is not heat labile. However, when these same preparations are treated with crystalline papain all of their activity becomes heat labile.

Although pink cobalamin protein(8) stimulated liver homogenates to combine with Vit. B_{12}, receptor proteins purified by ammonium sulfate fractionation were not stimulated by this curious Vit. B_{12} containing protein. This unexplained phenomenon supports the view that stimulation of purified receptor protein by IFC is a function of its intrinsic factor content. More extensive studies are needed to clarify this point.

A comparison of receptor proteins from serum and liver (homogenates), provides evidence that intrinsic factor may be absorbed into the blood stream of the rat from the intestine. Although other explanations are not precluded, the most plausible explanation of the data shown in Fig. 3 is that rat serum contains a material that acts like IF in the system under investigation. Also, the data presented extend and support a previously stated hypothesis(9,2) that intrinsic factor is absorbed into the blood stream where it acts not only to conserve the dietary Vit. B_{12} by enhancing its combination with receptor proteins of serum but also facilitates absorption of Vit. B_{12} by peripheral tissues by causing it to combine wtih the receptor proteins of the various tissues.

Summary. Data have been presented which show that intrinsic factor containing materials will stimulate receptor proteins to combine Vit. B_{12} of tissues as well as serum. Further, the receptor proteins of tissues are located intracellularly in the microsome and soluble protein fraction of liver homogenates. The evidence suggests that intrinsic factor aids in absorption of Vit. B_{12} by stimulating the intracellular receptor proteins to combine with Vit. B_{12}.

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Competitive Transfer of Sorbose and Glucose in Placenta of Rabbit. (23903)

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Previous studies on the placental transfer of simple sugars have suggested that an active transport mechanism is involved rather than one of simple diffusion(1-5). A differential permeability of the placenta toward the aldo- and keto-hexoses, respectively, has been noted in all species studied (sheep, guinea pig, rat, rabbit, monkey). In at least one of these (monkey) a competitive inhibition of fructose from mother to fetus by excess of glucose in maternal circulation has been suggested(4).

The purpose of the present study was to investigate the possibility of a competitive inhibition of sorbose transfer by glucose in the placenta of the rabbit at term. The findings indicate a significant depression of the "permeability constant" for sorbose in the presence of excess glucose.

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Materials and methods. Rabbits in the last 5 days of pregnancy, *i.e.* from about 25th to 29th day, were used. The experimental procedure has been fully described elsewhere(5) and will be only briefly outlined here. Animals were anesthetized with sodium nembutal and the abdomen opened. Maternal and fetal blood samples were obtained at serial intervals during intravenous infusion of l-sorbose alone or l-sorbose combined with d(+) glucose. A constant speed motor-driven syringe delivering 1.6 ml/minute was used. The jugular vein was cannulated with a polyethylene tube. Since serial blood samples in a single fetus are technically difficult to obtain in the rabbit, whole fetuses were removed at times selected. Two fetuses were removed at a time, each acting as a control for the other. The method gives reproducible results, and its validity has been discussed(5). The type of anesthesia also was shown to be without deleterious effect on permeability of the placenta to the simple sugars. An arbitrary "permeability coefficient," as originally devised by Karvonen and Raïhä(3), was calculated after graphic recording of the maternal and fetal blood sugar levels over the time interval selected. It was calculated as:

$$K = \frac{\text{Rise in fetal blood sugar in mg \%}}{\text{Time in min.} \times \text{avg maternal-fetal gradient in mg \%}}$$

and is thus expressed as the rise in fetal blood sugar level/minute/mg % of gradient from maternal to fetal blood. Total reducing substance was estimated colorimetrically by the method of Somogyi(6). Sorbose was estimated colorimetrically by modified procedure for fructose(7). The latter method gave adequate reproducibility in the presence of large excess of glucose. Glucose was observed to give "apparent sorbose" values of 1 to 3% so that corrections were made by use of duplicate blanks. In any event, the direction of the error due to glucose was in favor of increased placental transfer of sorbose rather than the reverse.

TABLE I. Permeability Coefficient (K) for Sorbose Alone in the Rabbit Placenta Near Term.

% sorbose infused	Infusion interval in min.	K
10	11–46	.0095
10	13–44	.0099
15	14–40	.0115
15	10–39	.0121
15	16–37	.0116
20	14–41	.0082
40	15–39	.0119

Mean coef. = .0110. Stand. dev. = ± .0017.

