Translocation – Physiologic Mechanism or Clinical Problem?

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Translocation, defined as the escape from the intestinal tract of bacteria and their toxins to extraluminal sites, is still a matter of controversy. A large body of evidence, derived from both experimental and clinical studies, suggests that it indeed occurs, yet its clinical significance remains to become established.

According to present concepts some form of bacterial passage across the intestinal barrier may occur even under physiologic conditions. Certain microorganisms may reach the submucosal space either within macrophages; or by active transcellular or intercellular penetration; or by endocytosis, absorption, or diffusion. During this passage or on their further way towards the mesenteric lymph nodes, intracellular or free bacteria may be killed by the host's defense system (grade 0 translocation). Viable germs in the mesenteric lymph nodes (grade I translocation) are a common finding in a huge variety of pathologic and experimental conditions. The spread of bacteria beyond this level leads to their detection within the circulation and in different organs (grade II). Although the lymphatics are an important route, some bacteria may also enter small venules and reach the portal system while others have been shown to find an intercellular passage across the muscularis propria into the peritoneal cavity. Whether systemic spread has to be regarded as the decisive step in the development of a septic response (grade III) still remains unproven.

Differences in reported translocation rates to specific extraluminal sites may reflect differences of culture methods, of the species involved, and of the respective model. It turned out that the magnitude of translocation – and thus probably the detectable grade – basically depends on three different factors: the bacterial factor, which is mostly related to a disturbed colonization resistance with subsequent bacterial overgrowth; the bowel wall factor, combining morphologic and physiologic alterations; and the defense factor, which encompasses all antibacterial effects (such as phagocytosis and intracellular killing) both locally and systemically.

Under most pathologic conditions at least one of these factors will come into play. In this issue two rat models of translocation are presented: methotrexate-induced enterocolitis – a well-established model for the beneficial effects of enteral diets – and obstructive jaundice [1, 2]. With both models all three factors eventually become influential. Methotrexate directly disrupts the mucosal barrier, alters bowel physiology, allows for bacterial overgrowth, and decreases the capacity of host defense. Intra-luminal bile depletion also may lead to mucosal damage, to alterations of gut propulsion, to bacterial overgrowth, and to immunodepression.

Both papers offer therapeutic approaches: Continuous intragastric infusion of three different strains of *lactobacilli* prior to methotrexate [1] and orally fed lactulose [2]. Both regimens lowered translocation rates, reduced overgrowth with pathogenic bacteria, improved mucosal constituents and structure respectively, and dampened inflammatory reactions.

The role of both *lactobacilli* and lactulose in the re-establishment of normal intestinal microflora and for epithelial nutrition is well known. Whether additional beneficial effects are involved in the restoration of host defense is less clear. Both 'bacteriotherapy' and lactulose-enriched enteral diets may well establish their place in the clinical setting, where the prevention of translocation might reduce spontaneous bacterial peritonitis and bacteremia in cirrhotic patients and secondary infection in patients with pancreatic necroses.

References

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