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DETERMINING THE TYPE OF PROSTAGLANDINS EXCRETED
FROM THE SMOOTH MUSCLES UNDER THE INFLUENCE
OF THE ACTIVATING SERUM FACTOR IN WOMEN
WITH PATHOLOGICAL PREGNANCY

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In our previous works we established that the blood sera of women with early or late toxicosis and habitual abortions contains water soluble glycopeptide with a molecular weight of about 2000 causing the excretion of prostaglandins from the smooth muscles (7).

Having in mind the considerable role played by prostaglandins during pregnancy and labour (6, 9), a clarification as to which type the excreted prostaglandins are is of very real significance. The blocking of the action of the factor with SC 19 220 shows that these prostaglandins may be of type E or F, as SC 19 220 blocks only their excitative action in investigations of smooth-muscle preparations (4, 11).

According to published data (1, 3) the group E prostaglandins stimulate the storage of iodine in the thyroid glands of rats. This action is explained by the rise in the level of cAMP. $\text{PGF}_{2\alpha}$ does not noticeably affect this accumulation as it realises its effect by changing the level of cGMP which is not linked with the storage of iodine.

On the other hand, differences exist in the effects of prostaglandins from the E and F groups on the contractile activity of the smooth muscles of the circular layer of the gastro-intestinal tract of different animals (2).

The aim of the present study is, on the basis of the difference in the effects of the prostaglandins from these two groups on the biological subjects mentioned, to establish whether the activating factor X realises its action on the smooth muscles through PGF or through PGE .

METHOD

For the physiological test smooth muscle preparations from the corpus region of the stomach (circular, without mucosa) were prepared and from the right uterine horn of rat (longitudinally), 10–12 mm long and about 2–3 mm wide.

The thyroid glands needed for the investigation were prepared from 90 rats and in order to avoid the individual difference in metabolism of the test animals the 2 lobes of the gland from one and the same rat were put in different groups.

Both the thyroid glands and the smooth muscle preparations were placed in physiological solution with $t^{\circ}=35^{\circ}\text{C}$ and nonstop aeration (the components of the solution and the mixture for aeration are given in our previous work) (8, 10). Treatment with ^{131}I was carried out in the way described in publications (1), the determination of activity being made with a scintillation counter after 48 hours drying at $t^{\circ}=60^{\circ}\text{C}$.

RESULTS

In fig 1 (on the left) the introduction of blood serum 1 % from a woman with spontaneous abortion onto the smooth muscle preparations from the uterus (cut

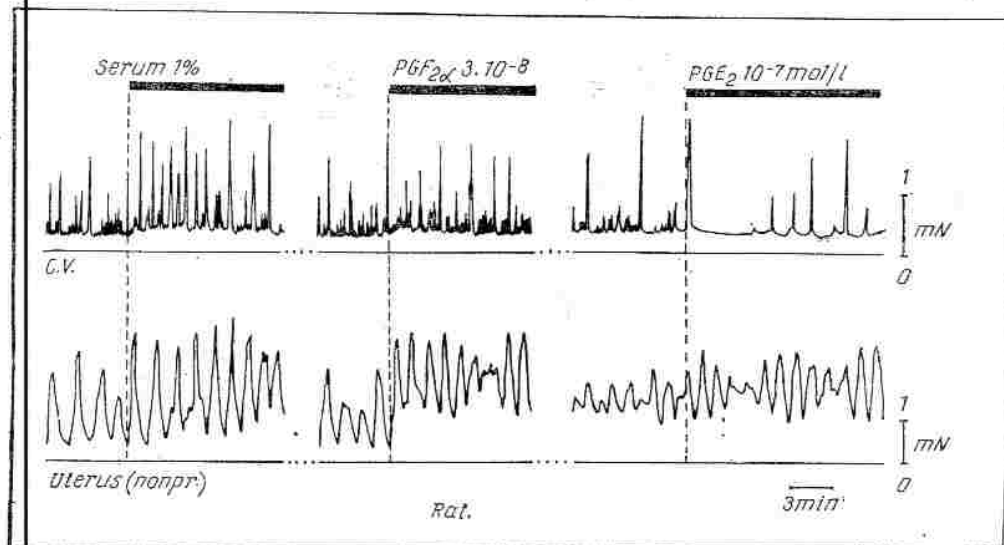


Fig. 1. The circular preparation from stomach reacts with an activating effect to only $\text{PGF}_{2\alpha}$, i. e. analogically to the blood serum of a woman with spontaneous abortion

longitudinally) and from the corpus region of rat stomach (circular) is shown. A clearly expressed activation from application of the serum can be seen — an increase of tonus (in the corpus preparation) and frequency (in the uterus preparation). In the centre and to the right of the same figure the effect of an exogenous introduction of $\text{PGF}_{2\alpha}$ and PGE_2 on the same preparations is shown. On introduction of $\text{PGF}_{2\alpha}$ in a dose of $3 \cdot 10^{-8}$ mol/l an activating effect is observed in both investigated preparations — a picture similar in effect to that with blood serum. Application of PGE_2 provokes an activation of the longitudinal strips of uterus and a suppression of the circular preparation from the corpus region of the stomach.

Table 1 shows the results from the exogenous introduction of $\text{PGF}_{2\alpha}$ and PGE_2 in a concentration of 10^{-6} mol/l on an accumulation of ^{131}I from the thyroid glands of rat.

