EDITORIAL

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Autonomic Denervation and Western Diseases

For an internist, "autonomic denervation" may suggest rare clinical situations such as Shy-Drager syndrome, Charcot-Marie-Tooth disease, or orthostatic hypotension. For a gynecologist, autonomic denervation is rapidly becoming the basis of most of our clinical work. Injuries to branches of the pelvic plexi cause endometriosis, adenomyosis, and many painful pelvic conditions, including vulvodynia, dyspareunia, and irritative bladder and bowel symptoms.[1] These injuries result from difficult first labors, minor gynecologic surgery requiring traction to the uterine cervix or unnecessarily vigorous curettage, and persistent straining during defecation. Latent periods of 5 to 15 years between the primary injury and the subsequent clinical presentation depend on the site, nature, and extent of the original neurologic injury. Injuries to branches of the cardiac, celiac, and pelvic plexi may contribute to clinical conditions presenting to internists?[2]

Burkitt and Trowell[3] found that Africans had lower daily stool weights (110 vs 454 g) and shorter intestinal transit times (12 vs 40 hours) than Europeans and that they did not suffer from Western diseases.[3] One of their students provided later epidemiologic evidence for endemic straining during defecation (30%-40%) in an urban Western population.[4] In that survey, 1% of women achieved successful defecation less than once per week, and, 0.3% less than once per month![4] Persistent straining during defecation causes injuries to autonomic nerves with specific neurohistochemical signatures in every pelvic organ.[1,2] Constipated, supine infants suffer different injuries from adolescents, adults, and the elderly owing to their varying sizes, shapes, and patterns of straining. Recurrent and varying and incoordinate Valsalva maneuvers, that are all-too-obvious in the second stage of labor, may explain some cases of denervation and reinnervation in extra-pelvic organs.

Unexplained autonomic denervation and reinnervation may contribute to Western diseases through several secondary mechanisms, including visceral and ductal dysfunction, tissue hyperplasia and hypoplasia, opportunist infection, and pain and central nervous system "sensitization."[2] Appendicitis, cholecystitis, pancreatitis, inflammatory bowel diseases, interstitial cystitis, allergic rhinitis, asthma, cardiac arrhythmias, hypertension, rectal hypersensitivity, anal fissure, intervertebral disc pain, and erosive lichen planus demonstrate reinnervation in a significant proportion of patients. Some "autoimmune" conditions, including type 1 diabetes, show clear evidence of denervation of the end organ. Further swathes of morbidity result from the layered consequences of obesity, including diverse metabolic and endocrine complications, herniae, hemorrhoids, and varicose veins.[2]

Lower abdominal pain remains a common reason for a woman of reproductive age to consult a physician. The description of the pain often has a "neuropathic" flavor; the pain is persistent and associated with nonspecific, autonomic symptoms, such as headache, nausea, vomiting, and fainting. In the absence of "endometriosis," generic labels such as "irritable bowel syndrome," "fibromyalgia," and "chronic fatigue" often find their way into the case record. In a gynecology clinic, there is almost always a clear history of a source of autonomic injury: prior difficult labor, gynecologic surgery, and persistent straining during defecation. Diagnostic laparoscopy or magnetic resonance imaging demonstrate corresponding asymmetric injuries to the pelvic supports and their associated neurovascular bundles. Neuroimmunohistochemical findings may include reinnervation in the viscus itself or its supporting ligaments.[1,2]

Persistent straining during defecation also results in the clinical enigma of advanced "endometriosis."[1] Injuries to uterine and tubal nerves cause incoordinate dysmotility with retrograde menstruation, as well as fusion of the rectum and vagina. Adhesion of ectopic endometrium to injured pelvic tissues (eg, myofascial supports or small bowel in Crohn's disease) causes further adhesions. Difficult vaginal delivery and traction to myofascial supports during gynecologic surgery also contribute to varying clinical phenotypes. Pain and subfertility result from these injuries rather than any effects of the macroscopic lesions of endometriosis.[1,2] Similar mechanisms may result in coexisting irritative bladder and bowel symptoms that may develop into some patterns of interstitial cystitis and rectal hypersensitivity.

Nineteenth century clinicians, including Lee in 1841 and Frankenhauser in 1867, produced their dissections of the pelvic and cardiac plexi in cadaveric material preserved in alcohol.[5] Modern undergraduate teaching takes place in formalin-embalmed cadavers. Formalin destroys autonomic nerves, not only in the great plexi of the thorax, abdomen and pelvis but also in subtle neuroanatomy in and around each viscus. This obscure neuroanatomy, together with unsuspected sources of

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injury, varying latent periods, and heterogeneous secondary mechanisms, has restricted these lines of inquiry. Temple and Burkitt[6] warned that we may lose several decades in our pursuit of "complex" mechanisms of disease, including genomic and epigenomic processes, before returning to consider the primary influences of diet, bowel habit, and lifestyle.[6] Burkitt and Trowell also suggested that most cancers were also Western diseases with similar etiological origins.

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