

# THE EFFECT OF HIGH ASCORBIC ACID DOSES ON THE COURSE OF PREGNANCY IN THE GUINEA PIG AND ON THE PROGENY

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Vitamins have recently been widely employed in medicine and dispensed in doses of considerable size and for extended periods of time. In this connection the question of the overdosing of vitamins should be carefully studied [3]. This applies in every respect to ascorbic acid (AK) which is often used in addition to specific therapeutic measures and also as an independent form of medical treatment. Data obtained in recent years has provided evidence to show that the organism reacts anomalously to a surplus of AK [1, 4].

The present work is a continuation of some investigations which we made earlier on the effects of AK in the sexual sphere [2]. There are one or two works in the literature dealing with this question [4, 5]. The aim of the work was to study the effects of AK on the course of pregnancy in the guinea pig and on the progeny.

## EXPERIMENTAL METHOD

The effect of different doses of AK on the course of pregnancy and on the condition of the progeny was studied in 50 female guinea pigs having an average weight of 320 g. To one group of ten guinea pigs AK was administered per oral in doses of 500 mg to each animal daily throughout the whole pregnancy from the day of conception. Another group comprising 15 guinea pigs was fed with 50 mg per animal for a similar period. Two control groups of guinea pigs, each comprising 25 animals, were administered per oral with a quantity of physiological solution equal in volume to the solution of AK (0.2-0.4 ml).

Males were kept with the females from the first day of observation. Vaginal smears were taken daily in order to establish the time of conception. For histological examination the organs were fixed in 5% formalin solution and embedded in paraffin wax. The sections were stained in hematoxylin-eosin and by Von Gieson's method. The experiments were carried out during summer and autumn and the animals fed on the usual rations for these seasons.

## EXPERIMENTAL RESULTS

The daily administration of a solution containing 500 mg AK to female guinea pigs led to abortions, stillbirths and to the death of young rats during the first hours or days of life (Table 1).

Abortions were noted in three females which proved to be pregnant at the beginning of the experiment: — in one on the 4th day, in one on the 5th day and in one on the 25th day following the administration of AK. On dissection, the horns of the uterus in two of the females were found to be hypertrophied and devoid of fetuses and in the other female the uterus contained two fetuses in a mummified condition.

In the females of the experimental groups, deaths among the offspring occurred usually in the first minutes or hours of life. In the females of the control group, pregnancy proceeded without complications and viable young were born upon which observations were made up to the age of six months. A daily administration of 50 mg AK to female guinea pigs throughout the course of pregnancy also led to abortions, stillbirths and to the early death of the offspring, but in a somewhat lower percentage of instances (Table 2).

TABLE 1. Course and Results of Pregnancies in Guinea Pigs Administered Daily with 500 mg AK

Animal group	Number of animals			Progeny			Died after giving birth	Remained alive
	total	carrying young	abortions	total	born alive	stillborn		
Experimental	10	7	3	12	8	4	6	2
Control	10	10	—	13	13	—	—	13

TABLE 2. Course and Results of Pregnancies in Guinea Pigs Administered Daily with 50 mg AK

Animal group	Number of animals			Progeny			Died in first hours of life	Remained alive
	total	carrying young	abortions	total	born alive	stillborn		
Experimental	15	13	2	15	10	5	3	7
Controls	12	12	—	17	17	—	—	17