Analogically to the data cited in publications a raised storage of iodine from the thyroid gland in the presence of PGE_2 is seen. Addition of $\text{PGF}_{2\alpha}$ does not result in significant changes in the accumulation of the isotope.

Table 1

Effect of introduction of prostaglandins on accumulation of ^{131}J in the thyroid gland of rat

Group	Specific activity, (imp/min. mg)	Relative activity
Controls	503.51 \pm 3.52	1.00
PGF _{2α} · 10 ⁻⁵ mol/l	495.46 \pm 10.13	0.98
PGE ₂ · 10 ⁻⁵ mol/l	866.54 \pm 9.46	1.72

Table 2

Effect of accumulation of ^{131}J in the thyroid gland of rat upon the introduction of blood serum of a women with pathological pregnancy and indomethacin

Group	Specific activity, (imp/min. mg)	Relative activity
Controls	503.51 \pm 3.52	1
Serum X 4 %	367.60 \pm 16.15	0.73
Indomethacin 10 ⁻⁵ mol/l	119.72 \pm 36.29	0.24

In table 2 the results are shown of the relative activity of ^{131}J in the thyroid glands added after the introduction into the solution of blood serum from a woman with spontaneous abortion.

The presence of the blood serum reliably reduces the accumulation of iodine in the thyrocytes. At the bottom the results of the accumulation of ^{131}J after treatment with Indomethacin 10⁻⁵ mol/l are given.

DISCUSSION

Comparison of the direct effect of blood serum and exogenously introduced prostaglandins on the contractile activity of smooth-muscle preparations shows that the picture produced by the effect of blood serum is analogical to that produced by the effect of PGF_{2 α} . While the uterus preparations are affected by both the pharmacological substances in a way similar to that of blood serum — activating, the circular preparations from the corpus region of the stomach react differently to the prostaglandins — by activation on the introduction of PGF_{2 α} (i. e. as with the serum) and by inhibition on the introduction of PGE₂. These results give us the right to confirm that under the influence of the blood serum factor prostaglandins mainly of the type F_{2 α} are released.

Analysis of the data for accumulation of ^{131}J in the thyroid glands of rat in a normal state and when affected by exogenous prostaglandins it is seen that PGE₂ stimulates accumulation of the isotope which corresponds to announcements made by other authors (3), while PGF_{2 α} does not act essentially, within the framework of experimental error, upon this storage.

Under the influence of blood serum the iodine accumulation is reduced sharply which speaks of the fact that in no case when under the influence of serum factor X does a raised excretion of the prostaglandin type E_2 occur. The effect of this accumulation can be explained by a movement of the synthesis of the prostaglandins in the thyrocytes in the direction of $PGF_{2\alpha}$, upon which there is a sharp suppression of the synthesis of PGE_2 by the cells of the thyroid gland.

The powerful inhibitory effect of indomethacin on the accumulation of iodine according to us is an indication that in the cells of the thyroid gland prostaglandins of group E are synthesised which seem to participate in the regulatory function of the gland. This explains why the effect of the thyrotropic hormone on the thyroid gland depends on its prostaglandin synthesis being preserved (12).

It is clear that upon being influenced by the factor, the synthesis of prostaglandins of the E group is suppressed, as a result of which we obtain a picture analogical with the picture upon influence with indomethacin.

The proofs shown in our previous studies (7, 8, 10) that under the influence of serum factor X an excretion of prostaglandins from the smooth muscle cells is set off and the fact that this effect is inhibited by SC 19 220 shows that under the influence of the excitative serum factor prostaglandins of the type F or E are excreted. The results of our present work eliminate the possibility of excretion being affected by prostaglandins of group E in consequence of which we can confirm that under the influence of the activating serum factor prostaglandins of type $F_{2\alpha}$ are released. In addition to which the results with thyroid glands permit us to confirm that the activating serum factor inhibits prostaglandin synthesis of group E at the expense of increased synthesis of prostaglandins of group F.

CONCLUSIONS

1. Endogenous prostaglandins from group E which probably play a part in the accumulation of iodine are synthesised in the thyrocytes.
2. Under the influence of an activating serum factor present in the blood of women with the type of pathological pregnancy studied an affected excretion of prostaglandins of type $F_{2\alpha}$ from the smooth muscles is set off.

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ОПРЕДЕЛЕНИЕ ТИПА ПРОСТАГЛАНДИНОВ, ВЫДЕЛЯЕМЫХ
ГЛАДКИМИ МЫШЦАМИ ПОД ДЕЙСТВИЕМ ВОЗБУЖДАЮЩЕГО
СЫВОРОТОЧНОГО ФАКТОРА, У ЖЕНЩИН С ПАТОЛОГИЕЙ
БЕРЕМЕННОСТИ

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Резюме

В предыдущих работах было показано, что в сыворотке крови женщин с ранними и поздними токсикозами беременных и со спонтанными абортами женщин содержится низкомолекулярный воднорастворимый полипептид с мол. весом около 2000, под действием которого выделяются простагландины, преимущественно типа $F_{2\alpha}$. С помощью физиологического теста и биомодели, используя различный эффект различных простагландинов на спонтанную сократительную активность гладкомышечных препаратов и накопление йода в щитовидных железах, был подтвержден тип выделяемых гладкими мышцами простагландинов путем прямого влияния сыворотки на накопление изотопа