TABLE II. Permeability Coefficient (K) for Sorbose in Presence of Excess Glucose in Rabbit Placenta Near Term.

% sorbose infused	Infusion interval in min.	K
15	12–36	.0029
15	15–39	.0044
15	16–41	.0046
15	15–48	.0041

Mean coef. = .0040. Stand. dev. = ± .00076.

Results. Infusion of l-sorbose alone. The permeability coefficient K was first calculated for sorbose alone (Table I). From these figures it is apparent that no significant variation in value of K takes place with increasing concentrations of sorbose in the infusion mixture.

Infusion of d(+) glucose and l-sorbose. An attempt was made to saturate the placental transfer mechanism by preliminary infusion of 50% aqueous solution of glucose. By this means a maternal blood glucose level of about 2000 mg % was achieved. The placental transfer of sorbose was then determined, as described above, by a continued infusion of 15% sorbose combined with 15% glucose. It was found necessary to add this amount of glucose to the sorbose solution to maintain the maternal glucose at the aforementioned level. The results are shown in Table II. The difference of means for sorbose alone and for sorbose in the presence of glucose is significant ($p = < .001$) and indicates a depression of permeability coefficient for sorbose by glucose.

Discussion. The results indicate that there is a significant inhibition of sorbose transfer from mother to fetus in the presence of an elevated maternal blood glucose. Such an inhibition could reasonably be expected if glucose and sorbose share a common mechanism during their passage across the rabbit placenta. It is possible that a "carrier" mechanism might be involved, as suggested on the basis of kinetic data in sheep by Widdas(1),

although no evidence is available as to its nature. That it is impossible to saturate the placental transport system even by elevating maternal blood glucose to unphysiological levels, often fatal, has been observed(5). Thus, a complete inhibition of sorbose transfer could not be obtained by raising the level of maternal glucose. It is possible, of course, that more than one mechanism may be involved. The elucidation of the character of the placental mechanism for transport of sugar remains to be accomplished.

Summary. Sorbose alone and with glucose have been infused intravenously into pregnant rabbits near term, and permeability coefficients for sorbose under these 2 conditions have been calculated. It has been shown that there is a significant depression of permeability coefficient for sorbose when the maternal blood is overloaded with glucose. The results have been interpreted as indicating a competitive inhibition by glucose of sorbose transfer across the placenta.

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Role of Common Ions in Production of Increased Oxygen Consumption by Ouabain.* (23904)

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Since Ringer published his classical papers (1) it has become increasingly apparent that the common ions potassium and calcium alter the heart beat. More recent work(2-5) indicates that the toxic effects of digitalis may be altered by potassium and calcium, and the reports of Holland, Greig, and Dunn(6) and of Vick and Kahn(7) show that digitalis may enhance loss of potassium from the heart. Because of the importance of these common ions to the heart beat and to some actions of digitalis, it was thought desirable to investigate their relation to another effect of digitalis, namely increased oxygen consumption.

Methods. Hearts from embryos of chicken eggs incubated 5 days were dissected into Locke solution of the following composition: NaCl 9.00 g; KCl 0.42 g; $CaCl_2 \cdot 2H_2O$ 0.32 g; $NaHCO_3$ 0.20 g; dextrose 1 g; the solution was adjusted to pH 7.2-7.4. The hearts were then placed in a cartesian diver and experiments were performed as previously described (8,9). After a 10-minute period the same solution (for control experiments) or ouabain was added and observations on beat and measurement of oxygen consumption continued for 30 minutes. Similar experiments were carried out using each of following solutions: Locke without potassium; Locke with 4 × potassium; Locke without calcium; Locke with 4 × calcium (sodium bicarbonate was omitted). The hearts were kept in these solutions for about 30 minutes before observations and measurements were started. The results of each experiment were graphed, and a master graph for each group of experiments was constructed by averaging and graphing oxygen consumption at each even-numbered minute. Control experiments(8), recently supplemented by others, indicate that oxygen consumption during the entire 40-minute period is linear; therefore a curve of control oxygen consumption of each experiment was obtained by extending the curve of oxygen consumption during the 10-minute control period by dotted

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