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Bugs in the system

Bugs play a large role in our life. Bugs can be either good, or bad for us. Microorganisms, such as gut microbiota, are usually beneficial to us. They provide a barrier to pathogenic organisms and help to digest our food. However, microbiota also produce Trimethylamine-N-oxide (TMAO), a metabolite of dietary phosphatidylcholine and L-carnitine, that has been recently been shown to increase the risk of arterial thrombotic events, such as myocardial infarction and stroke. In this issue of Thrombosis Research, Reiner and colleagues have investigated whether plasma levels of TMAO also associate with recurrent venous thromboembolism, major or non-major bleeding, and mortality in a cohort study of elderly patients with acute VTE [1]. While they show that both extremely low and extremely high plasma levels are associated with increased mortality, they could not find associations between TMAO plasma levels and risk of recurrent VTE or bleeding. Thus, TMAO levels appear to be mainly associated with arterial thrombosis.

One other example of the dramatic effects microorganisms may have on human health is sepsis. Bacterial infection can lead to excessive activation of the immune system, leading to organ failure and eventually death. Sepsis may also lead to disseminated intravascular coagulation, a condition in which the formation of microvascular thrombi further contributes to organ damage. The international Society of Thrombosis and Haemostasis (ISTH) has developed a tool to facilitate the diagnosis of DIC and one of the criteria taken into account by this tool is an increase in D-dimer levels, the latter being a break down product of fibrin. However, as sepsis also inhibits fibrin breakdown, D-dimer levels may not be an appropriate criterium for the diagnosis of DIC. Indeed, in this issue, Semeraro and colleagues show that D-dimer levels in the normal range, rather that enhanced D-dimer levels, are associated with higher mortality in septic patients [2]. Thus, it appears that the ISTH diagnostic tool needs some refining.

Venous thromboembolism (VTE) is a major complication following lower-leg cast immobilization and knee arthroscopic surgery. Patients undergoing lower-leg cast immobilization or knee arthroscopic surgery are often given thromboprophylaxis to prevent VTE, but a recent study has shown that thromboprophylaxis was not effective for symptomatic VTE reduction. Apparently, there are bugs in our understanding of the system. In a narrative review, Nemeth and Cannegieter discuss the necessity of thromboprophylaxis in these patients and perform meta analyses on the efficacy of thromboprophylaxis in patients with lower-leg cast immobilization and knee arthroscopic surgery [3]. They conclude that there was no clear benefit of thromboprophylaxis on the prevention of *symptomatic* VTE, while in contrast, this seemed to prevent *asymptomatic* DVT. In lower-leg cast patients, thromboprophylaxis appeared to reduce symptomatic VTE. Nevertheless, they advise caution and the validity of these results may be questioned as many trials had several methodological weaknesses. Therefore, more research is warranted to remove the bugs from the system.

References

[1] Martin F. Reiner, Daniel Muller, Sara Gobbato, Odile Stalder, Andreas Limacher, Nicole R. Bonetti, Lisa Pasterk, Marie Mean, Nicolas Rodondi, Drahomir Aujesky, Anne Angelillo-Scherrer, Christian M. Matter, Thomas F. Luscher, Giovanni G. Camici, Arnold von Eckardstein, Jurg H. Beer, Gut microbiota-dependent trimethylamine-*N*-oxide (TMAO) shows a Ushaped association with mortality but not with recurrent venous thromboembolism, Thromb Res. 174 (2019) 40–47.

[2] Fabrizio Semeraro, Concetta T. Ammollo, Pietro Caironi, Serge Masson, Roberto Latini, Mauro Panigada, Nicola Semeraro, Luciano Gattinoni, Mario Colucci, Low D-dimer levels in sepsis: Good or bad? Thromb Res. 174 (2019) 13–15.

[3] Banne Nemeth, Suzanne C. Cannegieter, Venous thrombosis following lower-leg cast immobilization and knee arthroscopy: From a population-based approach to individualized therapy, Thromb Res. 174 (2019) 62–75.

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