of the toxicity experiments the correlation coefficient was calculated. This was found to be −0.84 which is significant at the 0.01 level, according to Snedecor's table of probability (*8*), indicating a very high degree of significance and correlation.

Table 1 presents the physical constants of the alkyl derivatives of *n*-phenyl carbamic acid, the boiling point of the parent alcohol, melting point of the derivative, density of the derivative, and refractive index.

Table 2 shows the molecular refractivity, and "Q function" of the phytotoxicity of these alkyl groups, as measured by the growth in milligrams per plant.

TABLE 2

Alkyl group	Molar refractivity at 91° C ± 0.1° C	Q function	Growth of plants mg/plant
Methyl	40.6	28.9	99.7
Ethyl	53.7	35.8	35.4
Propyl	52.2	29.7	104.2
Isopropyl	50.5	52.2	0.00
Butyl	58.9	29.2	122.3
Sec-butyl	33.2	10.0	124.8
Isobutyl	35.5	26.2	119.3
Amyl	59.9	27.2	121.0
Isoamyl	62.5	26.0	131.0
None (control) ...	...	...	**124.3**

The formula (*8*) used for calculating the correlation coefficient is as follows:

$$r_{xy} = \frac{N\Sigma xy - TxTy}{\sqrt{N(\Sigma x^2) - (Tx)^2 N(\Sigma y^2) - (Ty)^2}}$$

It was found that the molecular refractivity itself would not correlate as well with phytotoxicity as did the so-called Q function in this series.

Certain other derivatives were tested, notably those of *m*-chlorophenyl carbamic acid, to see if the Q function would fall within the same range as those by phenyl carbamic acid derivations. This was not found to be the case; therefore, it is reasoned that the values given in the tables apply only to a homologous series. It is interesting to note, however, that certain fundamental physical measurements made to elucidate something of the geometry of the molecule can be correlated with toxicity. If sufficient information appertaining to physical configuration as related to biological activity were amassed, it would enable the biologist and chemist to predict the activity of a compound and prepare biologically potent materials.

In the author's laboratory it has been possible to demonstrate the effect of iso-propyl-*n*-phenyl carbamate on certain enzymes of germinating Gramineae seedlings as evidenced by lack of color or weak color in treated plants compared to untreated plants when using 2,3,5-triphenyl tetrazolium chloride to indicate the reaction. Preliminary evidence also indicates the possibility of reversing the poisoning action of iso-propyl-*n*-phenyl carbamate by meta inositol.

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The Relationship between Human Serum Cholinesterase and Serum Albumin

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In a recent paper (*5*) we reviewed the literature on the variation of human serum cholinesterase (pseudocholinesterase) in various pathological states and presented our observations on the decrease of this enzyme in patients with malignancy, and in pregnant women. In an attempt to explain this decrease, we have studied further serum cholinesterase levels in numerous diseases and have observed what we consider to be a general principle applicable to this phenomenon.

In the process of explaining the influence of disease on this enzyme, we noticed an apparent correlation between the serum albumin and cholinesterase levels. In order to establish such a relationship we studied the level of these two substances in a variety of diseases, and are presenting here the results obtained with a series of 294 patients seen routinely at our hospital and diagnosed as having the usual variety of diseases to be expected in a group of general hospital admissions.

In tests for serum cholinesterase, we have followed the procedure of Mazur and Bodansky (*6*), who modified the method of Ammon (*1*). The production of acetic acid from acetylcholine was followed at 37° C by means of the liberation of carbon dioxide from a bicarbonate-carbonic acid buffer in Warburg flasks. These vessels were gassed at room temperature with a mixture of 93% oxygen and 7% carbon dioxide. At zero time, the acetylcholine was tipped into the serum and bicarbonate mixture. Readings were made at 20 min, at which time the readings fell on a zero order curve. Albumin determinations were made by our own modification of the Biuret method, which we shall describe elsewhere.

