Doses of atropine less than 20 mg or of nembutal less than 10 mg cannot be used to demonstrate the above described phenomenon; by using 20-25 mg of atropine it is often possible to show severe depression following 15 mg of nembutal on the first day, but even then there is no anesthesia or complete relaxation. Smaller doses of nembutal (5-10 mg) do not produce complete relaxation and anesthesia irrespective of the dose of atropine.

Six dogs received 0.075 mg of strychnine sulfate (by vein); to 3 additional dogs the same dose was given twice within one hour without producing convulsions. To 5 dogs a dose of 50 mg of atropine was given which produced motor depression ("weakness of the limbs") and somnolence. Each of these 5 dogs received in about 30 minutes a dose of 0.075 mg of strychnine. Every one of these animals stood up almost immediately following injection, showed motor excitement and developed within a few minutes typical strychnine convulsions. Two of these 5 dogs died of convulsions. The surviving animals were given the same dose of strychnine the following day, but no convulsions were noted.

These experiments prove that (a) atropine, until appreciable elimination occurs, shows synergism with an aliphatic hypnotic; (b) large doses of the same drug synergize with a spinal convulsant, and (c) hypnotics may antagonize atropine stimulation and convulsants may oppose atropine depression. It other words, atropine, like morphine, has a twofold action on the central nervous system. Whether or not these actions can be explained by the acetylcholine-blocking effect of atropine still remains to be determined.

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Anaphylaxis in the Pregnant Rat.

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Attempts have been made to elucidate the rôle of the endocrine glands in determining the susceptibility of animals to anaphylactic shock. Kepinow and Lanzenberg[1] found that thyroidectomy protected the guinea pig and rabbit against anaphylactic shock by in-

[1] Kepinow, L., and Lanzenberg, A., *Compt. rend. Soc. de Biol.*, 1922, **86**, 204, 906.

hibiting active sensitization with antigen. This, however, could not be repeated by Applemans[2] nor Yun;[3] and Fleisher and Wilhelmj[4] thought the protection was much less complete than the former authors believed. Blom[5] demonstrated the converse, that injection of thyroid preparations to sensitized guinea-pigs during the period of sensitization or shortly before the shocking dose, markedly increased the severity of anaphylactic shock; his method of injecting the shocking dose of antigen directly into the heart is, however, open to question.

Adrenalectomy was shown by Kepinow,[6] in guinea pigs, and Flashman,[7] and Wyman,[8] in rats, to increase the susceptibility of these animals to anaphylactic shock. Epinephrin has long been known to protect against the symptoms of anaphylaxis.[9] Wolfram and Zwemer[10] showed that cortin administered from 2 to 6 hours before a shocking dose protected a large proportion of guinea pigs against anaphylaxis; and Dragstedt, Mills and Mead[11] noted that cortical extract administered to dogs 48 hours to 5 minutes before diminished the severity of, but did not prevent anaphylactic shock.

Administration of parathyroid extract has led to contradictory results. Levinson and Matthews[12] claimed that amounts sufficient to raise the blood calcium of dogs to 15 mg % was without influence on the frequency of anaphylactic shock. Hajós,[13] on the other hand, found that the injection of parathyroid extract (Collip) decreased the sensitivity of guinea pigs to anaphylaxis.

Hajós also reported that, while anterior pituitary extracts were without influence on anaphylaxis in the guinea pig, posterior lobe extract caused a decrease in sensitivity. Cruveilheir and his associates,[14] however, found that the gonadotropic hormone adminis-

