mitotic figures were counted in one section containing several small fragments of pancreatic tissue. Thereafter, the number of mitoses decreased to approximately normal rarity by the end of 24 hours. The distribution of acinar cells in mitosis appeared to be completely haphazard. The even smaller numbers of mitotic figures observed in the pancreatic ductular epithelium of control animals were not discernibly increased in the experimental animals. No mitotic figures were seen among islet cells at any time.

With the exception of slight degenerative changes in the convoluted tubules of the kidneys and the irregular occurrence of slight fatty metamorphosis of the liver, no significant alterations were observed in organs other than the pancreas, including the other endocrine organs. Histological alterations of the adrenal medulla similar to those described by Hard and Carr[6] were encountered irregularly in both experimental and control animals.

Sections of the liver from diabetic animals were found histologically to be lacking in glycogen. The heart muscle contained some stainable glycogen but this was not distinctly greater in quantity than normal. The deposition of glycogen in the renal tubular epithelium, especially of the loops of Henle, was satisfactorily demonstrated in several diabetic animals.

Summary. Alloxan administered to hooded rats in single subcutaneous injection in doses of 175 to 350 mg per kg of body weight regularly produced rapid selective necrosis of the islets of Langerhans and characteristic fluctuations of the blood sugar level. During the first 24 hours, irrespective of dosage, a blood sugar curve of typical form was obtained. Thereafter, following the higher doses of alloxan, the blood sugar rose rapidly to very high values and death occurred in a state resembling diabetic coma. With the lower doses employed the animals survived for periods up to several months with persistent diabetes. Histological alterations in the islets of Langerhans conformed to those described by previous investigators in white rats following alloxan. In addition, a great increase was observed in the activity of mitotic division in acinar cells of the pancreas during the first 24 hours after injection of alloxan.

14785

Transmission of Penicillin Through Human Placenta.*

HARRY J. GREENE AND GLADYS L. HOBBY.

From the Kings County Hospital, Brooklyn, N.Y., and the Biological Laboratory of Chas. Pfizer & Co., Brooklyn, N.Y.

This study was undertaken to determine the existence of a placental barrier to penicillin.

Experimental. Four normal patients were selected while in active labor. Delivery was expected within 2 hours. Penicillin,† dissolved in normal saline, was administered intravenously. Ten cubic centimeters of saline were used irrespective of the dose administered. The calcium salt of penicillin was used in one case, the sodium salt in the remainder.

Samples of the maternal blood were taken for assay at intervals from the time of injection up to and including the time of delivery. At the time that the baby was separated from the placenta, placental cord blood was withdrawn into a sterile test tube. In one instance (Case 1) a pipette was inserted into the uterus following spontaneous expression of the placenta. Blood was aspirated from the uterus for assay. In Case 3 the amniotic sac was perforated about 5 minutes prior to delivery and amniotic fluid obtained for assay.

* This manuscript was submitted for publication June 1, 1944.

† The penicillin used throughout this study was supplied through the kindness of Mr. John L. Smith, Chas. Pfizer & Co., Brooklyn, N. Y.

TABLE I.
Amount of Penicillin in Maternal Blood at Intervals Following Intravenous Administration.

Cases	Dosage (units)	Maternal blood ½ hr	1 hr	1½ hr	2 hr
		Units per cc			
1 H.B.	100,000	0.32	0.16	—	0.04
2 M.P.M.	100,000	2.56	0.32	0.16	0.01

TABLE II.
Amount of Penicillin in Maternal and Placental Cord Blood at Time of Delivery.

Cases	Dosage (units)	Time* (hr)	Maternal blood (units/cc)	Placental cord blood (units/cc)	Amniotic fluid
1 H.B.	100,000 Ca	2	0.04	0.02	
2 M.P.M.	100,000 Na	2	0.01	0.02	
3 L.C.	20,000 Na	½	0.19	0.05	Neg.
4 A.B.	20,000 Na	1	0.094	<0.047	

* Time is period elapsed from the administration of penicillin to delivery of infant.

In each case blood was allowed to clot and was then stored over-night at refrigerator temperature. On the following day the serum was withdrawn using sterile precautions.

Serum was tested for the presence of penicillin by the method of Dawson, Hobby, *et al.*[1,2] Hemolytic streptococcus (strain C203Mv) was used throughout. The serum was diluted serially from 1:2 to 1:512 in a phosphate buffered beef infusion medium. Hemolytic streptococci were added in an amount sufficient to give a final dilution of 10^{-6}. Incubation was carried out at 37°C for 24 to 30 hours. Standard penicillin of known unitage, diluted serially from 3 to 0.0012 Units per cc, was run simultaneously.

In 2 cases, determinations of the amount of penicillin in the maternal blood were made at one-half hour intervals following injection in order to ascertain rapidity of elimination from the blood stream in the woman in labor. As shown in Table I, penicillin was eliminated at approximately the same rate as was previously demonstrated in other patients by Rammelkamp & Keefer[3] and by Dawson *et al.* [1]

It is evident from Table II that penicillin surmounts the placental barrier. When one hundred thousand units were used, the concentration in cord blood was relatively high even though 2 hours had elapsed following administration of the penicillin. When twenty thousand units were used the concentration in cord blood one-half hour after administration was adequate to inhibit sensitive bacteria. If the time was extended to one hour, the amount in the cord blood was insignificant. Except for one instance, there was a lower level in the cord blood than in maternal blood. There was no evidence of toxicity to mother or baby.

Summary. Penicillin was administered to 4 normal patients in active labor. Two patients received one hundred thousand units each. Both showed significant amounts of penicillin in the maternal and placental cord blood, 2 hours after administration. Two patients received twenty thousand units of penicillin each. The patient who received it one-half hour before delivery showed ample penicillin in the maternal and placental cord blood but not in the amniotic fluid. The patient who received penicillin one hour before delivery showed significant penicillin in the maternal blood but none in the placental cord blood.

1 Dawson, M. H., Hobby, G. L., Meyer, K., and Chaffee, E., *Ann. Int. Med.*, 1943, **19**, 707.

2 Hobby, G. L., Meyer, K., and Chaffee, E., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 277.

3 Rammelkamp, C. H., and Keefer, C. S., *J. Clin. Invest.*, 1943, **22**, 425.