Postpartum Changes in the Mechanical Responses of the Circular Muscle of Rat Uterus

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Abstract The circular muscle strips were isolated from rat uterus 10–60 h after parturition, and the electrical and mechanical responses were investigated. The muscle strips exhibited a variety of contractile activity ranging from frequent spontaneous contractions generated on an elevated muscle tone to a sustained contracture, when incubated with Mg-free Krebs solution. The muscle tone was lowered, and phasic contractions were abolished when the external Ca was removed. Muscle tone was also lowered by addition of 1.2 mM Mg, 1 mM spermidine, or 1 mM tetracaine. The membrane potential was about -25 mV in a muscle which exhibited a contracture, and the membrane was hyperpolarized by 20–25 mV by the application of 1.2 mM Mg or 1 mM spermidine. Addition of indomethacin ($1.5\text{--}4.5 \times 10^{-5}$ M) caused a gradual decrease in muscle tone, and the membrane was hyperpolarized. In view of the above results, it is hypothesized that Ca-influx was increased, for which prostaglandin(s) was probably responsible, in the circular muscle of postpartum rat uterus, thereby elevating the muscle tone in Mg-free solution.

Key words: postpartum myometrium, Mg, tetracaine, spermidine, indomethacin.

After parturition the rat uterus returns to its preparturient size in about 4 days. This is accomplished by cellular atrophy and cell destruction. The former occurs mainly in the myometrium as a simple reversal of the hypertrophy induced during pregnancy (MORTON and GOLDSPIK, 1986). Maximum number and size of gap junctions between myometrial cells declined rapidly within a day after delivery (PURI and GARFIELD, 1982; SAITO *et al.*, 1985). The membrane activity of postpartum myometrium has also been a subject of several investigators. The action potential of the circular muscle of near-term rat uterus is composed of spike activity (OSA and FUJINO, 1978; KAWARABAYASHI and MARSHALL, 1981; BENGTSOON *et al.*, 1984), and transformed into the plateau potential about 40 h after the parturition

(KISHIKAWA, 1981; MARUTA *et al.*, 1985a). Thus, the uterine muscle membrane is one of the targets of postpartum hormonal effects. It was found in the preliminary experiment that in the circular muscle excised from the rat about 10–40 h after parturition, the muscle tone was elevated and spontaneous contractions were very frequent during incubation with Mg-free Krebs solution. In some preparations, the muscle strip underwent a persistent contracture. This feature strongly contrasted to that observed in the prepartum preparation (OSA and OGASAWARA, 1983).

To investigate how and why the muscle tone of the postpartum circular muscle was elevated in Mg-free Krebs solution is the main subject of present study. Particular attention was directed to the effects of Mg, tetracaine, and spermidine which are supposed to reduce the Ca-influx (FEINSTEIN, 1965; HASHIMOTO *et al.*, 1973; ALTURA and ALTURA, 1981; CHIDECKEL *et al.*, 1985; MARUTA *et al.*, 1985b; OSA and MARUTA, 1986). It is hypothesized that Ca-influx, for which the raised synthesis of prostaglandins is probably responsible, is increased in the circular myometrial tissue of postpartum rat uterus.

METHODS

Wistar rats weighing 250–300 g were used. Proestrous rats were housed with males overnight, and Day 1 of pregnancy was the day that sperms were found in the vaginal smear. Delivery usually occurred on Day 22 or Day 23 of pregnancy. The present work was carried out on uteri taken from animals sacrificed between 10 and 60 h after the delivery of the first newborn. The uterus was cut open along the mesometrium, and the endometrium was removed carefully using jeweler's forceps. Circular and longitudinal muscle strips were dissected with fine scissors from the antimesometrial part of ovarian portion of the uterus.

