

Description of the aetiology of endometriosis based on injuries to pelvic nerves. Persistent straining or difficult vaginal delivery, injures these nerves resulting in “endometriosis”.

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ENDOMETRIOSIS:

THE ELUSIVE EPIPHENOMENON.

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John Sampson described retrograde menstruation as the pathophysiological mechanism for ectopic endometrium in the pelvis though subsequent theories have not advanced this view (Sampson, 1927). Solving the enigma of endometriosis depends on explaining the frequent paradoxes in the clinical expression of the condition. For example, young, nulliparous women often present with persistent pain and subfertility associated with advanced endometriosis and hypertrophic myofascial supports (AFS grade III/IV, Fig 1a-d). Multiparous women typically present with similar symptoms together with injured and atrophic, uterosacral ligaments, and minor deposits of endometriosis (AFS grade I/II). In some cases women have persistent pelvic pain before the appearance of endometriosis; others develop pain after surgical removal of their pelvic organs and every visible, spot of endometriosis. Specific evidence that deposits of endometriosis cause pain is limited yet much surgical effort is expended in removing them. These observations have prompted the view that endometriosis is a manifestation rather than a cause of chronic pelvic pain (Slocumb, 1992).

The denervation-reinnervation view

In many women with chronic pelvic pain with, or without, endometriosis, there are abnormalities of the fascial supports, blood vessels and nerves in the lower pelvis (Fig 1-3). Improving laparoscopic techniques describe frequent, postpartum injuries to the uterosacral ligaments (Fig 1a-d). Allen and Masters originally described the relationship between difficult intrapartum episodes, myofascial injuries and subsequent pelvic pain (Allen, 1955). At the same time Taylor described pelvic vascular congestion and hyperaemia in association with chronic pelvic pain (Taylor, 1948, Beard, 1984). Recent studies confirm abnormal nerves in the myometrium, endometrium, cervix, uterosacral ligaments and retroperitoneum in women with chronic pelvic pain with, or without, endometriosis (Atwal, 2005; Tokushige, 2006, 2007). Interpreting the significance of these wide-ranging injuries to muscles, ligaments, nerves and blood vessels in women with chronic pelvic pain, remains empirical rather than based on specific sequences of events.

Branches of the inferior hypogastric plexi converge on the uterovaginal plexus at the vaginal vault where they are vulnerable to injury (Fig 2, Spackman, 2006). In nulliparous women with extensive endometriosis there is often a clear history of straining to achieve defaecation; in multiparous women there is often a prior, difficult, intrapartum episode (Atwal, 2005). In both circumstances there are injuries to uterine nerves with aberrant neural regeneration in characteristic patterns (Fig. 3b-d, Atwal, 2005; Tokushige,

2006, 2007). In the nulliparous uterus with chronic pelvic pain, the most frequent findings are injured nerves regrowing along small blood vessels (Fig 3d, Atwal, 2005). In the multiparous woman, collateral sprouting of nerve fibres with widespread stromal regeneration is typical of traumatic injury following tearing of nerve bundles (Fig 3b-3c, Quinn, 2002)

Different patterns of neural injury cause aberrant reinnervation in many pelvic organs though particularly those at the junction of the uterus and vagina i.e. the uterine isthmus, cervix, vagina and uterosacral ligaments (Tokushige, 2006, 2007). Aberrant reinnervation results in "allodyniae" where "light touch causes pain or discomfort" (Cervero, 2000) e.g. chronic pelvic pain (Atwal, 2005), dyspareunia (Quinn, 2006), vulvodynia (Westrom, 1998), dysmenorrhea (Atwal, 2005) irritative bladder symptoms (Christmas, 1990) and rectal hypersensitivity (Chan, 2003). Dyspolar uterine activity causes retrograde menstruation that may contribute to dysmenorrhea and subfertility (Leyendecker, 1996). The sequence of events in the denervation-reinnervation view is set out in Table 1.

- 1) Injury to uterine nerves through prolonged straining to achieve defaecation or traumatic vaginal delivery (denervation)
- 2) Aberrant reinnervation takes place in those anatomical features at the junction fo the uterus and vagina
- 3) Aberrant reinnervation results in dyspolar uterine contractility, and, retrograde menstruation delivering endometrium to the pelvic cavity.
- 4) Ectopic endometrium adheres to injured peritoneal surfaces in dependent areas of the pelvis including the uterosacral ligaments

Table 1

Different laparoscopic “phenotypes” results from differing patterns of injury. Teenage, nulliparous women with chronic pelvic pain and “endometriosis” strain during defaecation (Atwal, 2005). Recurrent injuries result in hypertrophic uterosacral ligaments with fusion of rectum to vagina, and, large volumes of endometriosis (AFS grades III/IV, Fig 1d). In multiparous women with chronic pelvic pain and “endometriosis” intrapartum injuries tear myofascial supports (Fig 1b-c). Avulsion of one or both uterosacral ligaments is not unusual though more commonly asymmetrical uterosacral scarring and atrophy coexists with neovascularisation of adjacent peritoneal surfaces (Fig 1b-c). Retrograde menstruation delivers endometrium to these injured surfaces though there may be little, or none, if breast-feeding, or, contraception prevents menstruation during repair of the intrapartum injury.

