What Is HUS and What Is TTP?

N.

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Dear Sir,

If I might be allowed, I would like to use your columns to comment on this issue which has been discussed recently by Remuzzi [1], but which, in my opinion, is far too important to allow a one-sided view. It is important because so many infants die of haemolytic-uraemia syndrome (HUS), and yet we wallow in academic discussions without embarking on practical solutions. My comments will apply also to the views of Neil [2].

Remuzzi's [1] description of HUS is accurate to fine detail. In spite of the fact that he clearly distinguishes the role of endotoxins in causing HUS from a different syndrome caused by anti-endothelial antibodies, he insists on amalgamating HUS and TTP simply because he has no certain clinical means of distinguishing them. I have indicated elsewhere [3] that correct reading of the older literature indicates that HUS and TTP are different. Moreover, if one starts from the assumption that HUS in infants is commonly caused by endotoxaemia (arising from the bowel or urinary tract), albeit in certain areas of the world viruses or rickettsiae could play some part, and that TTP (usually of middle-aged ladies) is an auto-immune reflection of production of antibodies to endothelial cells, then at least the scene is set for a practical approach to the situation. The fact that prostacyclin deficiency (by oestrogen administration or poisoning by ciclosporin or mitomycin C) may complicate either situation should not delude us into thinking that this final common pathway is the basis for definition of a clinical syndrome. Rather in the case of HUS we should all be searching for lipid A toxin at the onset of the illness and thus for a rise of lipid A antibodies in the ensuing days, and in the case of TTP we should be looking for better techniques for detecting antibodies to endothelium. Like endotoxin, they are going to be evanescent because of the absorption capacity of the endothelial surface.

Only when we have the results of such researches shall we be in a position to correctly formulate our definitions.

Meantime I would like to comment on some associated problems. Firstly, much publicity has been given to the verotoxin of certain *Escherichia coli*. Nevertheless

lipid A toxin is the most powerful toxin known with respect to its potential for vasoconstriction and mediation of endothelial cell damage. Rather verotoxin is a cytotoxin that enables certain pathogens to penetrate the gut mucosa. Quite clearly, if the mucosa is breached, endotoxaemia will follow. In experimental pathology certain viruses have been shown to cause such a sequence of events.

Secondly, in my opinion, von Willebrand factor is receiving more than its fair share of attention. It has been demonstrated that the deposition of fibrin on vascular endothelium leads to the release of von Willebrand factor [4]. The fact that the size of the monomers is different in HUS may merely reflect the nature of the damage to endothelium, without shedding light on the cause of the problem. All the same, analysis of this situation could be productive.

Thirdly, it is clear to all who work with DIC problems that infusion of fresh plasma that contains antithrombin III ought to be beneficial [5]. So much the better if it also contains a PGI₂-stimulating or protective factor. Yet it is my opinion that it will be those plasmas that contain good anti-lipid A antibodies that could confer the most benefit for sick wee infants.

References

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