Unfractionated heparin enhances platelet aggregation in HD patients [4,5]. Regarding the effect of LMWH, in one study it did not alter ADP- or collagen-induced platelet aggregation during dialysis [6], but in another one no differences between unfractionated heparin and LMWH were observed [7]. The positive impact of LMWH on platelet aggregation, found in our study, could be the result of the reduced microthrombus formation accompanied by less fibrinolytic mechanism activation and fibrinogen fragments production during the HD procedure. Sreedhara et al. showed that platelet dysfunction in chronic HD patients results from decreased GpIIb/IIIa availability due to receptor occupancy by fibrinogen fragments [8]. Additionally, Sobel et al. have detected that unfractionated heparin directly binds to GpIIb/IIIa modulating its function [9]. This aspect has not been extensively evaluated for LMWH.

In our opinion, the effect of LMWH on PLT function in HD patients needs further evaluation.

**Conflict of interest statement.** None declared.

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**Editorial Note:** Dr Gritters et al. have been invited to reply to this letter but we did not receive a response in time.


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**Letter and Reply**

Advance Access publication 25 December 2008

**Mystery of pentraxin-3 not yet resolved: still a long way to its prime time in surgery**

Sir,

With great interest we read the article [1]. Since pentraxin 3 (PTX3) is a leading topic of our own research, we feel that we might add some comments on the authors’ findings. It was their declaration that PTX3 levels increase dramatically after surgery that incited us to open this discussion. On the basis of our current knowledge, we must strongly argue against this unfounded contention. While there is no doubt that plasma concentrations of PTX3 do increase in sepsis and in endotoxic shock, just the same as they do after myocardial infarction, to the best of our knowledge no one has up till now established PTX3 levels after surgery. The authors did not address this issue in their study. The disputable contention of theirs has been extracted from a surgical study performed by Hampel and co-workers [2].

Nevertheless, we must insist that ‘living kidney donation’ represents a tiny and an altogether specific fraction among surgical patients. This specificity, which resides in expanling one kidney from a healthy organ donor, has most probably elicited the increase of PTX3 levels in the quoted study. Moreover, this PTX3 elevation went hand in hand with increase of plasma CRP (C-reactive protein) levels, which also is an unusual finding [3–5]. Of note, the questionable declaration about PTX3 rising dramatically after surgery has been borrowed from a study that included all in all six patients.

As far as PTX3 research is concerned, we must concede that the surgical community seems to stand hesitatingly apart from the scientific mainstream. Three years ago, when we designed our own study that was intended to gain insight into PTX3’s behaviour in cardiac surgical patients, we started by searching the Medline database for similar studies in order to avoid any duplicity. However, using the mesh headings: ‘pentraxin 3’, ‘coronary artery bypass grafting’ (CABG), ‘cardiac surgery’, ‘cardiopulmonary bypass’ (CPB), or quite simply ‘surgery’, we did not find any relevant reference.

Our PTX3 study, realized in the autumn of 2005, searched for an answer to the question: ‘Does cardiac surgery increase plasma levels of PTX3 similarly to or differently from CRP?’ We randomly enrolled 40 CABG patients to be operated either with the use of CPB or avoiding CPB [6]. Study participants were purposely confined to otherwise healthy subjects in whom an uneventful peri- or postoperative course was expected. Since the heart is supposed for an answer to the question: ‘Does cardiac surgery increase plasma levels of PTX3 similarly to or differently from CRP?’ We randomly enrolled 40 CABG patients to be operated either with the use of CPB or avoiding CPB [6]. Study participants were purposely confined to otherwise healthy subjects in whom an uneventful peri- or postoperative course was expected. Since the heart is supposed to represent one of the most important sites of PTX3 production, even if the inflammatory process attacks primarily another organ, e.g. the brain [7], our aim was to set...
normal’ postoperative PTX3 levels in cardiac surgical patients. We assumed that any deviation from these reference PTX3 levels might supply prognostic information of an as yet unpredictable value, similar to myocardial infarction patients. Moreover, surgical manipulation of the heart can be expected to set off local PTX3 production, which in turn would influence systemic PTX3 levels.

There were no major complications in any patient of either group. Plasma CRP levels displayed typical elevations, attaining 100-fold of their basal levels. Contrary to our expectations, the plasma levels of PTX3 did not exceed 2.0 ng/ml in any patient or at any time point investigated. On the basis of our results, we feel competent to claim that, in contrast to CRP, an uneventful surgical procedure executed on the heart, irrespective of the use of CPB, does not elicit any increase in plasma PTX3 concentrations (Figure 1). An as yet open question is presented by the PTX3 response in patients affected by complications. Results from our larger study that enrolled at-risk cardiac patients are now being evaluated.

Results published by Michael Boehme and his team differ in some basic aspects from what has so far been established concerning PTX3 behaviour in human biology and disease. The authors found that PTX3 production in whole blood of patients is very slow, increasing only after 48 h and attaining a plateau after 72–96 h. This is in striking contrast not only to myocardial infarction patients [3,4] but also to patients suffering from multiple injuries and/or sepsis, in whom plasma levels of PTX3 peak much earlier, i.e. about 8 h after the onset of the index event, regularly preceding peak levels of CRP [5]. Furthermore, increased PTX3 levels in renal failure patients discerned those suffering from concomitant coronary and/or peripheral artery disease(s) from their counterparts who were free from vascular diseases. This correlation between levels of inflammatory markers and the presence or absence of CAD (coronary artery disease) was reported to be most important for PTX3, whereas it was almost insignificant for CRP. This is really a unique finding. In our CAD patients, we observed virtually no correlation between PTX3 levels and disease presence, its angiographic extent or the gravity of disease symptoms.

For all the comments we have made, we think that the study by Boehme and co-workers merits profound attention for shedding new light on PTX3 kinetics in patients with end-stage renal disease. The most likely explanation for both Boehme’s and Hampel’s unique findings is renal failure or a sudden loss of a kidney ensuing in alteration of many metabolic pathways, including those that involve PTX3. We can only speculate that PTX3 is catabolized and eliminated from the human body preferentially via the kidneys. Further studies are warranted to confirm or refute this hypothesis.

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Reply

Sir,
We read with great curiosity the comments by Kunes et al. regarding our publication [1].

A large part of their comments is related to pentraxin levels after surgery. Kunes et al. doubt that pentraxin levels