The causes of reduced fecundity associated with endometriosis and other infertility diagnoses remain controversial, but some may reflect defective endometrial receptivity. Abnormal decidual development also may underlie pregnancy complications such as preeclampsia and preterm birth. Microdomains composed of gap junctions, which facilitate cell-cell communication and promote decidualization, may be responsible. Connexin (Cx) 43, the protein subunit responsible for the majority of gap junctions in human endometrium, is progressively upregulated by hormones during decidualization. However, pharmacological or genetic inhibition of Cx43 blocks morphological and biochemical decidualization of endometrial stromal cells (ESC) in vitro. We recently tested the hypothesis that women with endometriosis have reduced Cx43 concentrations in eutopic endometrium compared to unaffected controls. Consenting subjects undergoing laparoscopic exploration and endometrial biopsies were recruited. Immunohistochemistry confirmed strong stromal Cx43 in tissue sections from controls, with reduced signals in endometriosis cases. Tissue lysates were subjected to Western blotting to quantify Cx43 protein levels. Actin was used as an internal control for total cellular protein. Western blot signals were compared by Mann-Whitney U-tests. The ratio (mean±SD) of Cx43/actin was 1.2±0.3 in endometriosis cases and 3.4±1.5 in control biopsies (Z=3.12, P<0.01). ESC cultured from eutopic biopsies were analyzed similarly and revealed a significantly lower ratio of Cx43/actin in ESC derived from endometriosis vs. control subjects (Z=3.58, P<0.01). Our results indicate that eutopic endometrial Cx43 concentrations in endometriosis cases are less than half those in controls, and that the levels in situ are accurately reflected in ESC isolated from the biopsies. Funded by the NIH SCPRIR U54 HD55787.