

Benzathine penicillin had the strongest toxic action if given on the fourth day of pregnancy: 30.6% of the embryos were resorbed. On the eighth 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.

LITERATURE CITED

1. V. K. Demidova, Nauch. Trudy Vyssh. Ucheb. Zaved. Litovsk. SSR, No. 5, 375 (1964).
2. A. P. Kiryushchenkov and V. G. Kurdyukova, in: Simulation, Methods of Study, and Experimental Treatment of Pathological Processes [in Russian], Moscow (1973), p. 76.
3. A. M. Chernukh and P. N. Aleksandrov, Pat. Fiziol., No. 3, 41 (1965).
4. C. K. Lowe, Brit. J. Prev. Soc. Med., 18, 14 (1964).
5. J. Warkany and E. Takaes, Arch. Path., 79, 65 (1965).

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

T. E. Pavlova

UDC 615.916:546.131].015.4:612.64

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 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-

Laboratory of Toxicology, Research Institute of Work Hygiene and Occupational Diseases, Academy of Medical Sciences of the USSR. Department of Biology, Moscow Medical Stomatological Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. A. Letavet.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 7, pp. 866-868, July, 1976. Original article submitted November 25, 1975.

This material is protected by copyright registered in the name of Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$7.50.

TABLE 1. Indices of Functions of Certain Organs in the Progeny of Rats Exposed to HCl

Age of progeny (in months)	Sex of progeny	Experimental conditions	Kidney function			Liver function	Content of neutral red in lungs after additional exposure to HCl (extinction units)	Relative weight of kidneys
			diuresis (in ml)	chlorides (in mg/ml)	protein (in mg/ml)	content of hippuric acid in urine (in mg)		
3	♂	Control	9,0±0,9	1,48±0,10	2,37±0,23	96,00±4,5	0,92±0,03	0,62±0,01
		Exposure to HCl on ninth day of pregnancy	10,0±1,3	1,20±0,06 <i>P</i> <0,05	2,85±0,27	93,6±2,8	1,16±0,04 <i>P</i> <0,001	0,61±0,02
		Exposure to HCl before pregnancy	7,8±0,7	0,88±0,07 <i>P</i> <0,001	3,25±0,24 <i>P</i> <0,02	81,2±3,2 <i>P</i> <0,05	1,15±0,07 <i>P</i> <0,02	0,66±0,01 <i>P</i> <0,02
		Control	6,7±0,4	1,20±0,16	0,71±0,12	81,3±3,7	1,04±0,06	0,66±0,02
3	♀	Exposure to HCl on ninth day of pregnancy	7,5±0,5	1,11±0,13	0,82±0,11	78,5±6,1	1,16±0,04	0,65±0,03
		Exposure to HCl before pregnancy	7,7±0,6	1,07±0,15	0,69±0,11	77,5±5,1	1,11±0,05	0,69±0,02

Legend. Values for *P* > 0.05 are not given.

tions the direct action of chemical compounds on the fetus or placenta has been studied. Comparatively few studies have been made of the state and development of the progeny in relation to the state of the mother during pregnancy [12].

Injury to maternal organs, especially the endocrine glands, heart, and liver, during pregnancy, is known to lead to the appearance of congenital anomalies and developmental defects of the homonymous organs and systems of the progeny [2-6, 9]. Murasheva [7, 8] and Romanova [10, 11] observed hypertrophy of the fetal lungs after unilateral pneumonectomy on pregnant rats. It is interesting to study the state of the organs in the progeny after chemical injury to the maternal lungs.

The object of this investigation was to study the characteristics of development and the functional stability of the organs in the progeny of animals with experimental lung injury. The harmful factor chosen was hydrogen chloride (HCl).

EXPERIMENTAL METHOD

Experiments were carried out on 160 sexually mature nulliparous female Wistar rats weighing 180-200 g. The groups consisted of 8-15 animals. To produce maximal lung damage the rats were made to inhale HCl (at the level $Cl_{50}=450$ mg/m³) once for a period of 1 h. The females of group 1 were exposed to the poison on the ninth day of pregnancy, when the anlage of the fetal lung appears. To exclude any direct action of HCl on the fetus, the females of group 2 were made to inhale the poison before the pregnancy. Mating of the females started from the 12th day after inhalation. The state of the mother was compared with the development of the progeny. To assess the state of the mother tests reflecting the state of the lungs (respiration rate, blood oxygen saturation, vital staining of the lung tissue [1]), the liver (the Quick-Pytel' test [14]), and the kidneys (diuresis, chlorides, protein [16]) were used and the relative weights of the organs also were determined. In the observations on the progeny attention was paid to the number of fetuses in the litter, the postnatal mortality, and the changes in weight until the age of 4 weeks. At the age of 2 and 3 months the progenies (females and males separately) were studied by various function tests. To study lung function, exposure to hypoxia was used. The respiration rate was determined in a pressure chamber at an "altitude" of 3500 m and the blood oxygen saturation was determined when the inspired air contained 10% oxygen. The effect of an additional exposure of the progeny to HCl (1/10 $Cl_{50}=52$ mg/m³) also was used, after which the adsorption of vital dye (Neutral Red) in the lungs was determined. During the investigation of hepatic and renal function of the progeny the same tests were used as on the mother. The oxygen consumption, the total serum protein, and the relative weights of the organs also were determined.

