contents. The other outstanding feature of the picture was the effectiveness of the beta lactose in producing a more acid condition throughout the whole length of the gut.

Although in general the reaction of the contents of the rabbit's intestine is more acid than that of the rat, the differences in the large bowel between the dextrose and alpha lactose are of approximately the same order of magnitude as those found in previous work. Unfortunately a strict analogy cannot be drawn because in the work with rats dextrose was not added to the control diet, but other workers have failed to find any change under its influence. In the case of the beta lactose, however, the differences exceed those found with rats. This is apparently due to the greater effectiveness of the beta form of the sugar. It may be that its greater solubility makes it more available for bacterial action.

The unique behavior of lactose in passing through the upper intestine has usually been ascribed to its comparatively low solubility. It may, however, be partly due to the relatively small amounts of lactase in the intestines of mature animals, particularly the rabbit. The failure to split lactose into the constituent monosaccharides perhaps hinders its absorption and allows it to reach the lower section of the bowel to become available there for bacterial consumption.

We are indebted to the Borden Company for the lactose used in this work.

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Cutaneous Absorption of Insulin.

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In a recent article on the cutaneous absorption of insulin Bruger and Flexner[1] came to the conclusion that "the absorption of insulin by the skin of rabbits is dependent upon the integrity of the integument. The intact skin shows little or no absorption, whereas a recently abraded skin, such as produced by shaving permits the absorption of an appreciable amount of insulin."

While there can be no doubt that actual abrasion of the skin permits absorption of insulin, there is evidence that absorption may occur under conditions where no abrasion can be detected or even

[1] Bruger, M., and Flexner, J., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 429.

suspected. In a series of some 250 individual experiments carried out during the past year, we have excellent evidence that the absorption of insulin through the skin of rabbits and of certain diabetics cannot be explained on the assumption that the procedures employed produce actual abrasions of the skin through which absorption of insulin occurred.

In all of the following observations the method employed in applying the insulin was identical. Glycerine was rubbed gently into the skin and 15 minutes later, insulin dissolved in a solution of diethylene glycol monoethyl ether was applied. The preliminary treatment of the skin, however, differed as will be indicated in the different experiments.

If the simple shaving of the rabbit's skin produced abrasions sufficient to permit insulin absorption, we should expect a marked fall in blood sugar almost uniformly if the application of insulin follows the shaving immediately. The following typical observation shows that this is not the case.

Rabbit No. 46. Insulin applied to abdomen 15 minutes after shaving.

Time	Blood Sugar	Remarks
9:45 A.M.	105	Insulin 25 units applied at 10:00 A.M.
11:45 "	108	
1:25 P.M.	114	
3:00 "	115	

Similar results were obtained in 28 experiments.

In the following group of experiments the rabbits were shaved 24 hours before the application of glycerine and insulin. We did not carry out any experiments as did Bruger and Flexner in which 6 and 7 days elapsed between the time of shaving and that of applying insulin, since our animals during this period developed a new growth of hair which we considered sufficient to interfere with the absorption of insulin.

Rabbit No. 38.

Time	Blood Sugar	Remarks
9:45 A.M.	134	10 units insulin applied 10:00 A.M.
11:35 "	59	
1:25 P.M.	103	
2:50 "	121	

Rabbit No. 49.

Time	Blood Sugar	Remarks
9:55 A.M.	175	10 units insulin applied 10:00 A.M.
11:50 "	67	
1:35 P.M.	104	
3:10 "	103	

Ten similar results were obtained.

Hermann[2] has laid great stress upon alkalinization of the skin before the application of insulin. In 5 experiments on rabbits, the skin of the abdomen, which had been shaved 24 and 48 hours before, was treated with a 1% solution of NaOH which was washed off in 5 minutes and then glycerin and the insulin solution applied. In all of these experiments a marked fall in blood sugar occurred.

The observations upon diabetic patients show even more strongly that abrasion of the skin is not the determining factor in insulin absorption from the skin. Thirty-four different observations were carried out. The insulin was applied to the anterior aspect of the thigh after preliminary treatment with glycerin. The area was not shaved.

In this group of 34 observations, 16 showed no change, 3 showed a fall of 20 mg., 6 a fall of 30 mg., 2 a fall of 50 mg., one a fall of 60 mg., 3 a fall of 70 mg., one a fall of 80 mg., and 2 a fall of 110 mg. The dose of insulin employed was 25 units and 50 units. The 2 following protocols are examples of observations where a marked fall in blood sugar occurred.

M.P. age 23 severe diabetes mellitus.

7/19/37	fasting blood sugar 282	7/11/37	307
	25 units of insulin applied after drawing blood		
	Blood sugar after 1 hr. 250		280
	" " " 2 " 210		250
	" " " 3 " 178		200
	" " " 4 "		204

A.C. age 40 severe diabetes mellitus.

5/18/37	25 units applied after drawing blood	
	Blood sugar after 1 hr. 210	
	" " " 2 " 195	
	" " " 3 " 189	

The fall in blood sugar in these patients could not have been caused by skin abrasions due to shaving since this procedure was not carried out. In these observations it should be stressed that in only slightly more than 50% was any definite fall in blood sugar observed. Also that in less than one-third was the fall 50 mg. or more. It was further observed that the same patient might on one day show a fall of 50 mg. or more and on a succeeding day prove quite refractory.

Conclusions. Cutaneous absorption of insulin occurs in rabbits and in patients independent of abrasions produced on the skin. This absorption is, however, very inconstant.

[2] Hermann, Siegwart, *Arch. f. exp. Path. u. Pharm.*, 1935, **179**, 529.