differed from the findings in man where experience with an A-prime infection caused rises in anti-Oti antibody. Using the more specific animal sera less evidence of cross inhibition between the Oti and other strains was obtained than between the A-prime strains of Rhodes and FMl. The Oti strain did not crossreact with the antisera to the PR8, Type A, strain. It should be pointed out, however, that anti-Oti serum gave as much inhibition of the Rhodes strain as anti-Rhodes serum did with the FMl strain. Further, there is considerable variation in the amount of cross reaction obtainable with strains of the A-prime group. In any event, it appears that this strain behaves like a type A strain and certainly does not have the characteristics of the swine strains described by Shope.[10] These data, while not decisive, taken together with the results obtained with human sera seem to warrant the inclusion of the Oti strain with the A-prime groups of 1947.

Discussion. The history of the Oti strain seems sufficiently accurate to accept the fact that it was originally isolated from infected swine in Korea where swine influenza is recognized largely as a low grade endemic disease and differs from the sharp epidemics described in the United States. The data presented in this paper call attention to the definite antigenic resemblance of this swine strain, isolated in 1939, to strains such as the A-prime group first prominently encountered in human disease in 1947. It may be that some of the peculiarities of that group of strains are related to their earlier adaptation in the animal host. If subsequent studies should increase the possibility that these infections of man arose from a swine host, it would represent a reversal of the sequence of host infection from that suggested earlier, by Koen[9] and Shope[10] for swine influenza recognized in the United States. On the other hand, the virus may have been of human origin, fortuitously detected in swine.

Conclusions. 1. A strain of swine influenza virus (Oti), isolated in 1939, has been reinvestigated by serological means and found antigenically to resemble some members of the human A-prime influenza virus group.

2. Significant increases in the levels of antibody against this swine strain of influenza virus were detected in the convalescent blood specimens of children who had had experience during the A-prime influenza epidemic of early 1947. High titers of antibody were also found against the current A-prime strains.

3. Adults involved in the same epidemic also showed significant antibody increases against the same swine strain and the current A-prime and Type A strains.

4. Results of cross hemagglutination inhibition tests with specific ferret anti-sera supported the observations made from the serological tests with human sera.

5. The relationship of this swine strain to members of the A-prime group has been discussed.

[9] Dorset, M., McBryde, C. N., and Niles, W. B., *J. Am. Vet. Assn.*, 1922-23, **62**, 162.

[10] Shope, R. E., *Harvey Lectures*, 1935-36, **31**, 183.

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17140. The Hyperglycemic Action of Some Analogs of Epinephrine

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The preparation in the chemical laboratories of this Institute of a series of compounds to be studied for bronchodilator action has made available to us a group of epinephrine analogs, all of which have this action to a desirable degree. They also lack some of the

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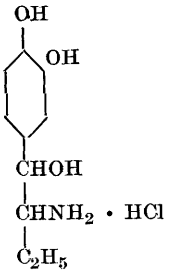
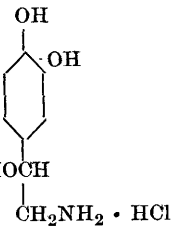
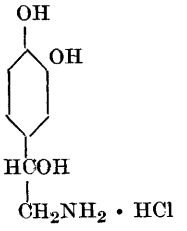
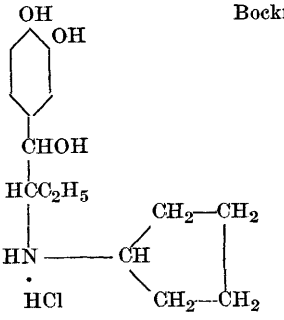
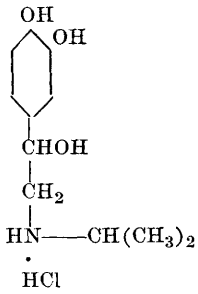
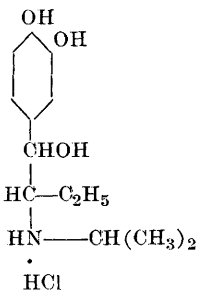
undesirable side effects of epinephrine, notably the abrupt pressor action.[1-3] The marked hyperglycemic action of epinephrine would also constitute an undesirable side effect, particularly if it were to be used for the treatment of bronchial asthma in diabetics. It was therefore of interest to determine whether these compounds have appreciable hyperglycemic actions, and the results of the study are included in this report. The recent resolution of arterenol (dl-norepinephrine) by Tullar[4] has provided the opportunity to study the pharmacology[5] and the hyperglycemic effects of the two optical isomers of this compound also. l-Arterenol is of particular interest because of its possible identity with Sympathin E.[6-8] The compounds studied and their structural formulae are given below:

Compound No.*	Chemical or trade name	Structural formula	Reference to method of preparation
Win 162	Butanefrine† hydrochloride (dl-ethylnorepinephrine hydrochloride)		Suter and Ruddy[9]
Win 273-6	l-Arterenol hydrochloride		Tullar[4]
Win 273-5	d-Arterenol hydrochloride		Tullar[4]
Win 515	dl-l-(3,4-dihydroxyphenyl)-2-cyclopentylaminobutanol hydrochloride		Boekmühl *et al.*[10]

Win 516-2	Isuprel† hydrochloride [dl-l-(3,4-dihydroxyphenyl)-2-isopropylaminoethanol-hydrochloride]		Scheuing and Thomä[11]
Win 3046	dl-l-(3,4-dihydroxyphenyl)-2-isopropylamino-1-butanol hydrochloride		Boekmühl *et al.*[10]

* Laboratory system of classification.
† Registered trade-marked names of Winthrop-Stearns Inc.

