from two to three times as potent as eserine and HETP and many times as potent as DFP. However, since the early parts of the inactivation curves of cholinesterase by specific antiesterases are steep and differ in character (unpublished results), the comparative estimate of the potency of the anti-

TABLE 1

SENSITIVITY OF ACETYLCHOLINESTERASE TO VARIOUS ANTIESTERASES

	DFP	HETP	Eserine	TEP
	Molar concentrations of inhibitor required to produce a 50 per cent inhibition of cholinesterase activity			
Roach cord (*1*).....	3.0×10^{-6}	4.0×10^{-6}	1.0×10^{-8}	—
Human serum (*6*)..	5.0×10^{-7}	—	5.0×10^{-6}	—
Horse serum (*6*)....	1.3×10^{-8}	—	—	—
Cockroach serum (*3*).....	—	1.0×10^{-7}	—	—
Rat brain (*3*).....	6.3×10^{-8}	1.6×10^{-8}	—	—
Dog (*4, 5, 7*).....	5.0×10^{-9}	4.0×10^{-10}	9.5×10^{-11}	8.5×10^{-11}
	Molar concentrations of the inhibitor required to produce a 100 per cent inhibition of cholinesterase activity			
Rat serum (*3*).....	—	2.0×10^{-9}	—	—
Dog (*4, 5, 7*).....	7.5×10^{-8}	1.0×10^{-9}	7.9×10^{-10}	3.3×10^{-10}

esterases may differ, depending on whether the 50 or 100 per cent inactivation point is taken as the index of activity. (See Table 1, specifically with reference to HETP and eserine.)

The efficiency of TEP seems to be especially remarkable, since in the presence of a wide range of its concentrations as

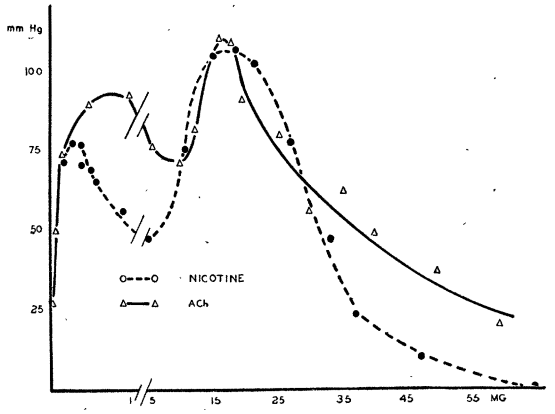

FIG. 3. Pressor response (ganglionic effect) in atropinized dogs to nicotine (0.1 mg./kg.) and acetylcholine (0.05 mg./kg.) (Abscissa—concentrations of eserine in mg./kg.; ordinate—pressor response in mm. of Hg of blood pressure.)

small a dose of ACh as 0.8γ/kg. is sufficient to elicit pressor responses. This figure compares favorably with that of Dale (*2*) of 2γ for the minimum amount of ACh necessary to stimulate on close intra-arterial injection the striated muscle of the frog, and with the minimal amounts previously estimated to be necessary to produce sympathetic ganglionic effects.

The second peak of the pressor response of ACh (Fig. 2), which occurs at considerable levels of TEP ranging from 15 to 20 mg./kg., is of particular interest. A similar peak occurs when the antiesterase used is eserine (Fig. 3; unpublished results). Also, the pressor effects of nicotine itself followed a double-peak curve with increasing amounts of eserine (Fig. 3). It is therefore tentatively suggested that the biphasic response to ACh elicited within a wide range of concentrations of different antiesterases is due to the effect of the latter on the sympathetic ganglia. The ganglia seem to be first depressed, and then, with higher concentrations of the antiesterases, rendered more responsive. Further research must determine whether this effect of the antiesterases on the ganglia is a direct one or related to the mechanism of the synaptic transmission.

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The Influence of Heredity on the Carotene Content of Corn[1]

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The extensive use of hybrid corn in recent years has emphasized the question of possible relationships between the heredity and nutritive content of corn and the possibility of producing hybrids of superior nutritive value. The early work of Hauge and Trost (*2*) pointed out that ordinary genetic factors controlled the vitamin A activity of dent corn, the genes responsible being the same as those governing development of the yellow endosperm. Recently Doty and associates (*1*) have reported that there is some indication that the amounts of the various amino acids in corn protein are related to the genetic constitution of corn hybrids, and that the physicochemical nature of the protein in the grain from two single cross hybrids was distinctly different. In general, however, information is lacking relative to the influence of the genetic constitution of corn on the nutritive value of the grain.

In the course of a comprehensive investigation dealing with this subject, crude carotene values were determined on the grain from all possible single cross combinations of 10 inbred lines of yellow dent corn, all of the same general maturity class and grown during the 1946 season. A 7 x 7 triple lattice design was used in the field experiment, thus providing for analysis three replicate samples of grain for each single cross. The field experiment was conducted near Chambersburg, Pennsylvania, the soil type and fertilizer treatment being the same on the three plots.

The corn was harvested at maturity, and the shelled corn was air-dried at room temperature for 10 days and stored in

[1] This investigation was supported by a grant from the Pennsylvania Farm Supply Cooperatives.

Authorized for publication as paper No. 1384 in the Journal Series of the Pennsylvania Agricultural Experiment Station.

air-tight containers at 0°C. until it was analyzed. Carotene estimations were made by the official A. O. A. C. method (*3*), modified by the use of Hyflo Supercel and magnesium oxide, 3:1, as the chromatographic adsorbent.