Microelectrode and tension records were made on muscle strips 1 mm wide and 5 mm long by a glass microelectrode filled with 3 M KCl and a force transducer, respectively, in the partition chamber as described by ABE and TOMITA (1968). For mechanical recording alone, a pair of muscle strips about 0.5 mm wide and 3 mm long dissected from the same animal were set up vertically in a recording chamber, and connected to force transducers. The solutions were continuously flowed at a rate of 8 ml/min, and the capacity of the chamber was 2 ml. Ag-AgCl electrodes were placed near ends of muscle strips, and electric pulse with 500 ms duration was applied when necessary. Stimulus intensity was about twice as strong as rheobase. The preparation was equilibrated with warm Krebs solution ($37 \pm 0.5^\circ\text{C}$, Mg-free) for 1–2 h before the experiment began.

The control solution (Mg-free Krebs solution) had the following composition (mM): NaCl 123.1, NaHCO_3 15.5, KCl 4.7, KH_2PO_4 1.2, CaCl_2 2.5, and glucose 11.5. It was equilibrated with a gas mixture of 95% O_2 + 5% CO_2 (pH of 7.4). A small amount of 1 M Mg solution was added to yield a desired concentration. Drugs used were tetracaine (Sigma), spermidine and spermine (Sigma), and glycoetherdiamine-tetraacetic acid (EGTA, Tokyo Kasei) which was titrated with

tris(hydroxymethyl) aminomethane to be pH of 7.4. Indomethacin (Sigma) was dissolved in ethanol, after the method described by SAKAMOTO *et al.* (1987), and added to the bathing solution. The final concentration of ethanol was less than 0.2%. Prostaglandins were the gift of Ono Pharmaceutical Company.

RESULTS

Postpartum preparations

Circular muscle strips were obtained from the postpartum rat uteri at periods ranging between 10 and 21 h after parturition, and incubated with Mg-free Krebs solution (Fig. 1). The contractile activity was full of varieties, exhibiting frequent spontaneous phasic contractions (A, B) or a sustained contracture

Fig. 1. Effects of raising external Mg on mechanical activity of circular muscle strips excised from rat uteri 10 (A), 14.5 (B), 16 (C), 21 h (D) after parturition of the first newborn. Mg concentrations in mM are indicated between vertical bars. Dots indicate the electrical stimulation (500 ms).

(C, D). Record A shows that increase in external Mg concentrations in steps decreased the frequency and amplitude of phasic contractions dose-dependently, and spontaneous contraction was abolished by 4.8 mM Mg. The basal muscle tone declined slightly by increasing external Mg concentrations. The spontaneous activity appeared with greater frequency in the preparation shown in record B. Raising external Mg concentration (0.6–4.8 mM) caused a lowering of basal muscle tone, and the amplitude of phasic contractions was heightened. Record C indicates that the muscle strip was spontaneously inactive and the electrical pulse was incapable of generating a phasic contraction. This contractile feature was proved to be a contracture, because application of Mg resulted in the depression of muscle tone, and caused a generation of spontaneous phasic contractions. Frequency of spontaneous activity was decreased when Mg concentration was raised to 4.8 mM. When Mg was removed, the muscle tension rose slowly then decayed, and phasic contractions of high frequency took place. Effects of external Mg application were somewhat different in the case of record D. When 0.6 or 1.2 mM Mg was applied, the muscle tone declined and phasic contractions were generated, and the muscle strip again underwent a contracture, the level of which was lower than that in the absence of Mg. When 2.4 or 4.8 mM Mg was applied, the generation of phasic contractions continued. The muscle tension rose slowly and decayed, and a contracture ensued, when Mg was removed.

