crease in the MA content in the median eminence found in the aging rats, coupled with persistence of a relatively high MA level in proestrus–estrus, is evidence of a disturbance of the liberation of MA from the nerve endings located in this region. On the other hand, comparison of the dynamics of the MA content and AP activity in the median eminence leads to the conclusion that the change in concentration and in the range of cyclic fluctuations in MA is not reflected in the transport processes in the blood vessels of the pituitary portal system.

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EFFECT OF ANTIBIOTICS OF THE PENICILLIN SERIES ON FETAL AND NEONATAL DEVELOPMENT IN RATS

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Penicillin, if injected into rats in large doses at different stages of pregnancy, had no adverse effect on the developing fetus or the newborn rat. Meanwhile benzathine penicillin (bicillin-3) caused resorption of the embryonic cells and acted adversely on development of the heart. Consequently, benzathine penicillin must not be used for the prevention of relapses of rheumatic fever on patients earlier than in the third trimester of pregnancy.

KEY WORDS: pregnancy; benzathine penicillin; penicillin; embryonic development.

Antibiotics are widely used for the treatment and prophylaxis of rheumatic fever in pregnancy.

Meanwhile the effect of various antibiotics on the intrauterine development of the fetus is not yet completely solved.

Evidence has been obtained that certain antibiotics, which pass easily through the placenta and also through the mother's milk, adversely affect the fetus and newborn infant [1-5].

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Penicillin (sodium salt) and, since 1952, the long-acting preparation benzathine penicillin, are widely used in obstetrics and gynecology.

The object of this investigation was to study experimentally the effect of certain antibiotics of the penicillin series used in the treatment of rheumatic fever on development of the fetus.

Interest was centered on the embryotropic action of benzathine penicillin.

EXPERIMENTAL METHOD

Experiments were carried out on 95 female albino rats weighing 180-200 g and on 187 newborn rats. Pregnancy was dated from the discovery of spermatozoa in the vaginal smear. Altogether five series of experiments were carried out.

Penicillin was injected in a large dose – 100,000 units (50,000 units twice a day) in series I from the third to the 12th day (end of organogenesis) of pregnancy, and in series II from the 13th to the 20th day (second half of pregnancy).

Benzathine penicillin (bicillin-3) was obtained from the L. A. Tarasevich State Institute of Standardization and Control of Medical and Biological Preparations. It was given as a single injection in a dose of 6,000 units, which maintained the blood level of penicillin for ten days. In series III benzathine penicillin was injected on the fourth day of pregnancy (the first critical period), in series IV on the eight day, and in series V on the 11th day of pregnancy (the second critical period). The animals were killed on the ninth, 11th, 15th, 20th, and 21st days of pregnancy and some of them were kept to obtain the progeny. To study morphological changes, the embryos were fixed in 10% formalin and in Susa fluid. Sections were stained with Heidenhain's iron–hematoxylin.

EXPERIMENTAL RESULTS

In the experiments of series I, in which albino rats from the third to the 12th day of embryonic development were given penicillin daily, in no case was resorption of the embryos observed (20 rats), whereas in the control series it was found in 10%. The litters of both the experimental and control groups contained on the average 9 or 10 young rats, evenly distributed between the uterine cornua. In their external appearance the embryos in the rats receiving penicillin were little different from the controls.

However, at the age of 15-20 days the embryos exceeded the controls in weight and size. For instance, the mean weight of the 20-day embryos was 2.66 ± 0.12 g compared with 2.2 ± 0.08 g in the control and their mean length 34 ± 1.5 mm compared with 31 ± 0.8 mm in the control. The weight of the heart, kidneys, lungs, and liver of the experimental embryos also exceeded the control weights by a statistically significant degree.

The weight (460.6 ± 23 mm) and size (13.7 ± 0.15 mm) of the placenta also were greater than in the control (447 ± 19 and 13.4 ± 0.1 mm, respectively).

In the animals of group 2, penicillin, when given during the second half of pregnancy, also had a statistically significant stimulating action.

The weight and size of the 20-day embryos and their organs were greater than normally, and this was especially true of the placenta (weight 546 ± 13 mg and size 15.5 ± 0.18 mm in the experimental series, 447 ± 19 mg and 15.5 ± 0.18 mm, respectively, in the control).

In both groups the time and act of parturition were indistinguishable from normal. No still births or postnatal deaths were observed.

The newborn rats were larger than the controls in weight and size and also in the weight of their internal organs (heart, lungs, liver, kidneys). In the postnatal period newborn rats born from mothers receiving penicillin during pregnancy preserved this difference in weight.

For instance, on the 15th day of postnatal development the newborn rats in the experimental group weighed 28% more than the control. They also differed externally from the control: Their hair was much better developed (thicker and more shining), and their eyes opened earlier than those of the control young rats.

Morphological investigations of the internal organs of the embryos showed no abnormality.

Penicillin thus had no teratogenic action and it stimulated fetal and neonatal development.

The study of the effect of benzathine penicillin on development of the rats showed that it has a marked effect on the process of embryogenesis. The effect of the antibiotic depended on the time of its administration.

Benzathine penicillin had the strongest toxic action if given on the fourth day of pregnancy: 30.6% of the embryos were resorbed. On the eight day 16.3% were resorbed, and on the 11th day 2%, i.e., fewer than in the control group (3.2%).

Embryos surviving after administration of benzathine penicillin developed normally in all series of experiments. In their size and weight they were indistinguishable from embryos in the control group. The study of the development of the heart of embryos in the antenatal period (on the ninth, 11th, 15th, and 21st days) and during the postnatal period (in rats five days after birth) revealed no significant changes compared with the control.

Some increase in the size of the heart and the more rapid differentiation of the myocardium were found only in 11-day embryos of the first and second experimental groups (the mothers received benzathine penicillin on the 4th and 8th days of pregnancy). Because of the adverse effect of benzathine penicillin on the developing fetus, the composition of the blood was studied. Benzathine penicillin, if injected into pregnant rats (on the fourth, eighth, and 11th days), had no significant effect on the hemoglobin concentration, the red and white cell counts, or the color index. All the changes observed were within normal limits for rats.

Penicillin, if administered during pregnancy, thus had no adverse effect on the embryo, fetus, or newborn rats, whereas benzathine penicillin had a toxic effect on the embryo and on the development of its heart.

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DISTURBANCE OF DEVELOPMENT OF THE PROGENY OF RATS EXPOSED TO HYDROGEN CHLORIDE

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Female Wistar rats were made to inhale hydrogen chloride gas once before pregnancy or on the ninth day of pregnancy. Besides marked disturbances of the state of the lungs, in the experimental rats of both groups changes in renal and hepatic function were observed. The disturbance of the state of the organs in the mother led to developmental changes in the organs of the progeny, manifested as a functional insufficiency of these organs in the postnatal period. A disturbance of of lung (after additional inhalation) and kidney function was found in male progeny of both groups, together with changes in liver function in the male progeny of animals exposed to HCl before pregnancy.

KEY WORDS: Hydrogen chloride; lungs; kidneys; injury to organs of the progeny.

The number of known congenital diseases has increased recently [15, 17] and, for that reason, the study of the mechanisms of embryonic disturbances is assuming ever greater importance [12, 13]. In most investiga-

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