

that this patient, who was first observed late in October, the seventh lunar month of her pregnancy, was just entering the stage of gestation during which the fetus gains excessively in weight. This is particularly well shown by the curves on fetal weight by Donaldson,¹ Streeter,⁵ and others.⁶ It is also during this time that the fetus stores considerable glycogen. Further, from the seventh month, according to Michel,⁷ the fat content of the fetus rises from about 2 per cent to 12 per cent at term. It is well known that the human fetus *in utero* obtains its nutrition chiefly through carbohydrates. There is no definite evidence that fat in any form passes the placental barrier. Therefore, carbohydrates not only furnish the greatest energy to the fetus, but they are used for the storage of glycogen in the fetus as well as being the chief source, if not the only source, from which the fat of the fetus is derived. It will be noted that the last two determinations do not show this marked drop. This, perhaps, suggests that the fetus is now adjusting its metabolism in such a way as to meet the demands of extrauterine life.

With these facts before us one can readily understand how these drops in blood sugar can occur in face of the already existing glycogen depletion as the result of hyperthyroidism and the additional burden of late pregnancy.

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The protective action of normal serum against placental
extract in vitro.

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In October, 1924, we presented a paper¹ confirming the work of Obata.² Obata reported that if normal serum is incubated

⁵ Streeter, G., Carnegie Inst. of Washington, 1920, xi, Pub. 145.

⁶ Rowley, W., *Am. J. Obst. and Gyn.*, 1923, xxiii.

⁷ Michel, *L'Obstetrique*, 1900, v, 252.

¹ Dieckmann, W. J., *Proc. Washington University Med. Soc.*, Oct., 1924.

² Obata, J., *J. Immunol.*, 1919, iv, 3.

with a saline extract of fresh placenta, the latter is no longer toxic to mice if injected intravenously; but that the serum of eclamptic patients obtained during a convulsion or a few minutes thereafter, does not possess this neutralizing power. After the convulsions have ceased, or very early in the puerperium, their sera have regained the full neutralizing power.

Dr. Leo Loeb suggested that we carry out similar work with placental extract *in vitro*. This suggestion is the basis on which the present work was carried out. It was noted by Dold³ and others⁴ that serum would neutralize the toxic action of tissue extracts. Loeb, Fleisher and Tuttle⁵ reported on the interaction between blood serum and tissue extract *in vitro* and found that the tissues contain constituents which can combine with a substance in the blood serum and thus lead to the production of a substance inhibiting the coagulation of the blood. Mills^{6, 7} obtained from lung extracts a protein called by him "tissue fibrinogen", which had marked coagulation properties. On adding serum to it and then both to the plasma, he obtained the initial marked decrease in clotting time, but on incubating them he found no increase. We found that we could not neutralize lung extract just as we did placental extract. His failure was due, we think, to an insufficient amount of serum. Furthermore, we were able to precipitate the active substance from placental extract with the method described by Mills for tissue fibrinogen. The clinical symptoms and postmortem findings after lethal doses of lung and placental extract are identical. Basing our opinion on Obata's work, we had, at the previous presentation, stated that the reaction was specific, but the above work demonstrates that the reaction is a general one.

The following table represents the optimum amounts of each substance as determined by us. We found that citrate plasma gave sharper end points than oxalate or fluoride. Determinations were all made at room temperature and with each unknown serum, a known normal serum was used as control.

Enough placental extract was used to cause complete clotting in 1 minute or less. Usually 0.1 cc. was sufficient.

³ Dold, H., *Zeit. f. Immunität.*, 1911, x, 53.

⁴ Dold, H., and Ogata, S., *Zeit. f. Immunität.*, 1912, xiii, 667.

⁵ Loeb, L., Fleisher, W. S., and Tuttle, S., *J. Biol. Chem.*, 1922, li, 461.

⁶ Mills, C. A., *J. Biol. Chem.*, 1921, xlv, 135.

⁷ Mills, C. A., and Matthews, S., *Am. J. Physiol.*, 1922, lx, 193.

	Control	Effect of extract	Serum and ex-tract not incub.	Serum and ex-tract inc. 2 hrs.
Citrate plasma	0.2 ml	0.2 ml	0.2 ml	0.2 ml
2 per cent CaCl ₂	0.2	0.2	0.2	0.2
Normal saline sol.	0.6	0.5	0.3	0.3
Placental extract		0.1	0.1	0.1
Serum			0.2	0.2
Total volume	1 ml.	1 ml.	1 ml.	1 ml.
Min. and max. clotting time	4-8 min.	45-90 sec.	10-50 sec.	3-8 min.
Ave. clotting time	6 min.	1 min.	30 sec.	4 min.

We found that sera from normal male or female, or from pregnant, parturient, or puerperal women had the power to increase the clotting time if incubated with placental extract. To date, we have had sera from four eclamptics. Two were on our own service and did not neutralize the extract. Two were from other hospitals. One, obtained by me, also did not neutralize. The other had normal detoxifying power. With reference to this sera, my information is that it was taken after the convulsion, but I do not know the interval which elapsed. Furthermore, the patient had only one convulsion and I do not know if the toxemia was a true eclampsia.

Summary: We believe that if normal serum and tissue extract are incubated together for one to two hours and then added to citrate plasma, the clotting time will be decidedly longer than if added immediately; but that eclamptic sera (although our series is small) if taken at the optimum time, will not increase the clotting time, thus indicating that the blood of eclamptic patients either is lacking or does not contain the usual amounts of certain substances always present in normal sera.*

* I wish to acknowledge the assistance of Mr. S. C. Roth in working out the details of the method.