Muscle strips were incubated with Mg-free solution containing 0.6 mM Ca, and effects of raising external Ca concentration were examined (Fig. 2). In the case of either A or B, muscle strips were spontaneously inactive, and electrical pulses caused a tiny contraction. In the case of record A, raising external Ca (1.2–4.8 mM) caused a generation of spontaneous phasic contractions, and the amplitude increased dose-dependently on the external Ca concentration. The basal muscle tension was elevated only slightly. In the case of record B, the level of muscle tone was elevated by increasing Ca concentration in steps from 0.6 to 2.4 mM, but the electrical pulses did not evoke a full-size phasic contraction. In the presence of 2.4 mM Ca, application of 1.2 mM Mg caused a lowering of muscle tone, and a generation of spontaneous phasic contractions. When Mg was removed, phasic contractions of high frequency were induced, and the amplitude was gradually decreased. The amplitude of phasic contractions was augmented by successive application of 4.8 mM Ca.

High frequency of phasic contractions and contracture of postpartum circular muscle in Mg-free solution suggest a membrane depolarization. Since it was shown that the membrane of smooth muscle was hyperpolarized in low K solution (CASTEELS and KURIYAMA, 1965), mechanical effects of reducing external K from 5.9 to 3 mM were examined (Fig. 3). A sustained contracture was transformed into a generation of phasic contractions produced on a lowered muscle tone in 3 mM K solution, and the phasic contractions ensued when K concentration was restored to 5.9 mM. The second application of 3 mM K solution caused a lowering of the level of maximal relaxation. Spontaneous activity was abolished, and the muscle was

Fig. 2. Contractions of postpartum circular muscle strips illustrating effects of different concentrations of external Ca added to Mg-free Krebs solution. Ca concentrations in mM are indicated between vertical bars. In record B, 1.2 mM Mg was applied (horizontal bar) in the presence of 2.4 mM Ca. Dots indicate electrical stimulation. Circular muscle strips were excised from rats 15 (A) and 28 h (B) after parturition, respectively.

Fig. 3. Contractions of postpartum circular muscle strips in Mg-free Krebs solution illustrating effects of reducing external K from 5.9 to 3.0 mM (vertical bars), and addition of 1 mM Mg (horizontal bar). Broken lines indicate the slack muscle tension level. Circular muscle strip was excised 46.5 h after parturition.

Fig. 4. Membrane activities (lower traces) of postpartum circular muscles of rat uterus illustrating effects of 1.2 mM Mg. Contractions were simultaneously recorded (upper traces). Muscles were excised 29 (A), 38 h (B) after parturition and incubated with Mg-free Krebs solution, and 1.2 mM Mg was applied at the time indicated by arrows. Ab and Bb are successive records of Aa and Ba, respectively. Interval between the end of Bb and the beginning of Bc was 4 min.

relaxed when 1 mM Mg was added.

The intracellular membrane activity of postpartum circular muscles exposed to Mg-free Krebs solution, and effects of adding 1.2 mM Mg were examined in the experiment shown in Fig. 4. In the case of record Aa, the membrane activity was composed of periodic bursts of spike potentials, and phasic contractions were generated in a one-to-one manner corresponding to each burst. The membrane was hyperpolarized by 2 mV, the amplitude of spike potential was augmented, and interval between action potential was prolonged, when 1.2 mM Mg was applied. At the steady state, the amplitude of slow potential increased (Fig. 4Ab). As the frequency of spontaneous activity decreased, the level of maximal relaxation was lowered (Fig. 4Aa). It is probable that in the Mg-free solution the successive contraction occurred before the preceding contraction was completely relaxed. In the case of record Ba, the membrane potential was -30 mV, and action potentials having very small amplitude occurred accompanied with phasic contractions. The membrane was gradually hyperpolarized by the application of 1.2 mM Mg, and was stabilized at -46 mV (Fig. 4Bc). The amplitude of action potential developed gradually exhibiting complicated shapes (Fig. 4Ba, Bb), and the steady response was the spike potential followed by plateau potential (Fig. 4Bc). The level of maximal

relaxation declined in the presence of 1.2 mM Mg.

