in anoxic shock they were shrunken and darkly stained, as if they were calcified.

Both types of shock produced in the cardiac musculature smaller or larger areas composed of pale staining swollen muscle cells. Only in exceptional cases were a few muscle cells definitely destroyed as was also indicated by the formation of reactive cellular proliferation. Its absence in most of the animals even if they had been frequently treated evidenced the reversibility of the changes described above. The skeletal musculature showed the same changes, but to a more marked degree, rupture of muscle fibres being visible in the iliopsoas muscle and in the musculature of the thigh. Here a definite reactive cellular proliferation was also noted. In the liver hydropic changes of hepatic cells were observed after exposure to insulin or anoxic shocks. Definite focal necroses of the liver were found only in those rabbits which had shown severe responses to insulin or anoxic shock. Fatty infiltration in the parenchymatous organs was not noted following anoxic shock, obviously because of the relatively short duration of a single shock period.

The hydropic changes in the heart, skeletal musculature and liver are usually reversible. In the brain, however, single ganglion cells of various areas are destroyed, and this perhaps is a necessary step in the effective therapy of schizophrenia. The great similarity of the symptomatology and anatomical changes produced either by insulin or anoxic shock might warrant a test as to the curative results obtainable by anoxic shock in schizophrenia.

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The Antigonadotropic Factor. The Quantitative Aspects of the Prolan-Antiprolan Reaction.

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The question as to whether or not the neutralization of prolan by antiprolan is subject to quantitative laws is of interest since it permits of certain conclusions in regard to the mechanism of this reaction. We know that fermentive processes are not subject to quantitative laws. On the other hand, adsorptive processes (*e. g.*, the toxin-antitoxin reaction) are so, subject to the deviation known

as Danysz's phenomenon. This phenomenon means: if a certain quantity of toxin is added to a certain quantity of antitoxin the mixture is more toxic if the toxin is added by a fractional method than if it were added at one dose. If, however, the reverse process is followed and the antitoxin is added to the toxin by this method the toxicity of the mixture is not greater than if the antitoxin were added all at once. Bordet described the same phenomenon in connection with hemolysins and Craw with agglutinins.

Following the technic indicated by Zondek and Sulman[1] we investigated whether Danysz's effect is also apparent in connection with the prolan-antiprolan reaction. In the first series of experiments we added prolan to antiprolan by the fractional method, in the second we followed the reverse method, adding antiprolan to prolan. The experimental order was chosen so that each time 10 RU of prolan or 10 PAU of antiprolan* were dissolved in 0.5 cc of water. The prolan powder had the titer of 1 mg = 100 RU, the antiprolan powder that of 1 mg = 1 PAU. We added the substance at intervals of 2 hours. During the whole experimental period, lasting 8 hours, the substances were kept in the incubator.

The experimental order is shown in Table I.

TABLE I.

1st series: Prolan is added to antiprolan.

Inf. rats R	Antiprolan PAU	Prolan RU	Method of addition	Gonadotropic reaction
1	30	30	1 dose	—
2	30	40	1 "	+
3	30	30	3 "	—
4	30	40	4 "	+

2nd series: Antiprolan is added to prolan.

Inf. rats R	Prolan RU	Antiprolan PAU	Method of addition	Gonadotropic reaction
5	40	30	1 dose	+
6	40	40	1 "	—
7	40	30	3 "	+
8	40	40	4 "	—

Table I shows that the neutralizing effect of prolan and antiprolan is subject to strictly quantitative laws. Even if we use 4 portions of 10 units each in every instance 40 units are neutralized, independent of whether prolan is added to antiprolan or the reverse.

The fact that the quantitative neutralization of prolan and antiprolan follows strict laws differentiates this reaction from fermentive

[1] Zondek, B., and Sulman, F., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 708.

* 1 PAU = 1 prolan anti-unit is the smallest amount of antiprolan able to annihilate the gonadotropic effect of 1 RU of prolan.

reactions and from most of the immune reactions. Even if we consider antiprolan formation *in vivo* as a process of immunization, yet antiprolan is distinguished from the other groups of immune bodies, which have hitherto been known, by the quantitative behavior of its *in vitro* reaction. The absence of the usual serologic reactions of prolan and antiprolan *in vitro* also demonstrates that we are considering a group of immune bodies of an exceptional type.

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Progonadotropic Augmentary Immune Sera after Protracted Injection of Hypophyseal Gonadotropic Hormone in Rabbits.

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Collip[1] as well as Thompson[2] showed that the injection of gonadotropic extracts of the pituitary gland occasionally led to the production of immune sera which augmented the gonadotropic effect of the antigen. Rowlands[3] was able to confirm these results. These synergistic sera exert their progonadotropic action exclusively on the gonadotropic extracts of hypophyseal origin (prosylan), not however on hormones derived from pregnancy blood or pregnancy urine (prolan). Thompson, therefore, explains the effect of the progonadotropic sera as acting through the formation of an augmentary factor, which is formed as an antihormone against Evans' antagonist[4] of the pituitary. The progonadotropic effect is invariably replaced by the anti-gonadotropic effect during the course of the immunization process. It is by no means the rule that the augmentary factor is produced following injection of gonadotropic extracts of hypophyseal origin. Its formation is, as a matter of fact, subject to laws which have hitherto been unknown.

In 14 cases in which we used protracted immunization with gonadotropic extracts from pregnancy blood, pregnant mare's blood, and pregnancy urine we have so far not detected the presence of a

1 Collip, J. B., *Canad. Med. Assn. J.*, 1937, **36**, 199.

2 Thompson, K. W., PROC. SOC. EXP. BIOL. AND MED., 1937, **35**, 640.

3 Rowlands, I. W., *Proc. Roy. Soc. London*, 1938, Ser. B, No. 837, **124**, 492.

4 Evans, H. M., Pencharz, R. I., and Simpson, M. E., *Univ. Calif. Publ. Anat.*, 1936, **1**, 237.