# Contractile Activity of Isolated Myometrium from Pregnant Women with Chronic Specific Urogenital Infections

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Contractile activity of the isolated myometrium from pregnant women with mycoplasma, chlamydial, and mixed mycoplasma-chlamydial infections of the urogenital system was studied *in vitro* by pharmacological methods. The amplitude of uterine contractions induced by oxytocin and prostaglandin $F_{2\alpha}$ decreased in women with mycoplasma infection, but increased during chlamydial and mixed infections. These data can help to predict pregnancy complications in women with specific urogenital infections.

**Key Words:** *human myometrium; contractile activity; pregnancy; specific urogenital infections*

Microbial agents play a growing role in the pathogenesis of diseases. The number of patients with infectious diseases and somatic pathologies caused by infectious agents constantly increases. These tendencies are also observed in obstetrics. Maternal infections contribute to the development of pregnancy complications and determine high perinatal mortality rate [1,4,5].

Microbiological characteristics of agents that cause women's diseases underwent considerable changes. Sexually transmitted infectious agents, including chlamydiae, mycoplasmas, ureaplasmas, and herpes simplex virus play an increasing role in the development of pathological processes. These microorganisms and genital facultative pathogenic bacteria cause chronic processes with mild symptoms that produce pronounced negative effects on women's reproductive health [3-5]. Previous studies revealed a relationship between specific intracellular infections, infertility, and premature labor. Pathogenic agents damage or directly infect the placental tissue, which results in chronic fetoplacental insufficiency, delayed intrauterine development of the fetus, chronic fetal hypoxia, and fetal infections [1,3-5]. The effects of infectious agents on the functional state and contractile activity of pregnant uterus remain unclear. Published data show that infected women are characterized by high incidence of labor abnormalities [6,7].

Here we studied induced contractions of the myometrium from pregnant women with specific urogenital infections.

## MATERIALS AND METHODS

Myometrium samples were taken from 22 pregnant women. During pregnancy these women were examined for sexually transmitted diseases. We assayed cervical swabs, urine, and blood. Immunofluorescence analysis, polymerase chain reaction, and DNA-DNA hybridization technique were used to evaluate the type of infectious agents. Pregnant women with activation of herpes virus, cytomegalovirus, and papillomavirus infections and/or chronic trichomoniasis were excluded from the study. We examined pregnant women with chlamydial ($n$=5), mycoplasma ($n$=5), and mixed mycoplasma-chlamydial infections ($n$=6). Women without specific genital infections served as the control ($n$=6).

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Infected pregnant women received antibiotics, immunomodulators, and local sanative preparations.

Indications for cesarean section were severe myopia and eye fundus pathology, breech presentation, large fetuses, 41 weeks' gestational age with incompetent labor passages, uterine scars after cesarean section and conservative myomectomy, long-lasting gestosis, chronic fetal hypoxia, and fetoplacental insufficiency. Each group included women with various diseases and different indications for cesarean delivery. Cesarean delivery was performed at 38-41 weeks' gestational age.

Myometrium samples were obtained during cesarean section before the beginning of labor activity. The sample was dissected from the upper zone of surgical wounds in the lower segment of the uterus. The tissue was immediately transferred in a modified Krebs solution (4-6°C). Preparations of the circular layer (2×10 mm, $n$=4-8) were made 5-8 h after surgery. Further experiments were performed using methods describe elsewhere [3].

After primary incubation contractions of the myometrium specimens were induced with 60 mM KCl and 0.1 mM histamine. The contractile response of muscle tissues to $10^{-10}$-$10^{-8}$ M oxytocin and $10^{-8}$-$10^{-6}$ M prostaglandin $F_{2\alpha}$ was evaluated. Contractile activity of the myometrium in response to 240 mM KCl was measured by the end of the experiments and taken as 100%.

The results were analyzed by Student's $t$ test. The differences were significant at $p$<0.05.

## RESULTS

In the control group, $10^{-10}$-$10^{-8}$ M oxytocin induced dose-dependent contractions of the isolated myometrium (Fig. 1, *a*). The contractile response to $10^{-8}$ M oxytocin was 73.4±8.3% of that induced by KCl (240 mM).

In women with chlamydial infection the strength of contractions induced by oxytocin was higher than in the control. In these women the contractile response to $10^{-8}$ M oxytocin attained 94.5±7.4% of that induced by 240 mM KCl. By contrast, in women with mycoplasma infection the contractile response to $10^{-10}$-$10^{-8}$ M oxytocin was less pronounced than in the control. In this group contractile activity of the myometrium induced by the highest dose of oxytocin was below 30% of the maximum KCl-induced response (Fig. 1). In women with mixed mycoplasma-chlamydial infection the contractile response induced by oxytocin in doses of $10^{-10}$ and $10^{-9}$ M surpassed the corresponding values in the control group by 22.2 ($p$<0.01) and 19.8% ($p$<0.01), respectively. Oxytocin in high doses induced similar responses in the control group and in women with mixed infections.

Experiments with prostaglandin $F_{2\alpha}$ produced similar results (Fig. 1, *b*). In women with chlamydial and mixed mycoplasma-chlamydial infections the strength of myometrial contractions was much higher than in the control. In the control group and women with chlamydial and mixed mycoplasma-chlamydial infections the strength of contractions induced by $10^{-6}$ M prostaglandin $F_{2\alpha}$ was 69.8±16.5, 99.9±7.1, and 94.9±8.6%, respectively. In women with mycoplasma infection, contractile activity of the isolated myometrium was lower than in the control. In these women the contractile response induced by prostaglandin $F_{2\alpha}$ in the highest dose was 27.3±12.4% of the maximum response ($p$<0.05).