Causes of pelvic denervation

Straining during defaecation is epidemic in Western societies (Heaton, 1993). Three per thousand women have stool frequencies of less than one per month, one per cent less than once per week (Heaton, 1993). The gender bias increases with age owing to the effects of vaginal delivery and hysterectomy. Persistent straining has effects from the uterus to the vulva depending on the shape of the pelvis, or, the pattern of straining (Quinn, 2007). Tortuous, pelvic blood vessels may escape the direct effects of straining though injuring their innervation may cause abnormal, accompanying, vascular patterns that are typical features in some women with chronic pelvic pain (Beard, 1984).

Allen and Masters established the original associations between intrapartum injuries, myofascial defects, and, subsequent gynaecological problems where the "postpartum cripple" suffered from a "universal joint cervix" (Allen, 1955). Their solution was to repair the fascial injuries though when Dr Allen returned to this subject he recognised hysterectomy to be an appropriate solution in some circumstances (Allen, 1971). In this second paper he drew attention to the role of premature maternal voluntary efforts and minor malpresentations in labour as sources of potential maternal injury. Recent studies confirm, and extend, these findings to include different forms of contemporary difficult intrapartum episodes (Quinn, 2002).

Consequences of pelvic denervation

Aside from the clinical phenotypes of chronic pelvic pain, injuries to pelvic nerves may cause loss of function, tissue hypoplasia (or hyperplasia), visceral dysmotility, susceptibility to infection, pain associated with aberrant reinnervation, and, "sensitisation" of the central nervous system (Jasmin, 2000). Women with endometriosis suffer adverse reproductive outcomes including subfertility, miscarriage, IUGR, preeclampsia, preterm labour with increased Caesarean section rates (Khong, 1997). Susceptibility to infection may promote infectious morbidity associated with recurrent urinary tract infections and vulvovaginal Candidiasis (Zondervan, 1999). Epidemiological studies of women with chronic pelvic pain confirm high rates of coexistent sensory symptoms in anatomically-adjacent organs including irritative bladder and bowel symptoms (Zondervan, 1999). Aberrant reinnervation results in different clinical syndromes in a variety of histopathological patterns in adjacent pelvic viscera (Christmas, 1990, Westrom 1998, Quinn 2002, Chan 2003, Tokushige 2006). Eventually new nerves infiltrate deposits of ectopic endometrium and may also contribute to symptoms (Anaf, 2002).

Hysterectomy for endometriosis may be complicated by recurrent pain within the medium term (MacDonald, 1998). Reasons for this may include continuing, straining to achieve defaecation creating further neurological lesions, or histopathological changes in the dorsal root ganglia where the pain is "stored" by sensitisation of the central nervous system (Jasmin, 2000).

Preventing chronic pelvic pain with, or without, endometriosis, may be both practical and achievable. Teenagers might avoid straining in the bathroom, their older sisters should avoid immoderate episodes in their first labours, and their mothers may need to consider fully the nature and extent of their proposed gynaecological surgery. Reducing immoderate intrapartum manoeuvres from nulliparous induction of labour to specific management of the second stage of labour, seems appropriate. Caesarean section may not remove the risk of neural injury since disruption of the uterine "angle" and the endometrial-myometrial interface, may result in neural injuries with wider clinical consequences in the form of adenomyosis over the medium term (Quinn, 2007).

Conclusions

Much of the pathoanatomy of endometriosis and its clinical associations may be explained by the consequences of uterine denervation. Aberrant reinnervation may account for common clinical symptoms and injuries to fascial supports may account for varying laparoscopic “phenotypes”. The denervation-reinnervation view proposes disordered uterine fundocervical polarity as the mechanism of retrograde menstruation. Widespread, pelvic neuropathic pain is difficult to treat though prevention by improving diets, bowel habits and intrapartum care, may be practicable. Developing these insights may avert some of the “aetiological confusion and therapeutic anarchy” that has characterised the history of this elusive epiphenomenon (Garry, 2004).

