patients with rhabdomyolysis secondary to trauma.6

- Whilst we agree that factors such as heterophile antibodies (HA) can cause interference in immunoassays (such as that used to assay cTnI) and thus produce true false positives, the incidence of interfering HAs is low.7 Furthermore, the majority of studies assessing the prognostic significance of cTnI make no effort to screen and correct for HAs.

Our study demonstrated that up to one third of patients undergoing bypass surgery for critical lower limb ischaemia (CLI) sustained peri-operative myocardial injury as manifest by an elevated cTnI. Regardless of the mechanism of injury, it is clear that myocardial cell damage occurs in a significant proportion of these patients and there is abundant evidence to demonstrate that acute elevations in cTnI are associated with adverse short and long-term prognosis in patients undergoing major vascular surgery.8,9 Jeganathan and Walker are keen to stress the importance of clinical context when investigating patients with CLI for coronary artery disease. This group has such a high incidence of coronary artery disease that further treatment of those patients experiencing a cTnI rise seems entirely appropriate.

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Vainas et al. investigated a possible effect of a 3-day azithromycin course on peripheral arterial disease (PAD) during 2 years. Peripheral arterial complications were observed in 23% of azithromycin-treated and 20% of placebo-treated patients. Vainas et al. concluded that a short-term course of azithromycin does not influence PAD.1 In contrast, our group showed that administration of roxithromycin for 28 days prevents progression of PAD in Chlamydia pneumoniae seropositive men. Limitation of walking distance to 200 m or less was observed in 20% of roxithromycin-treated and 65% of placebo-treated patients. Five invasive revascularizations were carried out in 20% of roxithromycin-treated patients compared to 29 interventions in 45% of placebo-treated patients during 2.7 years.2

The striking difference between the two studies regarding the effect of macrolides on PAD needs explanation. Patients were selected differently for the two studies. Vainas et al. selected patients who either had an IgA titer >16 (mean 28) EIUs or were C. pneumoniae seronegative. In contrast, an IgG titer ≥1/128 was inclusion criterion of our study, median C. pneumoniae antibody titers were 1/256 (IgG) and 1/64 (IgA). The percentage of patients undergoing severe impairment of PAD clearly differed between the placebo group of Vainas’ study (20%) and our study (65%). Duration of antibiotic treatment was different in the two studies. Azithromycin administered for 3 days—though characterized by a serum and tissue half life time of several days—is expected to have a less accentuated
anti-chlamydial effect than roxithromycin given for 28 days in our study.

A possible effect of macrolides on PAD depends on (I) selection of patients with clinically relevant endovascular infection with *C. pneumoniae* and (II) treatment of these patients with an effective regimen. The relevance of patient selection is often underestimated. We selected—in contrast to Vainas et al.—patients with high antibody titers (IgG ≥ 1/128) and a high clinical activity of peripheral atherosclerosis (severe impairment of PAD was observed in 65% of the placebo-treated patients). These features might indicate endovascular chlamydial disease. In our study, a significant association between *C. pneumoniae* seropositivity and incidence of PAD confirmed the involvement of *C. pneumoniae*. It is worth noting, that *C. pneumoniae* seropositivity was also significantly related to peripheral arterial events in the study by Vainas et al.

It will be subject of further studies to evaluate whether a high clinical activity of peripheral atherosclerosis in presence of high *C. pneumoniae* antibody titers is a reliable criterion for patient selection and whether administration of macrolides during 1 month is an optimum regimen. A further indicator of endovascular infection with *C. pneumoniae* might be elevated concentrations of serum homocysteine. In both Vainas’ and our study, *C. pneumoniae* antibodies were preferentially associated with atherosclerosis of peripheral arteries. Preference of *C. pneumoniae* for peripheral arteries is conceivable since peripheral arteries have a different embryological origin and a different histological constitution than coronary and cerebral arteries.

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Reply to: Effect of Macrolides on Peripheral Arterial Disease Depends on Patient Selection and Adequate Treatment. P.A. Krayenbuehl, P. Wiesli, T. Meier, G. Schulthess

We appreciate the interest of Krayenbuehl and colleagues in our recently published paper although we believe that their conclusions need some reconsideration.

Despite the promising initial reports suggesting a favourable effect of antibiotics on coronary events, recently published randomised clinical trials, enrolling more than 10,000 patients with acute and/or chronic coronary artery disease, failed to demonstrate any beneficial effect of prolonged antibiotic treatment (3 months–1 year) on coronary artery disease progression.

The assumption that *Chlamydia pneumoniae* is preferentially associated with peripheral arterial disease (PAD) and that antibiotic treatment of selected PAD-patients may prove effective needs some careful evaluation. Despite the different developmental origin of peripheral arteries, early histological studies have shown that *C. pneumoniae* DNA and proteins were ubiquitously present in atherosclerotic plaques throughout the body. Furthermore, it is believed that, after a respiratory tract infection, *C. pneumoniae* reaches the vasculature through infected alveolar macrophages. To the best of our knowledge, no regional differences in leucocyte–endothelial interactions have been reported, so that preferential homing of infected monocytes to peripheral atherosclerotic sites on the basis of different vascular