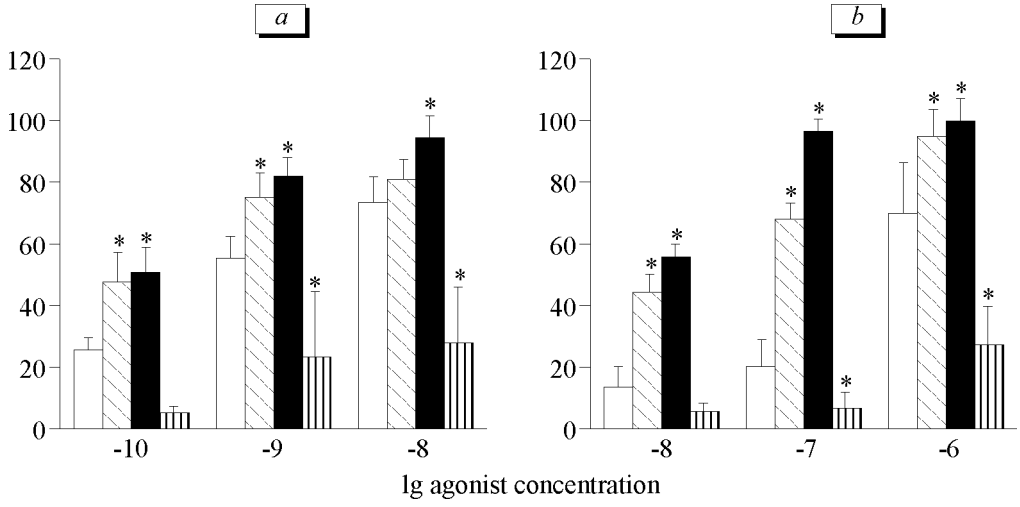


**Fig. 1.** Effects of specific urogenital infections on contractile activity of the isolated myometrium from pregnant women induced by oxytocin (*a*) and prostaglandin $F_{2\alpha}$ (*b*). Ordinate: strength of contractions of the isolated myometrium compared to that induced by 240 mM KCl. Slant shading: mixed infection; dark bars: chlamydial infection; vertical shading: mycoplasma infection. *$p$<0.05 compared to the control (light bars).

In the control group contractile activity of smooth muscle cells treated with 60 mM KCl and 0.1 mM histamine was 41.5±6.9 and 83±4.4%, respectively. In women with mixed mycoplasma-chlamydial infection, the contractile response induced by KCl and histamine was 71.9±8.5 and 109.2±12.2%, respectively. In women with chlamydial infection the strength of contractions was lower than in patients with mixed mycoplasma-chlamydial infection, but higher than in the control (49.2±13.9 and 86.1± 12.0% in response to KCl and histamine, respectively). In women with mycoplasma infection contractile activity did not differ from the control.

Thus, *in vitro* experiments showed that contractile activity of the isolated myometrium increases in women with chlamydial infection, but decreases during mycoplasma infection.

Clinical observations produced similar results. Women with chronic urogenital infections are characterized by high incidence of abnormalities in uterine contractile activity (UCA). Moreover, the type of disturbances in UCA depends on infectious agent. Mycoplasma infection is accompanied by primary UCA insufficiency. By contrast, mycoplasma infection leads to an abnormal increase in UCA, which results in precipitate delivery [6,7]. The mechanisms of these changes remain unclear.

Previous studies showed that not only the lower portions of the reproductive system, but also the uterine body (*e.g.,* endometrium and myometrium) can be infected with intracellular agents [3]. Our experiments were performed with the myometrium. Probably, infectious agents directly affected its contractile properties. On the other hand, various microbial agents are localized in different parts of the uterus. Chlamydiae are usually present in the posterior wall of the uterine body, while the anterior wall remains intact. By contrast, mycoplasmas infect the anterior wall of the uterine body. We examined samples from the anterior wall of the uterine body, which is not infected with chlamydiae. Therefore, it remains unclear whether chlamydiae directly modulate contractile activity of the myometrium.

Published data show that the long-term persistence of infectious agents is accompanied by morphological changes in the uterus. It should be emphasized that signs of inflammation are usually seen in the endometrium and subendometrial zone, while the myometrium is characterized by pronounced hemodynamic and atrophic changes [4]. Moreover, in most women with chlamydial and mycoplasma infections placentation occurs on the posterior and anterior walls of the uterus, respectively. Thus, hemodynamic characteristics differ in the myometrium and decidual membrane [3]. These data suggest that chronic specific urogenital infections impair trophic processes, which leads to disturbances in contractile activity of the myometrium.

It can be hypothesized that various factors, including different contamination of the uterine walls, localization of the placenta, regional blood flow, and morphological characteristics, determine contractile activity of the uterus and development of abnormalities (depending on the nature of infectious agents).

Our findings suggest that specific urogenital infections lead to various changes in contractile activity of human myometrium. Chlamydial and mixed mycoplasma-chlamydial infections are accompanied by an increase in contractile activity of the myometrium induced by specific and nonspecific agonists, while mycoplasma infection decreases the strength of myometrial contractions. Identification of the infection agent helps to predict and prevent pregnancy complications and perform adequate therapy.

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