



The promotion of tumor metastasis by surgery and stress: immunological basis and implications for psychoneuroimmunology.

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This mini-review emphasizes a psychoneuroimmunology (PNI) perspective of the hypothesis that stress and surgical excision of the primary tumor can promote tumor metastasis. It first establishes the empirical and theoretical basis for control of metastasis by cell-mediated immunity (CMI), as well as the interactive role of non-immunological risk factors. It then describes the various aspects of surgery that suppress CMI, and the neuroendocrine mechanisms mediating suppression by stress and surgery. Last, it briefly reviews the empirical evidence, from animal and human studies, for the promotion of metastasis by stress and surgery, with specific reference to the mediating role of CMI. It is concluded that: (a) Immunological mechanisms most likely play a role in limiting metastasis in patients with solid tumors. (b) Immunosuppression can be deleterious, especially when surgery is conducted early, before the tumor develops insurmountable mechanisms to escape immune destruction. (c) The most sensitive period for the establishment of metastases is the immediate aftermath of surgery. Interventions aiming at reducing stress and immunosuppression should thus strive to start beforehand. (d) Psychological and physiological insults activate similar neuroendocrine mechanisms of immunosuppression. Therefore, a multimodal therapeutic approach should be used to prevent tumor metastasis during the perioperative period. (e) Studies employing interventions aimed at reducing the surgical stress response should preferably assess immunological indices with an established clinical relevance, and follow up long-term recurrence provided sample size assure statistical power. (f) The progress toward earlier detection of cancer, and our growing understanding of immunosuppression, continuously improves the chances for successful PNI interventions.

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