Tetracaine is known as one of the smooth muscle relaxants. Its action is ascribed to the suppression of Ca-influx (FEINSTEIN, 1966; MARUTA and OSA, 1987). Figure 5 demonstrates effects of Ca removal, and application of 1 mM tetracaine in the presence of 2.5 mM Ca (Mg-free). In record A, the muscle exhibited phasic contractions. Ca omission together with application of 0.5 mM EGTA caused finally a muscle relaxation following the initial elevation of muscle tension. Application of 1 mM tetracaine also caused a relaxation. The recovery was very slow. In record B, the muscle exhibited a contracture, and Ca removal caused a muscle relaxation. The relaxation was rapid. Similarly, 1 mM tetracaine caused a muscle relaxation. The muscle was rapidly relaxed by 1 mM Mg, and the extent of relaxation was large.

It has been shown that spermidine or spermine depressed the phasic contraction of rat uterine muscle (HASHIMOTO *et al.*, 1973; MARUTA *et al.*, 1985b), and tonic contraction of trachealis muscle of guinea pig (CHIDECKEL *et al.*, 1985). Its action is very likely due to the suppression of Ca-influx. Figure 6 demonstrates effects of spermidine and spermine on 2 preparations which exhibited different patterns of contraction in Mg-free Krebs solution. In record A, the level of maximal relaxation was lowered, and the peak of phasic contraction exceeded the previous control by the application of 0.3 mM spermidine, the feature of which is reminiscent of the effects of Mg shown in Fig. 1B. Similar effects on the basal muscle tension was caused by 1 mM spermidine, and the amplitude of phasic contraction was slightly depressed. Later on, the muscle tone tended to elevate and the amplitude of phasic contraction decreased. Spermine (1 mM) strongly depressed the basal muscle tension, and spontaneous activity was abolished. In record B, the muscle exhibited a contracture, and the muscle tension was progressively increasing. Spermidine depressed the contracture in a dose-dependent manner. When 1 mM spermine was applied, the muscle underwent a strong relaxation, and phasic contractions having small amplitude were spontaneously generated. The second application of 1 mM spermidine caused initially a generation of phasic contractions; however, the muscle underwent a contracture again.

Effects of spermidine on the intracellular membrane activity are illustrated in Fig. 7. Periodic bursts of spike potential were the dominant membrane activity, and phasic contractions accompanied in the case of Fig. 7A. When 1 mM spermidine was applied, the resting membrane potential was not affected, but the frequency of spontaneous activity was decreased (Fig. 7Aa). The level of maximal relaxation slightly declined. The membrane was depolarized, and spike potentials were frequently generated, when spermidine was removed, and the muscle tone was elevated (Fig. 7Ab). The membrane potential was -27 mV, and the muscle underwent a contracture in the case of record B. Application of 1 mM spermidine caused an abrupt repolarization and the contracture was terminated (Fig. 7Ba). Action potentials composed of the initial spike followed by plateau were spontaneously generated (Fig. 7Bb). When 3 mM spermidine was subsequently applied, a main effect was the shortening of the plateau potential (Fig. 7Bc). The membrane

Fig. 5. Effects of Ca-depletion and 1 mM tetracaine on contractions in Mg-free Krebs solution of circular muscle strips excised from postpartum rat uteri 24 (A) and 38 h (B) after parturition. In record B, 1 mM Mg was applied (right). Dots indicate electrical stimulation, and broken lines indicate the slack muscle tension level.

Fig. 6. Contractions of postpartum circular muscle strips in Mg-free Krebs solution illustrating effects of spermidine and spermine which were applied during the periods indicated by horizontal bars. Concentration in mM are indicated by figures. Broken lines indicate the slack muscle tension level. Circular muscle strips were excised 23.5 (A), and 32 h (B) after parturition, respectively.