EXPERIMENTAL RESULTS

Exposure to HCl caused death of one-third of the animals in both groups with signs of severe dyspnea and cyanosis. The lungs of the dying rats were congested, with areas of edema and hemorrhage. Lung function was disturbed in the surviving females. On the 5th day after exposure the blood (mixed) oxygen saturation was lowered: $56.8 \pm 3.4\%$ in the pregnant rats compared with $68.7 \pm 2.7\%$ in the controls (*P* > 0.05); $5.29 \pm 4.2\%$ in the nonpregnant rats compared with $64.4 \pm 3.6\%$ in the controls (*P* > 0.05). An increase in adsorption of vital dye

(Neutral Red) by the lung tissue was observed in the pregnant rats on the eighth day after exposure to HCl (1.01 ± 0.05 extinction unit in the experimental rats, 0.77 ± 0.04 extinction unit in the controls; $P < 0.001$). This parameter was not determined in the nonpregnant animals.

Kidney function was disturbed in both groups of experimental females. An increase in the concentration of chlorides in the urine of the pregnant rats (1.48 ± 0.01 mg/ml compared with 0.94 ± 0.02 mg/ml in the control; $P > 0.01$) and in the protein concentration in the urine of the nonpregnant animals (1.53 ± 0.17 mg/ml compared with 0.78 ± 0.10 mg/ml in the control; $P > 0.001$) was observed.

Changes in liver function were found only in the pregnant animals: After loading with sodium benzoate the content of hippuric acid in the urine was increased (89.2 ± 2.3 mg compared with 73.1 ± 4.7 mg in the control; $P < 0.01$). No changes were found during this test in the nonpregnant rats. However, determination of the relative weights of the organs in the rats of group 2 revealed an increase in the relative weight of the liver (4.91 ± 0.13 in the experimental animals and 4.55 ± 0.15 in the controls; $P < 0.05$). The relative weights of the organs in the experimental pregnant animals were indistinguishable from those of the controls.

Observation on the development of the progeny showed an increase in mortality among the progeny of the rats of group 1 (exposed to HCl on the 9th day of pregnancy): $31.9 \pm 9.2\%$ in the experimental rats and $5.6 \pm 3.7\%$ in the controls ($P < 0.05$). The viability of the progeny of the animals of group 2 (exposed to HCl before pregnancy) was not reduced, but by the fourth week of development the gain in weight of the young rats was reduced: the males weighed 66.8 ± 2.4 g compared with 75.7 ± 2.3 g in the control ($P < 0.05$), the females weighed 63.2 ± 3.1 g compared with 72.2 ± 1.7 g in the control ($P < 0.02$).

Investigation of the functions of the organs of the young rats aged 2 months showed a change in kidney functions in the progenies of both groups of rats. The diuresis was increased (10.1 ± 0.8 ml in the experimental and 7.5 ± 0.7 ml in the control group; $P < 0.05$) and a decrease in the protein content in the urine of the male progeny (1.76 ± 0.11 mg/ml in the experimental and 2.26 ± 0.16 mg/ml in the control series; $P < 0.02$) after exposure to the poison on the ninth day of pregnancy. When HCl was inhaled before pregnancy, the diuresis of the male progeny was increased (10.1 ± 0.9 ml in the experimental and 7.5 ± 0.7 ml in the control series; $P < 0.05$), but in the female progeny it was reduced (6.5 ± 0.4 ml in the experimental and 8.6 ± 0.9 ml in the control series; $P < 0.05$). A study of the function of the organs in the rats aged 3 months also showed changes in the kidney function of the male progeny (Table 1). The concentration of chlorides in the urine of the progenies of the animals of group 1 was reduced and the protein concentration in the urine of the progenies of group 2 was increased.

The hypoxic test showed no disturbance of lung function in the progeny. However, additional exposure to HCl showed increased sensitivity of the male progeny to the action of this pathological agent. An increase in absorption of vital dye by the lung tissue of the male progeny of both groups of rats was observed (Table 1). In the male progenies obtained from the rats of group 2 liver function was disturbed: The quantity of hippuric acid in the urine was reduced (Table 1). The relative weight of the kidneys in these animals also was increased.

