

postmortem fracture haemorrhage, thus indicating the dogma is flawed.

**Method:** Sixty four female Sprague-Dawley rat femora were fractured using a uniform method consisting of a guillotine ramming system and constant load. Femora were fractured at postmortem intervals of 5, 10, 15, 30, 45, 60, 120, 240 and 480 minutes. Samples were histologically processed and examined for haemorrhage using light microscopy.

**Results:** Microhaemorrhage was observed in 31.3% of samples. Sources of haemorrhage included central venous sinus and periosteal vessels. There was no sole contributing source of haemorrhage. Fracture type had no effect on haemorrhage. Although results of logistic regression were not significant, the odds ratio indicated that postmortem interval increases the odds of haemorrhage (odds ratio=1.003,  $P=0.068$ ). No haemorrhage was observed at 30 minutes. Changes in blood viscosity over time as a result of postmortem changes in blood may explain this unexpected relationship.

**Conclusions:** Findings confirm that the current dogma is flawed which has major implications for the determination of fracture origin in medicolegal cases. Investigation of patterns in haemorrhage provided further insight into postmortem fracture haemorrhage and may be of use in medicolegal cases where fracture haemorrhage is observed.

### **Inhibition and reversal of cytoadherence in *Plasmodium falciparum* malaria**

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**Aim:** To investigate the ability of monoclonal antibodies to endothelial cell receptors to inhibit and reverse cytoadherence. Cytoadherence of erythrocytes infected with *Plasmodium falciparum* to endothelial cells contributes to the pathophysiology of cerebral malaria, the major cause of malaria-associated deaths. Parasite strains with different binding characteristics were used; IgG binding to

the endothelial cell receptors ICAM-1 and CD36, C24 binding to CD36 only.

**Methods:** Fluorescence activated cell sorting analysis was used to show that human dermal microvascular endothelial cells express ICAM-1 and CD36. Static and flow adhesion assays were used to show that both parasite strains adhere to human dermal microvascular endothelial cells. Following this, inhibition and reversal of binding of infected red blood cells to human dermal microvascular endothelial cells by  $\alpha$ ICAM-1 and  $\alpha$ CD36 monoclonal antibodies was assessed under both static and flow conditions. Human dermal microvascular endothelial cells were stimulated with tumour necrosis factor- $\alpha$  for 18 hours before assays, as this upregulated ICAM-1 expression.

**Results:** Strong inhibition and reversal of binding to human dermal microvascular endothelial cells was achieved.  $\alpha$ CD36 significantly reversed binding of C24 to human dermal microvascular endothelial cells under static (85% reversal) and flow (88%) conditions. For ItG under static conditions,  $\alpha$ ICAM-1 (83% reversal) and  $\alpha$ ICAM-1+ $\alpha$ CD36 (78%) had a similar efficacy when reversing cytoadherence than  $\alpha$ CD36 alone (57%). This was also observed under flow conditions.

**Conclusions:** These results show that adherence of infected red blood cells to endothelial cells can be prevented using monoclonal antibodies, and that adherent cells can be detached. There is a need for adjunct therapies for malaria; the prevention and reversal of cytoadherence to ICAM-1 is particularly relevant, as this has been linked with cerebral malaria.

### **Assessment of gastric function by non-invasive imaging: clinical studies in health and patients with functional dyspepsia**

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**Aim:** To assess whether non-invasive tests of gastric function can distinguish

patients with functional dyspepsia from healthy volunteers.

**Methods:** Patients with functional dyspepsia with normal endoscopy and 24-hour pH studies were recruited. The nutrient drink test assessed maximum ingested volume (0.75 kcal/ml at 40 ml/min). Gamma scintigraphy and magnetic resonance imaging assessed gastric function and dyspeptic symptoms after ingestion of 400 ml liquid test (0.75 kcal/ml at 40 ml/min) meal on two separate study days.

**Results:** Data from patients with functional dyspepsia ( $n=8$ , 7 female) were compared to two sex- and age-matched healthy volunteers. Patients with functional dyspepsia had a lower body mass index ( $P=0.023$ ) and tolerated a smaller maximum ingested volume than healthy volunteers ( $P=0.026$ , 95% confidence interval -765.8 ml to -54.3 ml).

With gamma scintigraphy, gastric meal volume immediately after ingestion tended to be lower in patients with functional dyspepsia than healthy volunteers (V0: median 325.9 ml vs 346.3 ml;  $P=0.177$ ) and gastric emptying rate T50 was significantly slower ( $P=0.009$ , 95% confidence interval -1.8 ml to -0.3 ml). No difference in gastric emptying half time (T50, the conventional measure) was present. With magnetic resonance imaging, measurements of gastric volume (meal and secretion) were larger than gamma scintigraphy ( $P<0.010$ ), but there were no differences between groups.

Compared to healthy volunteers, patients with functional dyspepsia scored dyspeptic symptoms higher after the 400 ml meal (nausea ( $P=0.001$ ), epigastric pain ( $P=0.002$ ) and bloating ( $P=0.052$ )). Normal postprandial sensations were similar (satiety ( $P=0.163$ ), fullness ( $P=0.416$ )) as was heartburn ( $P=0.292$ ).

**Conclusions:** Patients with functional dyspepsia can be distinguished from healthy volunteers by objective physiological measurements and reports of dyspeptic symptoms after a standardized 400 ml liquid nutrient test meal. The presence of rapid initial gastric emptying followed by slow later gastric emptying, as assessed by gamma scintigraphy, may be a useful diagnostic marker.