Fig. 7. Membrane activities (lower traces) of postpartum circular muscles of rat uterus illustrating effects of 1 mM spermidine. Contractions were simultaneously recorded (upper traces). Muscles were excised 29 (A), 39 h (B) after parturition and incubated with Mg-free Krebs solution, and 1 mM spermidine was applied at the time indicated by arrows. In record Bc, spermidine was further raised to 3 mM (arrows). Ab and Bb, Bc, Bd are successive records of Aa and Ba, respectively.

was depolarized and a contracture was produced when spermidine was removed (Fig. 7Bd).

Application of 10^{-6} M atropine or 10^{-6} M phentolamine did not change the mechanical responses, indicating that cholinergic or adrenergic mechanism was not involved in such elevation of muscle tension.

A possible involvement of prostaglandins on the elevation of muscle tone is illustrated in Fig. 8. Phasic contractions were frequently generated in the muscle strip shown in record A. The spontaneous contraction was little affected by the application of 2×10^{-5} M aspirin, whereas 4.5×10^{-5} M indomethacin lowered the level of maximal relaxation, and the amplitude of phasic contraction was decreased. On the other hand, the frequency of phasic contraction was increased. Application of 0.2% ethanol, the amount of which was contained in the 4.5×10^{-5} M indomethacin solution, caused a slight elevation of muscle tension. The muscle relaxed, and spontaneous contractions were abolished by addition of 1 mM Mg to the Mg-free Krebs solution. The muscle underwent a contracture illustrated in record B. Aspirin (2×10^{-5} M) slightly, and indomethacin (1.5×10^{-5} and

Fig. 8. Record A: effects of 2×10^{-5} M aspirin, 4.5×10^{-5} M indomethacin, 0.2% ethanol, and 1 mM Mg added to Mg-free Krebs solution on mechanical activity of the circular muscle strip excised 21 h after parturition. Record B: effects of 2×10^{-5} M aspirin, 1.5×10^{-5} and 4.5×10^{-5} M indomethacin, and 1 mM Mg on the circular muscle strip excised 35 h after parturition. Record C: effects of Ca-depletion and 4.5×10^{-5} M indomethacin. Circular muscle strip was obtained 40 h after parturition, and exposed to Mg-free Krebs solution. Broken lines indicate slack muscle tension level.

4.5×10^{-5} M) remarkably depressed the muscle tone. Mg (1 mM) caused a relaxation of the muscle, and spontaneous phasic contractions were generated. In the case of record C, the muscle tension was lowered, and phasic contractions were generated by 4.5×10^{-5} M indomethacin (right), and the level of maximal relaxation was nearly the same as that caused by omission of external Ca (left).

Effects of indomethacin on the membrane activity are shown in Fig. 9. The membrane potential was -35 mV, and spike potentials were continuously generated in Mg-free Krebs solution, and accordingly the muscle underwent a tetanic contracture (Fig. 9a). When 4.5×10^{-5} M indomethacin was applied, the membrane was once repolarized, and then an action potential exhibiting a long plateau was generated (Fig. 9a, b). The duration of action potential became progressively shorter in the presence of indomethacin, and the amplitude of the spike potential

Fig. 9. Membrane activities (lower traces) of postpartum circular muscle of rat uterus illustrating effects of 4.5×10^{-5} M indomethacin. Contractions were simultaneously recorded (upper traces). Muscle was excised 39 h after parturition and incubated with Mg-free Krebs solution, and indomethacin was applied during the time indicated by arrows.

generated on the plateau became larger. Phasic contractions were generated in a one-to-one manner accompanying the action potential. When indomethacin was removed (Fig. 9c), the plateau potential became gradually elongated (Fig. 9d, e).

