THE FORMATION OF PERITONEAL ADHESIONS

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The increased incidence of postoperative adhesions and their complications has focused attention on trying to understand the adhesion, adhesion formation, clinical consequences, and prevention of adhesion formation.

Adhesions are highly differentiated, formed through an intricate process involving a complex organ, the peritoneum, whose surface lining is the key site in adhesion formation.

The peritoneum, a serous membrane, serves a protective function for the contents of the abdominal cavity. Homeostasis is maintained by allowing exchange of molecules and production of peritoneal fluid. This provides an environment for optimal function of intra-abdominal organs. Forms of trauma to the peritoneum (i.e., mechanical, thermal, chemical, infectious, surgical, and/or ischemic) can result in the formation of peritoneal adhesions.

In 1919, it was shown that peritoneal healing differed from that of skin. When the peritoneal membrane is traumatized, a dynamic response results that produces a series of steps toward rapid regeneration in approximately five to seven days of the injured peritoneum via re-epithelialization, irrespective of the size of injury. Microscopic studies showed the new peritoneal cells are derived from mesodermal cells of the underlying granulation tissue, multipotent mesenchymal cells that are able to take the form of fibroblasts or mesothelial cells.

When a defect is made in the parietal peritoneum the entire surface becomes simultaneously epithelialized, differing from the gradual epidermalization from the borders as is found in skin wounds. Multiplication and migration of mesothelial cells from the margins of the wound *may* play a small part in the regenerative process, but it does not play a major role. The new mesothelium develops in the centre of a large peritoneal wound at the same time as it develops in the centre of a smaller one.

The stimulatory trauma induces deposition of a fibrin-rich exudate on the serosa which is infiltrated to various degrees with cells. Principal cellular elements in this cascade are leukocytes, including polymorphonuclear neutrophils and macrophages, and mesothelial cells. Macrophages are a major component of the leukocyte population exhibiting increased phagocytic, respiratory burst and secretory activity, and recruit new mesothelial cells onto the surface of the injury. The mesothelial cells form small islands throughout the injured area and proliferate into sheets of mesothelial cells accomplishing re-epithelialization via production of a fibrinous exudate usually within five to seven days after surgery.

The fibrin gel matrix developed in the cascade, a progenitor to temporary and/or long-term adhesions, results in the formation and insolubilization of fibrin polymers which interact with fibronectin and a series of amino acids. Apposed traumatized tissues bind via fibrin bridges organized by wound repair cells. These often support a rich vascular supply as well as neuronal elements.

In this step-wise series of events, a pivotal role is taken by the enzyme plasmin, and its promoters and inhibitors. It is mainly the tissue-type plasminogen activator/plasminogen activator inhibitor ratio which determines the rate of fibrinolysis

and therefore the rate of adhesion formation/dissolution. Protective fibrinolytic enzyme systems of the peritoneal mesothelium, such as the tissue plasminogen activator (tPA) system, can remove the fibrin gel matrix reducing adhesion formation.

In this scheme, adhesional links should be temporary and eliminated by the action of the fibrinolytic agents present in the peritoneum. Optimal repair of injured peritoneum typically occurs as the result of early mesothelial proliferation over the damaged surface, with little production of permanent fibrous adhesions. However, variable strength adhesions of viscera to viscera, or viscera to the peritoneal wall can also result. Events that inhibit early fibrinolysis through the production of cytokines can result in the production of plasminogen inhibitors, determining a greater number of more tenacious adhesional patterns.

Surgery has been shown to dramatically diminish fibrinolytic activity in at least two ways: (1) it increases levels of plasminogen activator inhibitors, and, (2) it reduces tissue oxygenation. And interestingly, a number of studies suggest that fewer adhesions appear when peritoneal rends remain open.

Peritoneal re-epithelialization and adhesion formation thus can be seen as alternative pathways following peritoneal injury. One of a number of pivotal events may be the extent of fibrinolysis. However, it is suggested that the rate of injury determines the rate and extent of the inflammatory response to that injury. In turn, the inflammatory reaction and the control of that reaction may also determine the extent of adhesion formation.

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