

vented the growth of the Gram-positive bacteria, *S. aureus* and *B. subtilis*, in a dilution of 1/100,000. Under similar conditions a 1/20,000 dilution of the chemical prevented the growth of *E. coli*.

The mixture of alkyl-dimethyl-benzyl ammonium chlorides investigated possesses high bactericidal efficacy, and has compared favorably with some of the best antiseptics in use.

9006 C

Integrity of the Skin in Relation to Cutaneous Absorption of Insulin.*

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Telfer¹ reported that insulin in the form of an ointment when rubbed into the skin of rabbits produced a fall in blood sugar. This work stimulated further investigations along similar lines and several reports from a number of workers² have appeared in the literature; however, the results on insulin inunction have by no means been uniform.

Of particular interest is a recent report by Major² who showed that a solution of insulin mixed with diethylene glycol monoethyl ether when rubbed into the skin of rabbits produced a marked fall in the blood sugar. The experimental procedure adopted by Major was as follows: the skin over the abdomen was shaved and several drops of glycerine first rubbed in over the shaved area. Ten to 15 minutes later, 25 units of insulin was applied. The blood sugar diminished markedly, and in a number of animals hypoglycemic convulsions ensued 3 to 4 hours later. Major further observed that in the course of repeated experiments on the same rabbits, some animals apparently became refractory after the insulin had been applied to the skin of the abdomen 3 or 4 times. He further stated that such animals were found not to be refractory if the hair was shaved off the back or thigh and the insulin applied on this fresh area.

Our frankly negative results on insulin inunction in humans (unreported studies) led us to believe that the positive results obtained

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¹ Telfer, S. V., *Brit. Med. J.*, 1923, **1**, 715.

² Major, R. H., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 775.

by Major may have depended in good measure, if not entirely, on the degree of the integrity of the skin. In other words, we felt that the application of insulin to an abraded (shaved) skin would permit the absorption of insulin; on the other hand, insulin applied to a depilated area several days after the shaving was carried out would not be absorbed to any appreciable extent since the previously abraded area had been given time to heal. Thus, we felt that true refractoriness of the skin to the dermal application of insulin, as contended by Major, may not actually exist.

Tables I, II and III prove our contention. In those rabbits in which a small area of the skin was first shaved and healing of the abrasions permitted for 5 to 7 days, the application of 50 units of insulin in diethylene glycol monoethyl ether failed to produce any effect on the blood sugar (Table I). Again, in those rabbits in

TABLE I.

Exp. No.	Rabbit No.	Area shaved	Days between shaving and insulin application	Time	Blood sugar, mg. %	Remarks
1	1	right back	5	10:22	124	glycerine applied 50 units insulin
				10:33-10:38		
				10:38-10:42		
				11:12	122	
				11:42	115	
				12:42	123	
				1:42	132	
2:42	125					
2	2	left back	6	11:17	114	glycerine applied 50 units insulin
				11:38-11:43		
				11:43-11:48		
				12:18	121	
				12:48	126	
				1:48	152	
				2:48	150	
3:48	150					
3	2	abdomen	5	10:10	96	glycerine applied 50 units insulin
				10:18-10:23		
				10:23-10:28		
				10:58	144	
				11:28	125	
				12:28	132	
				1:28	134	
2:28	125					
4	3	left back	7	10:39	139	glycerine applied 50 units insulin
				10:44-10:49		
				10:49-10:54		
				11:24	138	
				11:54	133	
				12:54	120	
				1:54	112	
2:54	115					

TABLE II.

Exp. No.	Rabbit No.	Area shaved	Minutes between shaving and insulin application	Time	Blood sugar, mg. %	Remarks
5	1	left back	15	11:14	99	
				11:28-11:33		glycerine applied
				11:33-11:38		50 units insulin
				12:08	66	
				12:38	53	weak, crawling
			1:38	36	convulsions, opisthotonus and death.	
6	2	right back	15	10:28	109	
				10:43-10:48		glycerine applied
				10:48-10:53		50 units insulin
				11:23	74	
				11:53	66	
				12:53	52	
			1:53	46	slight tremors	
			2:53	76		
7	4	left back	20	10:42	119	
				10:55-11:00		glycerine applied
				11:00-11:05		50 units insulin
				11:35	93	
				12:05	69	
				1:05	70	
			2:05	72		
			3:05	86		

TABLE III.

Exp. No.	Rabbit No.	Area shaved	Interim between shaving and insulin application	Time	Blood sugar, mg. %	Remarks
8	3	abdomen	7 days	10:15	130	
				10:32-10:37		glycerine applied
				10:37-10:42		50 units insulin
				11:12	188	
				11:42	183	
				12:42	130	
				1:42	120	
			2:42	143		
9	3	abdomen reshaved	15 min.	10:44	146	
				10:55-11:00		glycerine applied
				11:00-11:05		50 units insulin
				11:35	115	
				12:05	57	
				1:05	31	Convulsions. 8 cc. 50% glucose intravenously.
			2:40	73		

which an area of the skin was shaved and the insulin applied 15 to 20 minutes later, a distinct fall in the blood sugar occurred (Table

II). Of interest are the experiments on Rabbit 3 in Table III. On October 20 an area over the abdomen was shaved. Seven days later the application of 50 units of insulin to this area failed to decrease the blood sugar (in fact, there was a temporary rise in the blood sugar probably due to the excitement manifested by this animal). On the following day, this same abdominal area, upon which the previous application of insulin failed to produce any effect, was reshaved and 50 units of insulin rubbed in approximately 15 minutes later. There was a marked fall in the blood sugar requiring the intravenous administration of dextrose to overcome the hypoglycemic convulsions.

Conclusions. 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.

We are indebted to the Eli Lilly Company for a generous supply of powdered insulin.

9007 C

Fluctuations in Type 2 Pneumococcus Antibody During the Menstrual Cycle.*

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In the course of measuring the duration of the protective power of the sera of a number of persons who had been fed pneumococcal vaccine, fluctuating values for Type 2 were observed in the blood of 2 women. In the case of A.E.T., No. 10,† 1 cc. serum from blood drawn at 2 different times early in the investigation protected mice against approximately 500 fatal doses. Seven and a half months later the serum protected against only minimal numbers of pneumococci (*ca.* 5 fatal doses). However, after a lapse of 27½ months more the blood again protected well (*ca.* 5000 fatal doses per cc. See Table, 1/28/35). The other person's (L.P., No. 18†) blood possessed no protective power when first examined, then acquired

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† The initials and the numbers are those used in the report, "Oral Immunization of Humans against the Pneumococcus." *J. Immunol.*, 1934, **27**, 307.