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The Role of Collagen in Hernia Genesis

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There is a discrepancy between the number of publications on hernia in general and those addressing the role of collagen as an important pathophysiological factor in the development of hernia. On Medline, the search for "hernia" produces more than 14,000 references, whereas the search for "hernia" plus "collagen" or "connective tissue" yields only 25. This difference clearly illustrates that the pathophysiological factors for hernia formation have yet to be fully defined. Many papers address different surgical techniques and their outcomes. The aim of this chapter is to give an overview of the literature on the role of collagen in hernia genesis, with a focus on biomechanical tissue features.

Is Groin Hernia Secondary to Systemic Disease?

In addition to individual predisposition, many other factors are involved in the development of a hernia. For example, chronically raised intra-abdominal pressure secondary to obstructive pulmonary disease, ascites, hyperplasia of the prostate, constipation, and pregnancy, is considered a risk factor.[1] As pointed out by Peacock and Madden, indirect inguinal hernia may appear first in a man over 40 years of age. This is not clearly explained by failure of the processus vaginalis to become obliterated during development. In fact, 20% of males pass into adulthood with a patent processus vaginalis, but less than 50% of these develop clinical herniation.[2,3] Clearly, factors other than an open processus vaginalis must play a role in the development of an indirect hernia. Recurrent indirect hernia may follow high amputation of the peritoneal sac, but here too, more is at work than simple failure on the part of the surgeon.[3]

Other Diseases Associated with an Increased Risk of Hernia Formation

Epidemiological data show increased prevalence of inguinal hernia in some patients who exhibit altered connective tissue formation, as in osteogenesis imperfecta, *cutis laxa,* Ehlers-Danlos syndrome, and Marfan's syndrome. A Swedish study found that congenital hip dislocation in children was associated with an occurrence of inguinal hernia five times greater in girls and three times greater in boys.[4] Curiously, it has been reported that patients with indirect inguinal hernia tend to be hypermobile, as gauged by modified Carter-Wilkinson criteria: the ability to oppose passively both thumbs to the volar aspect of the forearms, or to hyperextend the fifth finger to more than 55° or the elbow to more than 190°. Patients who exhibited two of these three criteria were defined as hypermobile.[5] In a small study, 33% of patients with indirect inguinal hernia were found to be hypermobile versus 5% in the general population.[6] That patients with aneurysm of the abdominal aorta also are predisposed to hernia formation will be discussed later.

There is much evidence to suggest that hernia formation may depend on a systemic predisposition and that this may in turn be associated with abnormal metabolism of connective tissue.

Wound Healing and Collagen Formation

The development of biomechanical strength in wound tissue depends on several complicated steps in the formation of mature collagen. In brief, proliferating fibroblasts produce and secrete procollagen. These long triple helix molecules contain high concentrations of lysine and proline. In the presence of oxygen, vitamin C, and Fe^{++}, they undergo hydroxylation, with conversion of these amino acids to hydroxylysine and hydroxyproline. Procollagen converts extracellulary to tropocollagen. Strong crosslinks between several aligned tropocollagen molecules are created making up collagen fibrils and fibers in the wound cleft. The most abundant component of the later scar tissue is type I collagen. After day 5, there is a rapid increase in tensile strength of the wound in almost all types of tissue. After the proliferation phase of healing, the maturation phase involves equilibration between formation and degradation of collagen. Collagen fibers are reoriented and redistributed, leaving them more compact, thickened, and parallel to one another. Incremental increases in wound strength have been observed up to one year after wounding. During the healing process, the wound contracts due to the action of myofibroblasts.

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Experimental Studies on the Formation of Hernia

Male rats have been used for a hernia model. They have a peritoneum-lined sac extending into the scrotum on both sides. A fat deposit at the level of the abdominal wall prevents the transit of abdominal organs into the scrotum. The importance of the collagen integrity for the prevention of hernia formation was shown by Conner and Peacock.[2] Removal of the fat pad or transection of the external ring resulted in hernia formation in none of the animals, compared with 20% of the animals when the internal ring was transected. However, if systemic treatment with the lathyrogenic agent beta-amino-proprionitrile (BAPN) was applied with no concomitant surgery, 6 to 10% of the animals developed a hernia. When the internal ring was transected and BAPN was administered, 90% of the animals developed a hernia. BAPN is a highly effective blocker of the enzyme lysyl oxidase, which reduces hydroxylysine and impairs cross-link formation between collagen molecules. Collagen then becomes more soluble, with significantly less tensile strength. The combination of an anatomical defect and an abnormality of collagen cross-linking was needed to produce herniation in most animals.