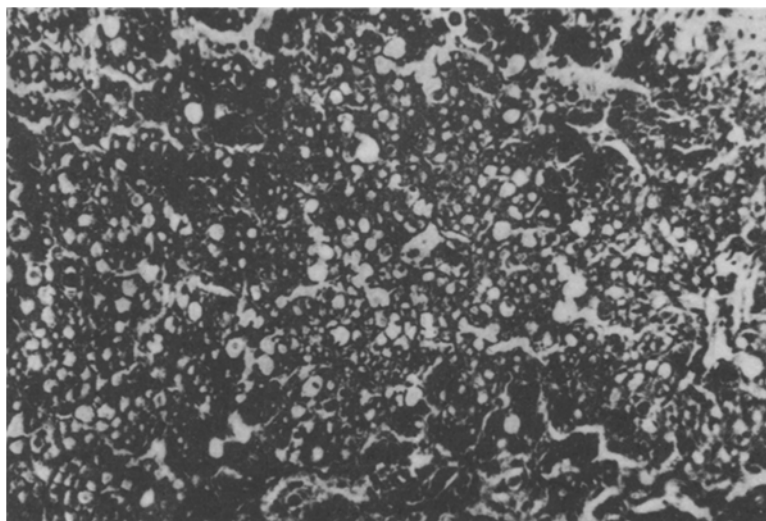


Fig. 1. Liver. Portion of adipose tissue mainly from the central parts of the lobule. Young animal from guinea pig No. 1004. Mother received an oral administration of 50 mg AK daily throughout the whole course of pregnancy. Microphotograph. Stained haematoxylin-eosin. Enlarged  $7 \times 10$ .

Out of 15 young animals born of 13 females, five were stillborn and three died during the first hours of life. A histomorphological study of the offspring belonging to females receiving large and small doses of AK revealed changes in the organs characteristic of hypoxia (Figs. 1 and 2). These changes were similar in all the offspring; they were different only in intensity.

Guinea pigs giving birth to nonviable young remained healthy from a clinical point of view for more than one year.

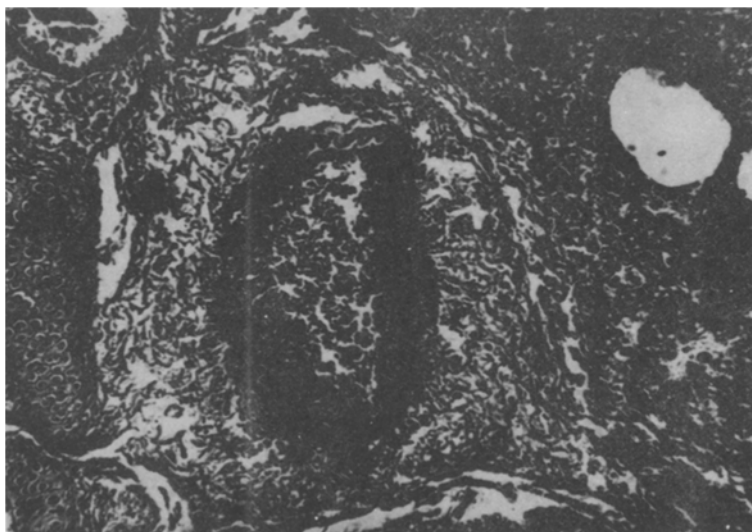


Fig. 2. Lung. Severe perivascular emphysema in the lung. Congestion and numerous haemorrhages in the perivascular tissue. Young animal from guinea pig No. 1004. Microphotograph. Stained haematoxylin-eosin. Enlarged 6 x 7.

The investigations carried out convinced us that, under special conditions of administration (large doses and for extended periods), had a negative action on the course of pregnancy in guinea pigs and on their progeny. The mechanism of these findings require elucidation.

#### SUMMARY

The work is a continuation of investigations made earlier by the author (Bull. of Exp. Biol. and Med. No. 10, 1962) on the effect of ascorbic acid on the function of the genital organs of female guinea pigs. This work contains data on the effect produced by ascorbic acid excess on the course of pregnancy and on the progeny.

It was shown that prolonged (during the whole course of pregnancy) daily per oral administration of ascorbic acid to female guinea pigs (high doses — 500 mg per animal, and physiological doses 50 mg per animal) led to pathology of pregnancy and of the progeny.

This pathology is manifested by a considerable percentage of abortions at various periods, as well as by stillbirths and by birth of nonviable progeny. Histomorphological examination of internal organs of stillborn and nonviable animals revealed marked tissue hypoxia.

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