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Observations on Impermeability of Guinea Pig Placenta to the Foreign Protein Ricin, a Phytotoxin.

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The placenta has been reported as permeable to such substances as amino-acids,¹ creatinine and creatine,² peptone,³ insulin,⁴ bacterial antibodies,^{5, 6} and allergens.⁷ Ascoli⁸ showed that the placenta was impermeable to albumins, but he suggested the possibility of a proteolytic ferment which might aid in the transfer of these substances.

To further the study of placental permeability ricin was injected into a fetus of each of 30 pregnant guinea pigs. Ricin was dissolved in physiologic salt solution and injected in amounts which varied from 6 to 350 lethal doses⁹ per kilo of the total weight of the pregnant mother. Saline solutions were injected into a fetus of each of 9 pregnant guinea pigs and this group served as controls. All of the pregnant guinea pigs were near full term and injections were made into the fetuses after laparotomy. Nembutal-ether anesthesia was used.

The mothers of the control group survived and pregnancy continued for an average of 10.4 days (6 hours to 20 days). All of the fetuses were normal at birth and they did not show any ill effects from the injection of the saline.

The results of the ricin-injected group are shown in Table I. One fetus in each litter was born dead and showed signs of ricin poisoning or one stillborn fetus was delivered too early to show characteristics of the poison, while the litter mates were alive at birth. One of the mothers gave birth to one fetus one day after operation and 3 other fetuses on the third day. One of the latter fetuses received the ricin and the mother lived. Three mothers were killed with an

¹ Slemmons, J. M., *The Nutrition of the Fœtus*, Yale University Press, 1919.

² Hunter, A., and Campbell, W. R., *J. Biol. Chem.*, 1918, **34**, 5.

³ Wertheimer, E., and Delezenne, G., *Compt. Rend. Soc. d. Biol.*, 1895, **10**, 191.

⁴ Carlson, A. J., and Drennan, F. M., *Am. J. Physiol.*, 1911, **28**, 391.

⁵ Staubli, C., *Centralbl. f. Bact. u. Parasitenk.*, *Bd.*, 1903, **33**, 458.

⁶ Bourquin, Helen, *Am. J. Physiol.*, 1922, **59**, 122.

⁷ Rosenau, M. J., and Anderson, J. F., *J. Am. Med. Assn.*, 1906, **47**, 1007.

⁸ Ascoli, A., *Z. f. Phys. Chem.*, 1902, **36**, 498.

⁹ Carmichael, E. B., *J. Pharm. and Exp. Therap.*, 1929, **35**, 193.

TABLE I.
Results Obtained by Injecting Several Lethal Doses of Ricin into One Fetus of Each of 33 Pregnant Guinea Pigs.

No. of pregnant animals used	Hr after injection until delivery	Mothers	
		Lived	Died
15	4.5- 16	14	1*
7	30 - 40	3	2*
			2†
5	50 - 96	4	1†
6	108 -150	5	1†

*Wound sepsis—gave anesthetic 7-125 hours after delivery.

†Ricin and autogenous toxins following premature delivery. Death 10-60 hours after delivery.

anesthetic following wound infection and self-evisceration. Four mothers died 10 to 60 hours after deliveries. Three of these mothers showed hemorrhages characteristic of ricin poisoning, due, we believe, to the injections being made into the uterus. The remaining mother that died spontaneously retained her litter 5 days and lived about 30 hours after the delivery. The mother did not show the hemorrhagic signs of ricin poisoning and we believe that autogenous toxins from the uterus were responsible for her death.

One of the numerous theories of the etiology of eclampsia is the absorption of fetal proteins or isoagglutinins with the consequent production of anaphylaxis or an hemagglutinative reaction. McQuarrie¹⁰ concluded that absorption of isoagglutinins did not occur in the intact placenta. Young^{11, 12} suggested that toxic products were absorbed from infarcts of the placenta caused by premature placental separation. Boucek¹³ confirms the conclusions of McQuarrie.

Our experiments with ricin support Ascoli, McQuarrie, and Boucek in demonstrating that the intact guinea pig placenta is impermeable to the toxic protein.

Conclusions. Although certain protein-like substances have been found to traverse the placenta, it seems that our experiments demonstrate that the guinea pig placenta is not permeable to the toxic protein ricin.

¹⁰ McQuarrie, I., *Johns Hopkins Hosp. Bull.*, 1923, **34**, 51.

¹¹ Young, J., *Proc. Roy. Soc. Med., Lond.*, 1914, **7**, 307.

¹² Young, J., and Miller, M. A., *Proc. Roy. Soc. Med., Lond.*, 1921, **14**, 247.

¹³ Boucek, C. M., *Am. J. Anat.*, 1928, **41**, 1.