In a previous study, Wirtschafter and Bentley showed that the effect of a lathyrogenic agent on hernia formation was dependent on the age of the rat.[7] Fifty percent of male rats 30 days old acquired a hernia after eating the lathyrogenic agent versus none of the rats 88 days old. This supports the view that the effect of lathyrism is due to failure in maturation of collagen fibers rather than collagenolysis.

Human Studies on the Formation of Hernia

Structural Studies on the Abdominal Wall

Peacock and Madden found major structural changes in the transversalis fascia of patients undergoing repair of either a unilateral indirect hernia appearing after the age of 40 years or a recurrent unilateral hernia of any kind without obvious cause for the recurrence.[3] In all the patients, a preperitoneal approach was used to expose both inguinal regions. Biopsies from the transversalis fascia were obtained from the edge of the defect and from an identical location in the fascia of the contralateral side. More than half of the patients had attenuation of the endopelvic fascia of the asymptomatic side, suggesting a metabolic abnormality of connective tissues in the area of the internal ring. It was concluded that a patent processus vaginalis does not by itself lead to herniation: structural abnormalities of the internal ring, acquired attenuation of transversalis fascia, or abnormal muscle function accompanying the congenital defect must also be present. The fascial defects were often noted on both sides of the epigastric vessels. The uncontrolled design of this study is a drawback.

Read took perioperative biopsies from the anterior rectus abdominis sheath close to the midline in patients referred with indirect or direct inguinal hernias.[8] Control samples were obtained similarly from patients without a hernia undergoing other surgical procedures. The anterior rectus sheath was found to be thinner in patients with hernia. Collagen normally contributes 80% to the dry weight of this tissue. In a later study from the same center, the mean collagen content of anterior rectus sheath tissue assessed as weight of hydroxyproline per weight of defatted fascia was 90 μg/mg for controls, 82 μg/mg for indirect hernia patients, and 75 μg/mg for direct hernia patients. The differences were significant between controls and patients with direct hernia and between patients with indirect and direct hernia.[9]

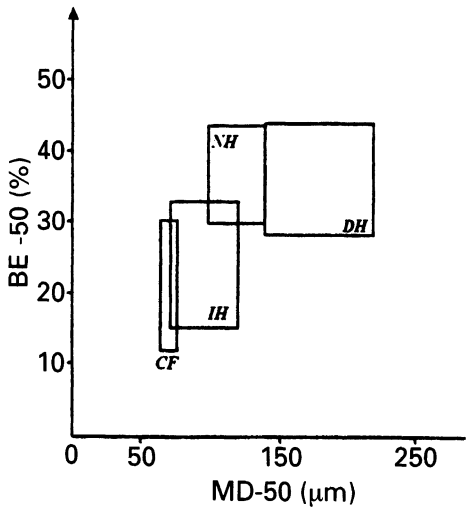

FIGURE 19.1. Plot of the biological elasticity at 50 mbar (BE-50) and maximum distension (MD) values. The rectangles are delineated by the mean value ± 2 S.E.M. for the transversalis fascia from the control subjects (CF), the indirect hernias (IH), the direct hernias (DH) and the nonherniated fascias (NH). Reprinted from Pans A, Piérard GE, Albert A, et al.,[10] with permission.

A large recent study supported the conclusion that tissue pathology is involved in hernia genesis.[10] Biopsies were taken during open preperitoneal hernia repairs from the transversalis fascia and rectus abdominis sheath on both sides in 63 hernia patients and 30 controls. The biopsies were subjected to biomechanical testing. Despite the difference in collagen content of the anterior rectus sheaths, no difference in elasticity or maximal distension was found between the groups. However, the biopsies from the transversalis fascia showed significantly higher levels of biological elasticity and maximal distension in direct hernia, compared with controls. Elasticity and distension measurements of the fascia in indirect hernia showed intermediate values (Fig. 19.1). Independent of the hernia type, there was a significant difference between the contralateral nonherniated fascia and the fascia of the controls. The fascia of the asymptomatic side of the hernia patient thus already presents pathological features at the time of surgery. This supports the proposition that the alterations of the fascia are the cause and not the product of hernia.

Studies on Proliferation and Synthesis

Cultured fibroblasts from biopsies showed a longer generation time and a lower incorporation of radioactively labeled (C^{14}) proline in patients with hernia, indicating lower rates of cell proliferation and retarded cellular biosynthesis. The lowest values were found in patients with direct hernia, but the number of patients was too small to allow for a proper statistical evaluation.[11] In a larger study, it was found that fibroblasts obtained from the in-