enough to meet the requirements of the experiment, *i. e.,* give a blood sugar raising effect equal to the blood sugar lowering effect of the insulin. Against a background of several hundred blood sugar curves we would judge that with the doses here used the epinephrin has little effect on the course of insulin action and asserts itself only after the action of the latter has passed off.

The lack of rapid return of blood sugar towards the initial level in the diabetic animal cannot be attributed to absence of mobilizable liver glycogen. Epinephrin alone causes the usual mobilization of sugar in the diabetic dog. When both drugs are given the delayed blood sugar rise also testifies to the presence of liver glycogen.

Unless secreted epinephrin has an altogether different action from injected epinephrin the conclusion seems warranted that the normal type of response to intravenous insulin with its early return to the normal is not due to epinephrin secretion.

8094 C

Placental Immunity. 1. A Method of Determining Dosage of Placental Globulin in Measles Prophylaxis.

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(Introduced by B. Schick.)

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Globulin extracted from human placenta has been found by McKhann and Chu[1] to be effective in measles prophylaxis. Our experiences with this preparation confirm their results. The dosage employed by us has, however, been larger than those previously recommended, and the percent of our cases completely protected was smaller. One reason for this discrepancy is that we treated only those children who were intimately exposed to measles in their own homes, and did not include children who were presumably exposed in hospitals, nurseries, schools, buses, playgrounds, etc. Results of measles prophylactic studies[2] made under such conditions are more accurate than those of institution epidemics.

The dosage of globulin extract from placenta is being determined by injecting various amounts under comparable conditions of exposure to children of a definite age range, as has previously

[1] McKhann, C. F., and Fu Tang Chu, *Am. J. Dis. Child.*, 1933, **45**, 475.
[2] Karelitz, S., and Schick, B., *J. Am. Med. Assn.*, 1935, **104**, 991.

been worked out for convalescent serum and immune adult blood. Since placentas vary in size, and in the amount of free blood obtained with them, and probably vary considerably in the amount of immune substance they contain, one can determine dosage in the manner mentioned above only when large numbers of placentas are pooled.

The determination of the prophylactic value of placental extract on the basis of its nitrogen content does not seem to be sufficiently reliable as yet, if we apply the knowledge that 2 samples of diphtheria antitoxin with the same nitrogen content may differ widely in their antitoxic titres. Our data indicate that this is also true of the placental globulin extracts. (Table I.)

TABLE I.

Placenta	—Globulin Extract— Quantity cc.	Nitrogen mg. %	Diphtheria Antitoxic Titre A—Extract units/cc.	B—Mat. Serum units/cc.	Nitrogen mg. %	Measles Prophylaxis Dose B/A times 10 cc.
1	100		.05	.05	2.48	10
2	"		.06	.09	2.48	15
3	"		.03	.04	2.44	13.3
4	"	3.72	.01	.02	1.92	20
5	"	2.67	.03	.03	1.37	10
6	"		.19	.11	1.55	5.7
7	"		.03	.02	1.83	6.6
8	"	2.56	.06	.05	1.98	8.3
9	"	3.75	.33	.11	2.28	3.3
10	"		.15	.06	2.18	4

Dosage of Globulin Extract is calculated to compare with 10 cc. of immune adult blood serum: If the comparison were to be made with a different quantity (X) of blood serum the calculation would be B/A times X, instead of B/A times 10, as above.

Both for academic as well as practical reasons it would seem desirable to be able to determine in each placenta the prophylactic value of its globulin content. To this end we (Karelitz) have suggested a working hypothesis—a procedure based on the following facts: 1. McKhann and coworkers[3] have found that the placental globulin extract as prepared by them contains both the diphtheria antitoxin and the measles antisubstance, when present at all. We[4] have confirmed these findings. 2. It has been shown[5] clinically that the globulin extracted from measles immune human blood serum is equally effective in measles prophylaxis as the equivalent quantities

[3] McKhann, C. F., and Coady, Harriet, *Southern Med. J.*, 1934, **27**, 20.