Intracellular membrane activities of the longitudinal muscles taken 20–60 h after parturition are illustrated in Fig. 10. In either case, the membrane potential was about -50 mV in the Mg-free Krebs solution, and bursts of spike potential were spontaneously generated. In the preparation taken 20 h after parturition, spike potentials were the predominant component (Fig. 10A). Phasic contractions arose from a well-defined baseline tension. The amplitude of spike potential was slightly larger in the presence of 1.2 mM Mg, and the duration of bursts became slightly shorter. The amplitude of accompanying contraction was slightly diminished. In the preparations taken a longer period after parturition (Fig. 10B, C), the slow potential became pronounced. The membrane was hyperpolarized by 2 mV in the presence of 1.2 mM Mg, and spontaneous activity was suppressed. Burst of spike potential was generated by the electrical pulse, and the amplitude of spike potential was generated by the electrical pulse, and the amplitude of spike potential was generally increased.

Fig. 10. Electrical activities (lower traces) of the postpartum longitudinal muscles illustrating effects of 1.2mM Mg (arrows). Contractions were simultaneously recorded (upper traces). Muscles were excised 20 (A), 39.5 (B), 60 (C) h after parturition, and equilibrated with Mg-free Krebs solution. Record Bb shows the recovery when external Mg was removed. Dots indicate the electrical stimulation.

However, the accompanying contraction was smaller. The baseline muscle tension was slightly depressed by 1.2mM Mg (Fig. 10B, C).

Prepartum preparations

The following experiments were carried out to facilitate comparison with mechanical responses in the postpartum circular muscle. Circular muscle strips excised from the prepartum rat on Day 22 of pregnancy exhibited spontaneous phasic contractions, when they were suspended under a slight stretch in Mg-free Krebs solution. The frequency ranged between 0 and 0.3 (min^{-1}). The muscle tone was slightly elevated and phasic contractions with greater amplitude were induced by application of 10^{-5} M PGE_2 (Fig. 11A). The maintained muscle tone was lowered, and the generation of spontaneous phasic contractions was suppressed by the application of Mg. Similar effects of Mg were caused in the $\text{PGF}_2\alpha$ -induced contractions (Fig. 11Ba). Beside the action of prostaglandin synthesis inhibitor, indomethacin is known as a Ca-antagonist for vascular smooth muscle (NORTHOVER, 1977) and myometrial muscle (ANDERSON *et al.*, 1981). However, record Bb indicates that 4.5×10^{-5} M indomethacin did not depress the contractile responses induced by $\text{PGF}_2\alpha$.

Fig. 11. Contractile responses of prepartum circular muscle strip exposed to Mg-free Krebs solution illustrating effects of 1.2 and 2.4 mM Mg (A, Ba), and 4.5×10^{-5} M indomethacin (Bb) during the application (arrows) of 10^{-5} M PGE_2 (A) and $\text{PGF}_2\alpha$ (B). Day 22 of pregnancy. Records A and B were on muscle strips taken from different animals. Dots indicate the electrical stimulation.

DISCUSSION

This study mainly describes the postpartum changes in mechanical responses of circular myometrium of rat. The changes observed in the Mg-free Krebs solution are collectively summarized so that a sequence of events is an elevation of muscle tone accompanied with frequent phasic contractions starting on the first postpartum day, followed by a sustained contracture about 30 h after the parturition. Because Mg is a natural constituent of blood serum, the tissue property *in vivo* is better reproduced *in vitro* by using the artificial saline solution containing a proper concentration of Mg. On the other hand, contrasting features between longitudinal and circular muscles were more pronounced, when they were exposed to the Mg-free solution (for longitudinal muscle, see Fig. 10). Thus, as several investigators have pointed out, physiological and pharmacological properties are more strongly changed by hormonal condition in the circular muscle than in the longitudinal muscle (OSA and FUJINO, 1978; ANDERSON *et al.*, 1981; KAWARABAYASHI and MARSHALL, 1981; KISHIKAWA, 1981; BENGTSSON *et al.*, 1984).