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Figure 1

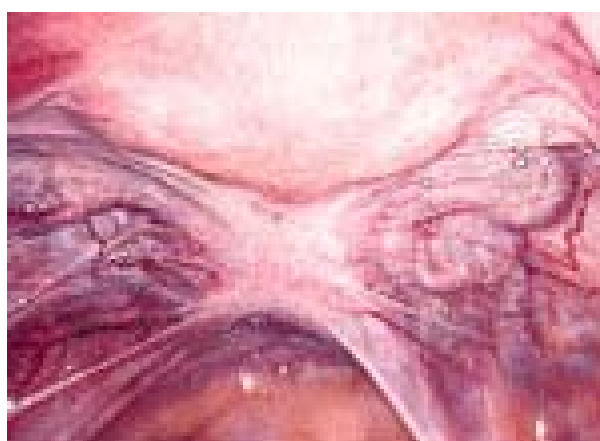
Injuries to the myofascial supports in women with chronic pelvic pain with, or without, endometriosis.

(a) normal uterosacral arch; (b) avulsion of right uterosacral ligament, and, (c) avulsion of left uterosacral ligament with pelvic varices, in women following traumatic vaginal deliveries, and, (d) symmetrical hypertrophy of uterosacral ligaments in a nulliparous woman with persistent straining during defaecation.

1a



1b



1c



1d

Figure 2

The nerve supply of the pelvic viscera in a fresh prosection preserved in methanol rather than formalin demonstrating (a) the superior hypogastric plexus, (b) the hypogastric nerve, c) the inferior hypogastric plexus, (d) the uterovaginal plexus, (e) parasympathetic fibres from sacral segments (S2-4).

Mixed autonomic nerves converge on Frankenhauser's uterovaginal nerve plexus at the vaginal vault where they are vulnerable to intrapartum injury or persistent, straining during defaecation.

This dissection was by Dr Ross Spackman and Dr Alice Roberts, University Department of Anatomy, Bristol.

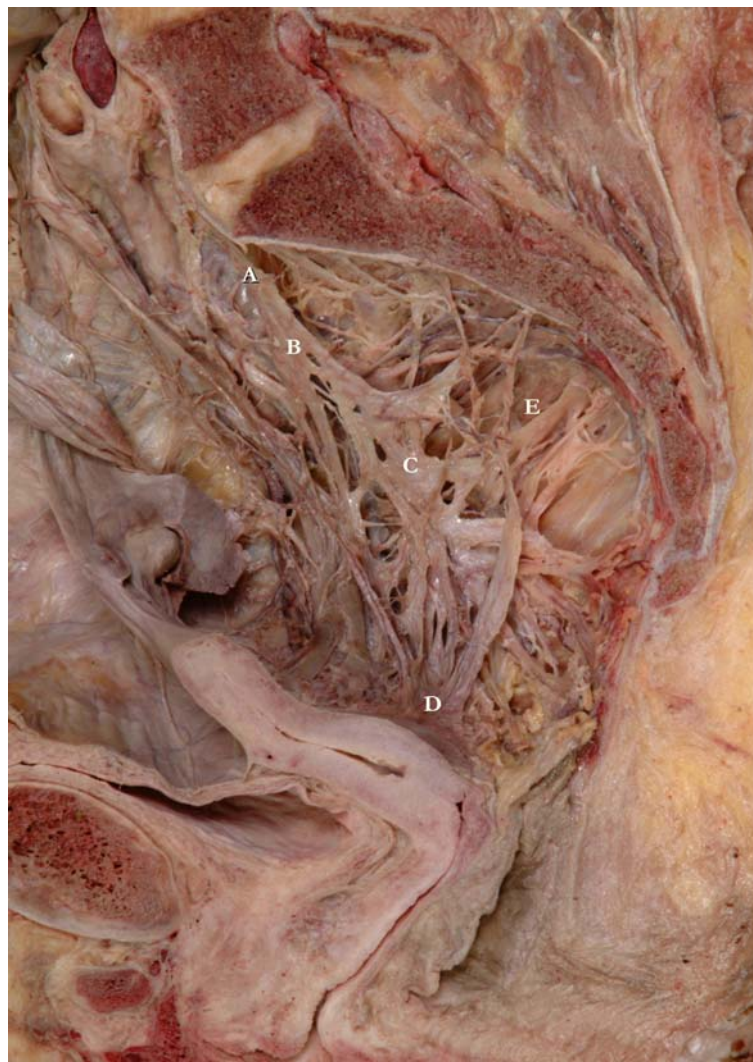


Figure 3**Different patterns of myometrial reinnervation following hysterectomy for chronic pelvic pain with, or without, endometriosis**

(a) sparsely-innervated, normal myometrium, (b) aberrant reinnervation in myometrial stroma, (c) collateral sprouting of nerve bundles following traumatic intrapartum injury, (d) perivascular nerve fibre proliferation around small blood vessels (x 200).