[4] Unpublished data of authors.

[5] Karelitz, S., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 793.

of blood serum. 3. The dosage of immune human blood serum in measles prophylaxis has been established in previous studies, to vary between 8-40 cc.

The deduction we have drawn is that the measles prophylactic value of that amount of human blood serum which contains one unit of diphtheria antitoxin should be equivalent to the amount of placental globulin extract which contains one unit of diphtheria antitoxin. For example: Blood serum obtained from a woman at the time she expels the placenta contains 0.05 units of diphtheria antitoxin per cc. The globulin extracted from her placenta has a diphtheria antitoxic titre of 0.10 units per cc. The placental globulin therefore contains twice the quantity of diphtheria antitoxin per cc. as does the circulating blood serum of this same person. Since it is known that the dosage of adult blood serum will vary from 8-40 cc., we believe, if our hypothesis is correct, that in this particular instance we would use just half as much globulin extract, namely 4-20 cc.

We have attempted to test our hypothesis in the following experiment: Blood was taken from 20 women at the time of the expulsion of the placenta. The bloods were permitted to clot and the diphtheria antitoxic titres of their sera were measured by the neutralization test. The placentas were individually extracted as has been suggested in the original paper by McKhann and Chu, and these globulin extracts, after being each diluted to 100 cc. volume, were studied for their diphtheria antitoxic titre. In the manner illustrated by the example cited the dosage of the various globulin extracts was determined, using the results obtained with 10 cc. of immune adult blood serum as the basis for our comparison.

Using the method described for arriving at the dosage of placental globulin extract, we have injected 60 children with the preparation from 10 placentas. As will be noted the dosage of globulin extract varied from 3.7 cc. to 20 cc., or from 5-30 doses from a placenta.

Our results are very similar to those obtained by various investigators[6, 7] with dosage of 10 cc. of adult serum. (Table II.)

The results indicate that our hypothesis was correct, since the placental extract and 10 cc. of adult serum yielded similar results. As pointed out above we calculated the dosage of globulin extract to be compared with 10 cc. of adult serum. The individual extracts

[6] Morales, E. G., and Mandry, O. C., *Am. J. Dis. Child.*, 1930, **39**, 1214.

[7] Karelitz, S., and Schick, B., *J. Am. Med. Assn.*, 1935, **104**, 991.

TABLE II.

	Dosage	No. Cases	Protected %	Modified %	Failed %
Morales & Mandry	10 cc. A.S.	138	40	40	20
Karelitz & Schick	10 cc. A.S.	70	42	41	17
Authors	3.3-20 cc. Globulin Extract	60	37	43	20

A.S.—Adult Serum.

are at present difficult to compare because of the small numbers of case reports received to date.

In the event that there is no diphtheria antitoxin either in the placenta or maternal circulation, this method fails. If, however, several placentas are pooled, it is possible to compare the diphtheria antitoxin of the globulin extract of the pooled placentas with the diphtheria antitoxic titre of the pooled specimen of 1 cc. of blood serum obtained from each mother at the time of expulsion of the placenta.

Conclusions. 1. By comparing the titre of diphtheria antitoxin of maternal blood and the globulin extracted from a placenta one may arrive at equivalents which are also equivalent in measles prophylaxis. This offers a method of measuring dosage of placental globulin extract. Ten experiments performed indicate that this, with the exception cited, is true. 2. The measles antibody and diphtheria antitoxin are both contained in the globulin fraction as extracted. 3. Globulin extract when properly applied as to dosage and conditions of exposure is effective in measles prophylaxis.

8095 C

Placental Immunity. 2. Comparison of Maternal Circulating Blood Immunity with that of Placental Fluid.

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In their study of the prophylactic value in measles of the globulin extracted from the human placenta McKhann and Chu[1] raised the question of the source of these antibodies. They believed that besides maternal and fetal blood there were possibly antibodies originating in the placental tissue as such.

[1] McKhann, C. F., and Fu Tang Chu, *J. Infect. Dis.*, 1933, **52**, 268.