The muscle tone was elevated by raising external Ca concentration (Fig. 2B), and suppressed by Ca-depletion (Figs. 5, 8). In addition, application of Mg, tetracaine, spermidine, and spermine, all of which are considered to be Ca-antagonists (FEINSTEIN, 1965; HASHIMOTO *et al.*, 1973; ALTURA and ALTURA, 1981; CHIDECKEL *et al.*, 1985; MARUTA *et al.*, 1985b; OSA and MARUTA, 1986; MARUTA and OSA, 1987), eliminated the contracture (Figs. 1, 5, 6). Therefore, Ca is likely influxed into the cell interior from outside the membrane, when the muscle tone is high.

The contracture was depressed in low K solution (Fig. 3), indicating a

membrane depolarization responsible for the above mechanical responses in the postpartum circular myometrium. The depolarization was in fact proved by microelectrode studies (Figs. 4, 7, 9). Mg and spermidine were shown to repolarize the membrane (Figs. 4, 7). Thence, the depolarization could be directly due to an increase in Ca permeability. A depolarization due to the increase in Ca permeability has been reported for the carbachol response in intestinal smooth muscle of guinea-pig (BOLTON and KITAMURA, 1983). An increase in Na permeability is also a probable causative candidate for the membrane depolarization. It has been reported that the myometria of mouse and rat are not hyperpolarized, but, instead, depolarized, and undergo a contracture in low Na solution (OSA, 1971; MASAHASHI and TOMITA, 1983). In the present study the depolarized membrane of the postpartum circular muscle was not hyperpolarized by lowering the external Na concentration (unpublished observation). Since the role of external Na on the membrane potential of uterine muscle is not yet fully understood, a conclusion concerning Na permeability is reserved.

The contracture was suppressed, and the membrane was repolarized by indomethacin (Figs. 8, 9). High concentration of indomethacin was required to produce the above effects, for which conclusions become controversial. Indomethacin is, on the one hand, a Ca-antagonist (NORTHOVER, 1977) and thus it is not strange that indomethacin suppressed the contracture; however, the same concentration of indomethacin (4.5×10^{-5} M) caused only a slight effect on the contractile response induced by $\text{PGF}_2\alpha$ in the prepartum circular myometrium (Fig. 11). Resistance of myometrial muscles *in vitro* to indomethacin has also been reported (ANDERSON *et al.*, 1981). The slow time course of depression of the contracture (Fig. 8), taken together with the above arguments, favors a view that a main effect of indomethacin in the present cases was an inhibition of cyclooxygenase activity. But this view is not compatible with the minor effects of aspirin (Fig. 8). Furthermore, provided that endogenous prostaglandins were the leading cause for the contracture, an excessive production should be assumed in postpartum circular myometrium, because PGE_2 and $\text{PGF}_2\alpha$ up to 10^{-5} M was not sufficient to produce a contracture in the prepartum circular myometrium (Fig. 11). For the above reasons, it is speculated at this moment that the synthesis of prostaglandins, probably other than PGE_2 and $\text{PGF}_2\alpha$, was raised in postpartum circular muscle tissue, and/or the sensitivity of membrane to prostaglandins was enhanced.

After the parturition, myometrial cells undergo atrophy, and proteolysis and collagenolysis occur (HARKNESS and HARKNESS, 1954; WOESSNER, 1965; HENELL *et al.*, 1983; ADAMS and FRIEDEN, 1985; MORTON and GOLDSPIK, 1986). These events effect a lower distensibility and a greater regression to the postpartum uterus. During the experiment reported previously (MARUTA *et al.*, 1985a), we experienced that the freshly excised postpartum circular muscle underwent a contracture *in vitro* for about 3 h in normal (Mg-containing) Krebs solution, as seen in Fig. 1D, then phasic contraction took place. The feature was puzzling at that time, and it is now speculated that the sequence of events depended on the gradual decrease of

prostaglandin synthesis *in vitro*, and so it is likely that the contracture is a physiologic status of postpartum circular myometrium *in vivo*. If so, the adaptive change of postpartum regression of uterine tissue may involve such a muscular contribution.

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