolling [a,b,*], Tsiri Agbenyega [c], Sanjeev Krishna [d,e,f], Peter G. Kremsner [e,f], Jakob P. Cramer [b]

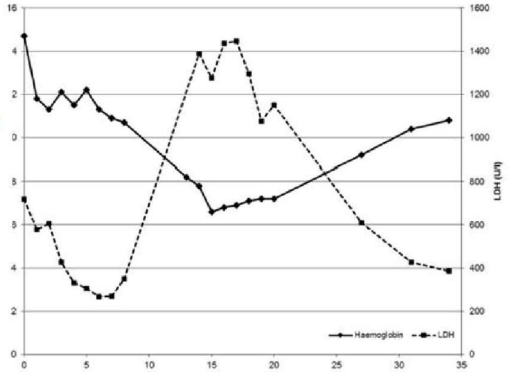


Figure 1 Typical time course of delayed haemolysis showing a secondary peak of LDH activity at the time of Hb nadir around Day 15 after the start of treatment with artesunate (Day 0). (adapted from original patient data of a patient reported in [30]).

Summary Artesunate has replaced quinine as the recommended first-line treatment of severe malaria as it clears parasites faster and lowers mortality. After artesunate's introduction, however, reports of delayed haemolysis have emerged. Typically, this adverse haemolytic event peaks two to three weeks after the acute phase of malaria, and can be severe enough to make blood transfusions necessary in the management of some patients. Delayed haemolysis has been detected in prospective studies in 7–21% of patients treated with artesunate. A confirmed risk factor in travellers is hyperparasitaemia, while additional in malaria-endemic countries young age has been shown to increase risk. The pathophysiology of this phenomenon has not yet been fully elucidated, but may include various combinations of delayed destruction of "pitted" erythrocytes and autoimmune aetiology.

All patients treated with parenteral artesunate should be followed up for at least four weeks to detect signs of haemolysis and to allow appropriate symptomatic treatment.

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