2 Applemans, R., *Compt. rend. Soc. de Biol.*, 1922, **87**, 1242.

3 Yun, *Zentralbl. f. d. ges. Hyg.*, 1930, **21**, 245, quoted by Blom.

4 Fleisher, M. S., and Wilhelmj, C. M., *Z. f. Immunität.*, 1927, **51**, 115.

5 Blom, T., *Z. f. Immunität.*, 1934, **83**, 373.

6 Kepinow, L., *Compt. rend. Soc. de Biol.*, 1922, **87**, 327.

7 Flashman, D. H., *J. Infect. Dis.*, 1926, **38**, 461.

8 Wyman, L. C., *Am. J. Physiol.*, 1929, **89**, 356.

9 Anderson, J. F., and Schultz, W. H., PROC. SOC. EXP. BIOL. AND MED., 1909, **7**, 32.

10 Wolfram, J., and Zwemer, R. L., *J. Exp. Med.*, 1935, **61**, 9.

11 Dragstedt, C., Mills, M., and Mead, F. B., *J. Pharm. and Exp. Therap.*, 1937, **59**, 359.

12 Levinson, S. A., and Matthews, S. A., PROC. SOC. EXP. BIOL. AND MED., 1926, **24**, 350.

13 Hajós, C., *Endocrinology*, 1926, **10**, 560.

14 Cruveilhier, L., Haguenau, J., Thieulin, G., and Viala, C., *Compt. rend. Soc. de Biol.*, 1938, **128**, 282.

tered prior to injection of the shocking dose of antigen decreased their susceptibility to anaphylaxis. This protection Solomonica and Kurzrok[15] showed to be true likewise for anterior pituitary extract and for pregnancy urine. Molomut[16] conversely found that following total hypophysectomy via the pharyngeal route susceptibility to anaphylaxis in the ordinarily refractory rat was markedly increased, despite the animals' general hypometabolism.

Hajós[10] administered ovarian, corpus luteum, and male sex hormone extracts to guinea pigs without effect on anaphylaxis. Solomonica and Kurzrok,[15] however, found that follicular hormone conferred protection to guinea pigs. Schafer[17] could not confirm this, and believed guinea pigs given large doses of follicular hormone had a slightly greater susceptibility to anaphylaxis than his control group.

The influence of pregnancy on anaphylaxis is not clear. Jackson[18] noted that of 8 animals who died of anaphylactic shock in a series of 10 female and 19 male rabbits, 6 were females. All of these females were either pregnant or "pseudo-pregnant," *i. e.*, histological examination of the uterus showed the endometrium to be under the influence of corpus luteum hormone, although no embryos were present. However, 3 of the 4 female rabbits who survived injection of a shocking dose of antigen were likewise pregnant; the precipitin titers of these animals were uniformly below the level found in all rabbits who died in anaphylactic shock. Those females who shocked fatally had all survived injection of a shocking dose of antigen while in a non-pregnant condition, although 5 of the 6 had precipitin titers as high as those present in animals dying in anaphylaxis.

A study was made of the effect of pregnancy on anaphylaxis in the rat. This animal was chosen because of its natural refractoriness to anaphylaxis, rendering any increased susceptibility to shock more readily apparent. Twelve stock female rats of the hooded strain, obtained from Dr. P. E. Smith, were mated with stock breeder males. The onset of pregnancy was dated from the time of appearance of spermatozoa in the vaginal smear. As soon as impregnated, the rats were segregated from the males; within 24-36 hours after the time of impregnation, 1 cc of normal horse serum was injected intravenously. This injection was repeated 3 and 6 days later. Eleven days after the last injection, a "shocking" dose of 1 cc of the same horse serum was injected intravenously. The progress of the animal was noted by clinical observation, and in 9 of the rats

[15] Solomonica, B., and Kurzrok, R., *Endocrinology*, 1936, **20**, 171.

[16] Personal communication.

[17] Schafer, W., *Zentralblatt f. Bakt.*, 1938, **140**, 260.

[18] Jackson, C., *J. Immunology*, 1935, **28**, 225.

by following the rectal temperatures. Results were compared with 17 normal nonpregnant female control rats of the same stock, sensitized and shocked in identical manner.

Table I tabulates the degree of shock in the pregnant and in the control animals. It can be seen that there is no significant difference between the frequency of anaphylactic shock in the pregnant and in the nonpregnant animals. Two severe shocks occurred in the pregnant group, and 4 in the nonpregnant, but no animals died of shock in either series. Impregnation was corroborated by either postmortem examination or the subsequent birth of young. The experience of sensitization and shock had no demonstrable effect on the number of rats in each litter.

It can be concluded that in the rat the endocrine rearrangements of pregnancy have no bearing on susceptibility to anaphylaxis.

TABLE I.

A. Anaphylaxis in Rats 18 Days Pregnant at the Time of Injection of the Shocking Dose of Antigen (1 cc horse serum intravenously).

Rat No.	Severity of Shock	Remarks
111	No shock	
120	"	
109	"	
102	Severe	Temp. dropped from 100.1 to 95.7°F
104	No shock	T. stationary
108	Mild	T. dropped to 96.7
115	"	T. " from 101.7 to 98.4
100	Severe	T. " " 101.7 to 96.8
110	No shock	T. " " 99.6 to 98.4
105	Mild	T. " " 98.5 to 96.0
114	No shock	T. stationary
122	"	T. stationary; only .5 cc horse serum given intravenously

B. Anaphylaxis in Control, Non-pregnant Female Rats.

Rat No.	Severity of Shock
37	No shock
38	"
39	"
40	"
41	"
42	"
43	"
64	"
61	Severe
62	Mild
63	Severe
65	Mild
66	No shock
67	"
68	Severe
69	"
70	No shock