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.

The demonstration by various authors that the titre of cord blood and maternal circulating blood for diphtheria antitoxin, scarlet fever antitoxin, and poliomyelitis virus neutralizing substance are alike in most instances, suggests the direct transplacental transmission of antibodies from the mother to the child.

We[2] reported that the globulin extracted from immune adult males' blood in the same manner as suggested by McKhann for placenta was equally effective in measles prophylaxis as the blood itself. In attempting to explain the striking results of McKhann and coworkers we suggested that possibly all of the extracellular placental fluid may be comparable to blood serum in its antibody content. In the course of several studies on placental immunity we obtained some evidence which seems to bear out this suggestion.

15-20 cc. of blood was drawn from a superficial vein of the mother at the time of expulsion of the placenta. This blood was permitted to clot, and the diphtheria antitoxic titre of the serum was measured by the toxic neutralizing test. The placenta plus what blood and fluid dropped into the receptacle with it was collected under sterile conditions. The fluid was decanted. The placenta was cut up into many small sections and squeezed in a simple orange hand press.

The fluid so obtained plus the blood which was decanted were mixed and measured, then centrifuged for 15 minutes under high speed. The sanguinous supernatant fluid was measured and its diphtheria antitoxic titre determined.

TABLE I.

Nos.	Placenta				Diphtheria Antitoxic Titre	
	Wt. Gm.	Fluid A	Supernatant Fluid B	B/A %	Placental Fluid U/cc.	Maternal Blood Serum U/cc.
1	880	150			.05	.05
2	755	150			.03	.03
3	1340	175			.05	.05
4	1050	360	290	80	.20	.20
5	900	90			.06	.06
6	575	33			.14	.16
7	580	140	110	78	.00	.00
8	770	225	155	69	.00	.00
9	585	125	75	60	.00	.00
10	920	325	210	65	.00	.02

As seen in Table I, in 8 out of 10 instances the antitoxic titre of the maternal circulating blood serum and that of the placental fluid were equal, and in the other 2 there was only a slight difference.

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

The placental fluid obtained as it was, must have been a mixture of maternal and fetal blood, interstitial fluid, some placental tissue, and possibly a slight amount of amniotic fluid. That it was not blood alone may be deducted from the fact that after centrifuging, the supernatant fluid varied from 60-80% of the total, instead of 40-45% as is usually obtained when blood is centrifuged. In addition the residue contained some placental fibres in all instances. It is not likely that laking of some of the blood caused this high percent of supernatant fluid.

Since the antitoxic titre of this supernatant fluid was identical with maternal blood serum, we may deduce that the interstitial fluid and placental blood probably have the same diphtheria antitoxic titre as does the maternal blood serum.

This evidence added to the fact that cord blood contains the same diphtheria antitoxic titre as does maternal blood, indicates that the immune substances of the placenta are probably due entirely to *passive immunity* transmitted from the mother to the placenta and from there to the fetus. Active immunity would result in such quantitative agreement between blood and placental fluid with such regularity, only if there is a constant interchange of antibodies between mother, placenta and fetus.

The determination of the diphtheria antitoxic titre of amniotic fluid is now in progress. In the first case analyzed no antitoxin was found in the amniotic fluid and none (less than 1/100 unit per cc.) was found either in the placenta or in the maternal circulating blood.

The information obtained in this study suggested its practical application in measles prophylaxis.

It has been shown by McKhann and Chu[8] and confirmed by us that the globulin, as extracted, contains the measles antibody as well as the diphtheria antitoxin. If the measles antibody is present at all, it may be assumed from the evidence presented that it would be contained in this placental fluid in the same proportion as in the serum of the maternal circulation, since that was true of the diphtheria antitoxin.

We might therefore use similar quantities of this fluid as we would use immune adult blood serum in measles prophylaxis. The truth of this hypothesis is now being tested.

If the placental globulin extract is used, its dosage may be determined by comparing the antitoxic titre of the extract with that of the placental fluid, instead of maternal blood as was suggested in a

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

previous paper.[4] This may be done because of the similar diphtheria antitoxic titre in maternal blood and placental fluid.

Conclusions. 1. The fluid obtained by squeezing the human placenta has the same diphtheria antitoxic titre as does the serum of the circulating blood of the mother drawn at the time of expulsion of the placenta. 2. This fluid is a mixture of maternal and fetal blood and tissue fluid, and possibly also a slight amount of amniotic fluid. 3. The diphtheria antitoxin titre of the placental blood, the circulating blood of the mother, and the placental tissue fluid are alike in most cases. 4. The antibody content of the placenta is probably entirely the result of transplacental transmission of the immune substance from mother to placenta, to fetus, and is probably passive in nature. 5. Since the globulin fraction carries with it both the diphtheria antitoxin and the measles antibody, it is suggested that this fluid be used in measles prophylaxis. 6. If the globulin of pooled placentas is to be used in measles prophylaxis, its dosage may be calculated by comparing its diphtheria antitoxic titre with that of the pooled placental fluid, and thus the necessity of obtaining maternal blood is obviated.

8096 C

Effects of Heavy Water on Mammalian Metabolism.

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Heavy water has hitherto not been subjected to serious pharmacological study in mammals; indeed it has been uncertain whether such activity exists to any significant extent. From its unusual physical characteristics, however, and its effects upon the behavior of lower forms of life (Urey,[1, 2] Barnes[3]) depression of function has been generally predicted in mammals. In particular, Barnes[4] has observed, for example, decrease in the rate of activity of the con-

[4] Karelitz, S., Greenwald, C. K., and Klein, A. J., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1359.

[1] Urey, Harold C., Cold Spring Harbor Symposia on Quantitative Biology, 1934, **2**, 47.

[2] Urey, H. C., and Teal, G. K., *Rev. Mod. Physics*, 1935, **7**, 34.

[3] Barnes, T. Cunliffe, and Jahn, Theo. L., *Quart. Rev. Biol.*, 1934, **9**, 292.

[4] Barnes, T. Cunliffe, and Gaw, H. Z., *J. Am. Chem. Soc.*, 1935, **57**, 590.