Journal of Reproductive Immunology
66 (2005) 161–173

JOURNAL OF REPRODUCTIVE IMMUNOLOGY

www.elsevier.com/locate/jreprimm

Macrophages and not granulocytes are involved in cervical ripening

Yoshiharu Sakamoto [a], Paul Moran [a], Judith N. Bulmer [b], Roger F. Searle [c], Stephen C. Robson [a,*]

[a] *School of Surgical and Reproductive Sciences, The Medical School, University of Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, UK*
[b] *School of Clinical and Laboratory Sciences, University of Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, UK*
[c] *School of Medical and Education Development, University of Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, UK*

Received 13 April 2005; accepted 19 April 2005

Abstract

To clarify the role of leucocytes in human cervical ripening and dilatation, cervical biopsies were obtained from six non-pregnant women, eight women undergoing early termination of pregnancy, 18 pregnant women undergoing elective Caesarean section at term (both with and without a ripe cervix as determined by Bishop score) and 11 women after term vaginal delivery. Leucocytes were localised by immunohistochemistry labelling and quantified in subepithelial and deep stromal areas. CD45+ leucocytes were more numerous in the subepithelial area of the cervix than in the deep stroma in all groups ($P < 0.01$). CD14+ macrophages and CD15+ granulocytes were increased in both the subepithelial and deep stromal areas only in the vaginal delivery group ($P < 0.01$). The number of macrophages in the ripening cervix (Bishop score above 4) was higher than in the unripe cervix (Bishop score 4 or less; $P < 0.05$) with no differences in other leucocyte populations. CD3+ CD8+ T cells in the subepithelial area were reduced in late pregnancy and after vaginal delivery ($P < 0.01$), but showed no relationship to Bishop score. Macrophages and granulocytes may be involved in the process of cervical dilatation, but macrophage infiltration into the ripening cervix before labour suggests their role in the ripening process. Reduced numbers of CD3+ CD8+ T-lymphocytes in late pregnancy and after vaginal delivery suggests that local immunity is down-regulated in the late pregnancy period.

* Corresponding author. Tel.: +44 191 282 4132; fax: +44 191 222 5066.
E-mail address: s.c.robson@ncl.ac.uk (S.C. Robson).

0165-0378/$ – see front matter
doi:10.1016/j.jri.2005.04.005

Regional differences in leucocyte subpopulations in the cervix indicate that leucocyte infiltration is likely to be regulated by local factors.

Keywords: Cervix; Ripening; Granulocyte; Macrophage; T-lymphocyte

1. Introduction

For most of gestation the human uterine cervix remains rigid and closed, but prior to labour it undergoes softening and effacement, a process termed ripening. Ripening occurs prior to dilatation proper, is a prerequisite for vaginal delivery and is associated with collagen remodelling and altered proteoglycan and water content (Junqueira et al., 1980; Osmers et al., 1993, 1995). Absence of normal ripening at term is associated with prolonged labour and post-term pregnancy, whereas premature ripening occurs as part of the preterm delivery syndrome or a second trimester abortion (Olah and Gee, 1992).

There is increasing evidence that the process of cervical dilatation resembles an inflammatory response (Liggins, 1981; Yellon et al., 2003). Leucocytes migrate into cervical stroma and mucus during labour reaching a density 2–3-fold higher than that found in late pregnancy (Luo et al., 2000; Young et al., 2002; Osman et al., 2003); the stromal infiltrate is composed principally of neutrophils and macrophages (Osman et al., 2003). Identical findings have been reported in the lower uterine segment during labour (Thomson et al., 1999; Winkler et al., 1999). In contrast, other workers reported an increase in macrophage and neutrophil numbers in cervical stroma during late pregnancy, but no further changes during labour (Bokstrom et al., 1997). This discrepancy may relate to differences in cervical ripening at the time of elective caesarean section, but no clinical information on the state of the cervix was provided in any of these studies. Furthermore, it is unclear whether leucocyte distribution is different in the cervical epithelium.

To determine if leucocyte influx into the cervix is a feature of cervical ripening or follows cervical dilatation in labour we compared leucocyte numbers in the cervical stroma and epithelium in women with and without a ripe cervix, as determined by Bishop's pelvic score.

2. Materials and methods

2.1. Subjects

Forty-three healthy women were recruited from the Obstetric and Gynaecology wards at the Royal Victoria Infirmary, Newcastle upon Tyne. The study was approved by the Joint Ethics Committee of the Newcastle and North Tyneside Health Authority and written informed consent was obtained from each subject. The non-pregnant group consisted of six regularly menstruating women (median age 42.5 [range 40–43] years, median parity 2 [range 1–4]), undergoing hysterectomy for non-malignant disease. None of the women