cocytes and platelets is not enough to produce shock seem to warrant the idea that the liberation of histamine constitutes a very important factor in localizing to the lung capillaries the emboli produced by the clumping of blood elements.

In 6 rabbits we have studied the effects of a previous injection of glycogen upon the course of anaphylactic shock and in 5 others, glycogen was given after the injection of the antigen. It became apparent (Table II and Fig. 1) that if a proper amount of glycogen is injected (1 to 3 g) and enough time is allowed to elapse (5 to 10 minutes) before injection of the serum, the blood histamine, the leucocytes, and the platelets are drastically reduced and shock will not occur after the injection of serum. This is clearly shown in rabbits 20 and 21. When an insufficient amount of glycogen is injected 1 to 2 minutes before the serum, the shock which occurs is either milder or unchanged. Given after the serum, glycogen rather aggravated the condition or had no effect at all.

Interesting enough is the fact that the leucopenia in anaphylactic shock probably derives from a different mechanism than that produced by glycogen, since under urethane anesthesia, glycogen produces a leucocytosis or no change in the leucocyte count, while anaphylactic shock produces a drop in leucocytes even under these anesthetics. Since histamine is bound to platelets, it seems logical to conclude that the reduction in blood histamine during anaphylactic shock in the rabbit depends upon the removal of the platelets from circulating blood, this being an inevitable occurrence during this kind of shock.[15]

Summary. Polysaccharides prepared from *Ascaris lumbricoides* and hydatid fluid, as well as liver glycogen, produce a sharp reduction in blood histamine in the unanesthetized rabbit or in those under Dial + ether anesthesia, urethane and chloralose anesthesia. Concomitantly, platelets almost disappear from circulating blood while the leucocytes are reduced only in the unanesthetized rabbit or in those under Dial + ether anesthesia. Under chloralose or urethane anesthesia, there was rather a leucocytosis after the injection of glycogen. Thus the conclusion was drawn that histamine is bound to platelets in rabbit blood. Glycogen has a definite inhibitory effect upon the course of anaphylactic shock, explained by the fact that glycogen *disperses* the blood elements, without a preferential allocation of those in the shock organ, while anaphylactic shock in the rabbit occurs as a consequence of the clumping of leucocytes and platelets in the lung capillaries and small vessels, which become a filter for agglutinated blood elements.

[15] Kopeloff, N., and Kopeloff, L. M., *J. Immunol.*, 1941, **40**, 471.

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Alloxan in Pregnant Rats.*

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Diabetes mellitus can be produced in rats by the injection of alloxan.[1] Although there is slight damage to other tissues of the body, the principal action of alloxan is the production of a selective necrosis of the beta cells of the islets of Langerhans. The diabetic state produced can be ameliorated by adrenalectomy[2] and by insulin therapy.[3]

In an attempt to produce offspring with

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[1] Dunn, J. S., and McLetchie, N. G. B., *Lancet*, 1943, **245**, 384.

[2] Janes, R. G., and Friedgood, C. E., *Endocrinology*, 1945, **36**, 62.

[3] Kaplan, N. O., Franks, M., and Friedgood, C. E., *Science*, 1945, in press.

diabetes mellitus, we undertook studies to determine whether alloxan passed through the placenta in quantities sufficient to produce the disease. Although some evidence seems to indicate that islet cells do not function before birth[4] we investigated what effect maternal hyperglycemia might have on the islet cells of the fetus.

Methods. (A) *Experiments to Determine Placental Transmission.* Sixteen rats, which were 18 to 20 days pregnant, were anesthetized (14 with pentobarbital intraperitoneally; 2 with vinethene inhalation). The abdomen was then opened, and the uterus incised longitudinally along the anti-mesometrial surface. Amniotic fluid was aspirated from several of the vesicles and these fetuses were then decapitated to obtain blood samples. Maternal blood was also drawn. These samples served as controls. A 5% solution of alloxan (200 mg/kg) was then injected into the inferior vena cava of the mother. Amniotic fluid was aspirated from the remaining vesicles one minute after the start of the alloxan injection, and the fetuses were removed and decapitated. The blood was collected on a watch glass, moistened with a 1% solution of heparin. Simultaneously a maternal blood sample was taken from the renal vein. Each of these samples was added to a strong tungstic acid solution. The filtrate separated from the tungstic acid precipitate was tested for the presence of alloxan by the qualitative method described by Leech and Bailey.[5]

(B) *Experiments on Maternal and Fetal Hyperglycemia.* Blood sugar studies were done on the following:

(1) Five normal 20-day-pregnant rats and their fetuses.

(2) Three normal mothers 1-2 day postpartum and their offspring.

(3) Three 20-day-pregnant diabetic mothers and their fetuses.

(4) One diabetic mother 1 day post-partum and her offspring.

The mothers made diabetic were given alloxan intraperitoneally (200 mg/kg in 5% solution) on the fourteenth day of gestation, and by the seventeenth day they showed polyphagia, polydypsia, marked polyuria (as high as 150 cc per 24 hours), a heavy 4+ glycosuria, and some had ketonuria.

Rats used in both experiments were from the Long-Evans strain.

Results. The control blood samples from both mother and fetus showed negative tests for alloxan. A faint blue reaction was detected in the control amniotic fluid; however, the substance giving this reaction was not determined. Following the injection of alloxan, a strong positive test for alloxan was obtained in the fetal as well as in the maternal blood. The amniotic fluid specimens drawn after the injection of alloxan gave a slightly more intense positive reaction than the control sample, but much less intense than the positive fetal blood specimens.

Blood sugar samples of the normal pregnant and postpartum mothers averaged 128 mg% (range 112-136 mg%). The blood sugar of the fetuses and of litters averaged 120 mg% (range 108-129 mg%).

Blood sugar values of the pregnant diabetic rats averaged 366 mg% (range 344-418 mg%). Their fetuses showed a slightly lower blood sugar value—average 327 mg% (range 292-373 mg%).

The diabetic maternal blood sugar one-day postpartum was 352 mg% while that of her offspring was 124 mg%.

When alloxan was injected into pregnant rats 6 hours to 4 days before parturition the mothers showed typical signs of diabetes mellitus whereas the litters were not diabetic. If the litters were placed with normal foster mothers, they developed normally, with no signs of diabetes mellitus, and the pancreatic islets showed no definite pathological change.

Summary. 1. In pregnant rats intravenously injected alloxan passes through the placenta into the fetal circulation within one to two minutes. 2. It does not, however, produce permanent diabetes in the offspring. 3. The blood sugar values of the fetus parallels at a lower level that of the diabetic mother until parturition.

[4] Hard, W. L., *Am. J. Anat.*, 1944, **75**, 369.

[5] Leech, R. S., and Bailey, C. C., *J. Biol. Chem.*, 1945, **156**, 525.