In a consecutive series of cases, a large number of dis-

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[2] Aided by a grant from the Cancer Research Grants Division, U. S. Public Health Service.

eases were studied, including pernicious anemia, tuberculosis, leukemia, tumors (benign and malignant), cirrhosis, infectious hepatitis, diabetes, and other conditions. The data to be presented for the series indicates a statistical correlation between cholinesterase and the albumin levels. In each individual case, within the limits of the normal range of variation for both cholinesterase and albumin, it is impossible to establish such a correlation. However, for values below the normal range, it is possible. Thus

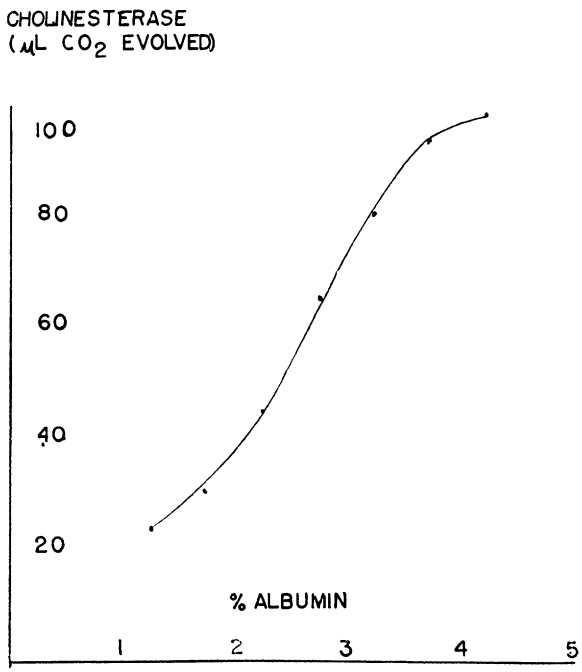

FIG. 1. Cholinesterase and serum albumin.

very low values for cholinesterase were always associated with low albumin values and vice versa. There was only one exception noted. If albumin was low due to increased urinary excretion, the cholinesterase in many cases was normal or higher than normal. In fact, we could predict albuminuria from the presence of a markedly elevated cholinesterase albumin ratio.

The relationship between serum albumin and cholinesterase in patients without albuminuria may be seen in Fig. 1. By dividing patient albumin values into groups varying by 0.5 g of albumin per 100 ml, and then averaging the cholinesterase values for each group, we see the definite relationship between the two. The detailed values for this group are given in Table 1.

Since numerous previous workers have noted the decrease in serum albumin in various diseases including cancer, our finding of the correlation of serum albumin and serum cholinesterase would obviate further work on the level of this enzyme in each individual disease. Rather, research now should be directed toward finding the mechanism involved in the relationship of the serum albumin and cholinesterase.

That the liver is involved in the production of serum cholinesterase may be deduced from the fact that patients with liver damage show a decrease in both albumin and cholinesterase. We have noted this, as have also Kunkel and Ward (*4*). Whether the liver damage affects the enzyme directly or indirectly (through its effect on albumin) remains to be determined.

In the same way, decrease in the enzyme in other diseases may be due primarily to decrease in albumin (which decrease may in turn be due to liver damage or protein intake deficiency), or to interference with a mechanism in which albumin hypothetically may help form the enzyme, or lastly, to a deficiency in a mechanism which forms both albumin and serum cholinesterase independently of each other.

TABLE 1

RELATIONSHIP BETWEEN SERUM ALBUMIN AND SERUM CHOLINESTERASE

Serum albumin g/100 ml	Number of patients	Cholinesterase average value	Cholinesterase standard deviation
1.1–1.5	4	24.0	9.24
1.6–2	13	30.7	8.82
2.1–2.5	23	45.2	18.4
2.6–3	55	65.9	17.8
3.1–3.5	99	80.9	23.4
3.6–4	82	93.6	19.5
4.1–4.5	18	98.7	14.5

The fact that normal or high values for serum cholinesterase are associated with low albumin values in some cases of kidney damage (observed also by Kunkel and Ward [*4*], and by Faber [*3*]) is to be expected. The smaller molecule of albumin readily passes through the kidney filter, which retains the larger cholinesterase molecule (*2*). In addition, it has been suggested by a number of workers that in glomerulonephritis there is a compensatory increase in albumin production. The exceptionally high cholinesterase levels encountered in some cases of albuminuria may be explained again on the basis of the correlation noted between serum cholinesterase and albumin production.

It has been demonstrated that the level of serum cholinesterase varies directly with that of serum albumin in various pathological states. There was only one exception noted; a low albumin associated with a normal or high serum cholinesterase is frequently observed in patients with albuminuria.

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