Exposure of both pregnant and nonpregnant rats to HCl thus caused a disturbance of the structures and functions of the lungs, kidneys, and liver. Changes in the mother led to a disturbance of embryogenesis and to functional abnormalities of the organs of the progeny during the postnatal period; changes in the progeny affected principally the same organs as were damaged in the mother. In fact, in the experimental females considerable lung damage was observed, and in their progeny there was increased sensitivity of the lungs to the action of the pathological agent. A fact that functional impairment of the lungs of the progeny was discovered only by the use of additional exposure to the poison is evidence of the great compensatory power of this organ in rats. Changes in the kidneys of the progeny were most severe. When the females were exposed to HCl before pregnancy, the subsequent pregnancy took place against the background of marked changes in the internal organs. This evidently explains the more severe disturbances of function in the progeny of these animals than in the progeny of rats exposed to the poison on the ninth day of pregnancy. In both groups of animals the male offspring were more sensitive than the female. The results thus showed that the disturbance of development of the progeny after exposure to HCl arises to some extent on account of interconnection between the homonymous organs of mother and fetus.

LITERATURE CITED

1. Ya. I. Azhipa, in: Response of the Organism to Small Doses of Ionizing Radiation [in Russian], Moscow (1962), pp. 98-123.
2. S. M. Bekker, Akush. Gin., No. 9, 59 (1968).
3. V. I. Bodyazhina and A. P. Kiryushchenkov, Vopr. Okhr. Mat., No. 12, 3 (1968).

4. O. E. Vyazov, The Immunology of Embryogenesis [in Russian], Moscow (1962).
5. O. E. Vyazov, A. I. Murashova, I. I. Orlova, et al., in: Proceedings of the 10th Scientific Conference on Age Morphology, Physiology, and Biochemistry, [in Russian], Vol. 1, Moscow (1971), pp. 92-93.
6. K. S. Lobyntsev, Yu. I. Savchenkov, and V. P. Tereshchenko, Abstracts of Proceedings of the 9th International Congress of Anatomists [in Russian], Moscow (1970), p. 112.
7. A. I. Murashova, Arkh. Anat., No. 8, 43 (1966).
8. A. I. Murashova, "An Experimental study of humoral connections between homonymous organs of mother and embryo in rats," Candidate's Dissertation, Moscow (1969).
9. E. I. Novikova and Yu. I. Barashnev, in: New Problems in Pediatrics, [in Russian], No. 5, Sofia (1968), pp. 29-37.
10. L. K. Romanova, Proceedings of a Scientific Conference on Regeneration and Transplantation of Organs and Tissues [in Russian], Gor'kii (1965), pp. 79-85.
11. L. K. Romanova, in: Conditions of Regeneration of Organs in Mammals [in Russian], Moscow (1972), p. 149.
12. L. K. Romanova, in: Problems in Establishment of Hygienic Standards During the Study of Late Effects of Exposure to Industrial Substances [in Russian], Moscow (1972), pp. 78-82.
13. I. V. Sanotskii, V. N. Fomenko, G. N. Zaeva, et al., Zh. Vsesoyuz. Khim. Obshch. im. D. I. Mendeleeva, 29, No. 2, 146 (1974).
14. N. G. Stepanova, Lab. Delo, No. 5, 49 (1962).
15. M. Ya. Studinikin and G. P. Borisova, Pediatriya, No. 8, 5 (1970).
16. N. I. Shumskaya and N. M. Karamzina, in: The Toxicology of New Industrial Chemicals [in Russian], No. 8, Moscow (1966), pp. 14-27.
17. B. Kaunelienė and S. Suksterienė, Sveikatos Apsauga, No. 4, 20 (1974).

EFFECT OF CORTISONE ON POSTTRAUMATIC REGENERATION OF MAMMALIAN SKELETAL MUSCLES

T. M. Kovalenko

UDC 616.74-001-003.93-02:615.357.453

Prolonged administration of cortisone to sexually immature rabbits and rats after previous injury to the tibialis anterior muscle inhibits the regeneration of skeletal muscle tissue, as manifested by delay in growth of the myosimplasts and muscle tubes. In rabbits by the 15th day after the operation the area of the muscular components of the regenerating focus was less than their area in the control. Analysis of the intensity of methionine-³H incorporation into the regenerating elements of the muscle tissue showed a significant decrease in uptake of the label into nuclear and cytoplasmic proteins of the myosimplasts of rats receiving cortisone. Inhibition of protein synthesis in the early stage of differentiation of muscle tissue was less marked than in mature differentiated muscle fibers of the intact muscle.

KEY WORDS: Regeneration of skeletal muscles; incorporation of methionine-³H; area of components of regenerating focus.

The investigation of the hormonal regulation of morphogenetic processes and, in particular, of processes of regeneration is an urgent problem of practical as well as theoretical importance [1, 7-9]. Hormones are known to control the synthesis of specific proteins in the tissues [6, 10, 11-13] and they can thus determine the direction of growth and differentiation of cells [2, 4].

Department of Biology, I. P. Pavlov First Leningrad Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR N.A. Yudaev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 7, pp. 868-871, July, 1976. Original article submitted May 30, 1975.

This material is protected by copyright registered in the name of Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$7.50.