Experimental methods. The compounds to be tested were injected subcutaneously into healthy adult rabbits (wt. 1.5-4 kg), following an 18 hr fast. They were administered in a volume of 1 cc of 0.9% NaCl/kg except in cases where solubility limitations required a larger volume. Control animals received the saline injection only. Blood samples were taken from the ear vein and were analyzed for glucose by the Folin-Malmros method,[12] or by a slight modification† of the Schales and Schales method.[13] Samples were usually taken at 1, 2, 3, and 5 hours after the injection. Analyses were also made before the injection, and any animal which gave a fasting blood sugar level of 130 mg% or more was rejected from that test. The results are presented in Table I. For purposes of simplification of the Table, only the peak rise of blood sugar, the extreme range of the rises in the several animals, and the approximate time of

[1] Lands, A. M., Nash, V. L., Dertinger, B. L., Granger, H. R., and McCarthy, H. M., *J. Pharm. and Exp. Therap.*, 1948, **92**, 369.

[2] Tainter, M. L., Cameron, W. M., Whitsell, L. J., and Hartman, M. M., *ibid.*, 1944, **81**, 269.

[3] Lands, A. M., Siegmund, O., and Ananenko, E., *Fed. Proc.*, 1949, **8**, 312.

[4] Tullar, B. F., *J.A.C.S.*, 1948, **70**, 2067.

[5] Ludueña, F. P., Ananenko, E., Siegmund, O., and Miller, L. C., *J. Pharm. and Exp. Therap.*, 1949, **95**, 155.

[6] Gaddum, J. H., and Goodwin, L. G., *J. Physiol.*, 1947, **105**, 357.

[7] West, G. B., *Pharm. J.*, 1947, **158**, 6.

[8] von Euler, U. S., *Science*, 1948, **107**, 422.

[9] Suter, C. M., and Ruddy, A. W., *J. A. C. S.*, 1944, **66**, 747.

[10] Bockmühl, M., Ehrhart, G., and Stein, L., U. S. Patent No. 2,083,001.

[11] Scheuing, G., and Thomä, O., U. S. Patent No. 2,308,232.

[12] Folin, O., and Malmros, H., *J. Biol. Chem.*, 1929, **83**, 115; Horvath, S. M., and Knehr, C. A., *ibid.*, 1941, **140**, 869.

† The authors state simply that a Folin-Wu filtrate is to be used. The filtrate was therefore prepared as follows: to 0.2 cc blood add 3.8 cc water followed by 3 cc of 0.67% sodium tungstate and 3 cc of 0.045 N. sulfuric acid. Centrifuge, and take 5 cc for analysis. If the blood sugar is found to exceed 300 mg %, the analysis is repeated on 2 cc of filtrate.

[13] Schales, O., and Schales, S. S., *Arch. Biochem.*, 1945, **8**, 285.

TABLE I.
Hyperglycemic Action of Some Epinephrine Analogs in the Rabbit.

Compound name or No.	Dose,* mg/kg	No. of rabbits	Rise in blood sugar, mg% Avg	Range	Time of peak rise, hr after inj.
l-epinephrine	0.15	3	106	18-157	3
,,	0.3	3	207	200-212	3
,,	0.5	3	495	462-552	2,4§
Win 162	1	3	11	7-14	2†
,,	2	3	20	14-31	2
,,	5	3	50	41-65	2
,,	10	6	76	56-96	2
l-arterenol	0.25	2	40	23-57	1
,,	0.5	4	35	18-44	2§
,,	1	3	96	53-149	3
,,	2	6	176	52-230	2
d-arterenol	2	4	17	5-31	2
,,	10	8	47	0-86	2-3‡
Win 515	10	4	61	43-106	1-2‡
,,	20	6	83	25-145	1-3‡
Isuprel	10	10	18	0-37	1-4‡§
,,	25	6	28	0-45	1§
Win 3046	5	5	52	20-85	1
,,	10	5	84	40-140	1-2‡
,,	20	6	71	36-98	1
Controls	0	8	2	—2-10	—

* All doses were calculated in terms of the free base.

† After it was established preliminarily that the peak response was at 2 hours after injection the subsequent observations were made only at that time.

‡ In these cases about as many animals showed peak responses at one time as another.

§ No observation was made at 3 hours in these cases.

this average peak are recorded in the Table.

Conclusions. Of the several compounds tested, only l-arterenol has a hyperglycemic action of the same order as that of l-epinephrine. Its activity can be placed at about 1/8 of that of epinephrine, while the d-isomer has about 1/20 of the activity of the l-isomer. Sahyun[14] found that dl-arterenol, 1 mg/kg, produced an average rise in blood sugar of 78 mg% 3 hrs after subcutaneous injection in 7 rabbits. This is considerably more activity than would be calculated from our observations on the separate isomers. However, if one of his rabbits (No. 8, Table II) is eliminated from consideration, the average rise becomes only 61 mg%, and the discrepancy is much less. Of the other compounds studied, Isuprel is clearly the least active. The approximate hyperglycemic activity of the whole series of compounds, taking l-epinephrine as 100, is as follows (all figures given have been calculated in terms of the free base): l-arterenol, 12; Win 3046, 1.7; Butanefrine, 1.6; Win 515, 0.7; d-arterenol, 0.6; and Isuprel, 0.12.

[14] Sahyun, M., *Arch. Intern. Pharm.*, 1933, **45**, 285.

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