Seed was not available for the Iowa I205 x Ohio 28 cross; hence, the carotene value for this combination is missing from the data. The range of yields of the other single cross combinations tested was from 71 to 123 bushels/acre.

The average difference between the highest and lowest of the three carotene values for the individual single crosses was of the order of 17 per cent, the values given in Table 1 being

TABLE 1

CAROTENE CONTENT OF CORN

(mg./lb.—15.5 per cent moisture basis)

	Nebraska 6	Wisconsin 8	Illinois M14	Illinois A	Indiana WF9	Ohio 28	Wisconsin 32	Ohio 51A	Wisconsin 22	Iowa I205
Nebraska 6		1.91	1.64	1.50	1.41	1.30	1.48	1.09	1.08	.67
Wisconsin 8	1.91		1.68	1.27	1.27	1.17	1.31	1.01	.88	1.07
Illinois M14	1.64	1.68		1.26	1.23	1.03	.93	1.17	.84	.70
Illinois A	1.50	1.27	1.26		.97	.95	.95	.93	.79	.66
Indiana WF9	1.41	1.27	1.23	.97		.93	.98	.79	.74	.62
Ohio 28	1.30	1.17	1.03	.95	.93		.88	.66	.72	—
Wisconsin 32	1.48	1.31	.93	.95	.98	.88		.79	.73	.58
Ohio 51A	1.09	1.01	1.17	.93	.79	.66	.79		.60	.53
Wisconsin 22	1.08	.88	.84	.79	.74	.72	.73	.60		.69
Iowa I205	.67	1.07	.70	.66	.62	—	.58	.53	.69	
Inbred line averages	1.34	1.29	1.16	1.03	.99	.96	.96	.84	.79	.69

Least significant difference between single crosses = .19 mg.

the means for three duplicate estimations. These data show that there are striking significant differences between the carotene contents of some of the inbred lines, irrespective of the lines with which they were crossed. On the average, combination of Nebraska 6 and Wisconsin 8 with other inbreds produced corn with the highest carotene content, while all crosses employing Iowa I205 were relatively low. The combination of Nebraska 6 with Wisconsin 8 produced corn with the highest carotene value of all the crosses.

The superior value of yellow corn over white corn as a source of carotene has been recognized for many years. However, little attention has been paid to the fact that different strains of yellow corn may vary greatly in carotene content among themselves. The results presented here show that the genetic constitution of corn may be responsible, in large part, for its content of carotene, and that, all other conditions being the same, different strains of yellow corn may vary widely in carotene content. The results suggest further that, in the development of new corn hybrids, attention should be given to the content of important nutritive factors, among which carotene is but one. Further work along this line is now in progress.

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Enhancement of Penicillin Blood Levels Following Oral Administration of Caronamide

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Daily dosages of 5,000,000–40,000,000 units of penicillin were required with or without enhancing agents in treatment of the last 15 patients of a consecutive series of 150 cases of subacute bacterial endocarditis infected with nonhemolytic streptococci, including the resistant *Streptococcus* s.b.e. (*6*, *9*). The penicillin was administered by continuous venoclysis for a span of at least 8 weeks, which was made possible technically by the conjoint use of heparin in the treatment program. These 15 patients, most of whom were treatment failures with penicillin per se before being admitted to our Clinic, received a total of 66,000,000–4,000,000,000 units of penicillin, the average being 630,000,000. At times streptomycin was also included in the treatment program. Of these 15 refractory patients, 3 (20 per cent) were unequivocal treatment failures despite these massive dosages, and 12 (80 per cent) were salvaged and considered cured by all clinical and laboratory criteria.

Early in our experience with this type of patient, it was found necessary to resort to agents for enhancing penicillin blood levels, primarily to obtain therapeutic values and also to conserve limited supplies of penicillin. In our studies in connection with the treatment of a case of subacute bacterial endocarditis infected with *Veillonella gazogenes* (*10*), curative levels of penicillin were obtained only by means of incorporating in the treatment program large amounts of PAH (sodium p-aminohippurate), as originally suggested by Beyer, Flippin, Verwey, and Woodward (*2*). Additional patients similarly treated were cured chiefly because of the penicillin-augmenting properties of PAH; the detailed data of these observations will be included in a forthcoming communication (7).

In conducting these studies with PAH it was soon evident that this agent, while extremely effective in augmenting penicillin levels by competing with the antibiotic for the tubular excretory apparatus, poses serious technical difficultues. It is ineffective when given by mouth and must necessarily be administered by vein in daily dosages of 200–240 grams. It has the additional disadvantages of unpleasant side-effects and a sclerosing effect on veins when given in the requisite concentration. As a result of all this, treatment cannot be continued uninterruptedly for any extended period.

Acknowledging the limitations imposed by intravenous administration and the necessity for large dosages of PAH, a new approach was sought by Beyer (*1*) which resulted in the development of the compound, caronamide (4′-carboxyphenylmethanesulfonanilide). Beyer found that the excretion of penicillin by a renal tubular transport mechanism could be physiologically inhibited reversibly. The basis for this effect is thought to be one of substrate competition between penicillin, which is excreted by the tubular, and caronamide, which is essentially refractory to excretion by that transport mechanism.

The purpose of this report is to present data indicating the capacity of orally administered caronamide to effectively en-