such a bias cannot be reduced by an increase of sample size.

In conclusion, then, it is possible to apply a simple correction for linkage to the formula for estimating the number of different genes. This correction, if the postulates on which it is based are met, applies to the average situation. In the case of any particular pair of parental strains, the actual distribution of differentiating loci on linkage groups may lead to a serious bias in estimates of gene number. Even in the absence of the complications due to linkage, the estimate of gene number is likely to be highly inaccurate except where the number of differentiating loci is relatively small.

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Correlation of Certain Physical Constants of Some Alkyl Esters of *n*-Phenyl Carbamic Acid, with Their Phytotoxicity[1]

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The toxicity of the alkyl ester derivatives of phenyl carbamic acids to members of the Gramineae family was first demonstrated in 1929 by Freisen (*4*), dealing with ethyl *n*-phenyl carbamate. Deysson (*2*) in 1945 demonstrated that this material acted, at least in part, as a mitotic poison, inhibiting cell division and causing subsequent death of the cell. This was a direct corroboration of the work done by Lefevre (*5*) in 1939.

Templeman and Sexton (*10*) in 1945 reported on the phytotoxicity of various carbamates, with the object of controlling certain weedy plants. In 1946 the same authors (*11*) announced their discovery of the phytotoxicity of isopropyl *n*-phenyl carbamate. Allard *et al.* (*1*) in 1946 further elaborated on this phytotoxicity. Numerous investigators have since published information concerning the merits of this chemical as a phytocide.

There have been many attempts to correlate chemical structure with the biological activity of a number of compounds. Frear *et al.* (*3*) undertook the study of some 5,000 organic chemicals to elucidate certain chemical structures which could be correlated with toxicity. They concluded that certain groupings in specific types of aporadicals produces a toxic entity. Tattersfield and Roberts (*9*) reported a study of physical properties and chemical constitution of organic compounds as related to their toxicity to the wireworm. These authors concluded that in any homologous series the most toxic compound would be the one with the highest vapor pressure if it possessed a sufficiently high molecular weight. Rubbo (*7*) demonstrated the correlation of the ionization constant to toxicity for mice and bacteria of derivatives in the acridine series.

Melander (*6*) was able to correlate the physical constants of various isomers of hexachlorcyclohexane with their toxicity. He found that the gamma isomer having the highest dipole moment also has the highest insect toxicity, whereas the other isomers have considerably lower dipole moments and accordingly lower toxicity.

In the present study of the series of alkyl esters of *n*-phenyl carbamic acids, it was reasoned that since molar refractivity is a function of the geometric configuration of a molecule in any homologous series, this measurement might offer a clue to the correlation of physical chemical properties with biological activity. Accordingly, the refractive index of this series of compounds was determined with an Abbe refractometer at 91° C ± 0.1°. The compounds have previously been purified by recrystallization from petroleum ether. The density of the compound was determined by the volume displacement method at 20° C.

The biological activity of the compound was determined by planting the seeds in triplicate in gallon cans that had been previously treated with an amount of material calculated to give 1 lb of active ingredient per acre. Notes were taken on the number of seedlings that emerged, and the plants were harvested after two weeks' growth, and weighed.

From the data derived from the refractive index and density measurements, molar refractivity was calculated according to the Lorentz-Lorenz (*12*) formula.

$$N = \frac{n^2 - 1}{n^2 + 2} \cdot \frac{M}{d}$$

A further calculation was made by multiplying the molecular refractivity by the factor of the melting point of the derivative divided by the boiling point of the parent alcohol.

$$Q = N \cdot \frac{\text{mp (derivative)}}{\text{bp (alcohol)}}$$

These calculations were made prior to obtaining the data from the toxicity experiment. After obtaining the data

TABLE 1

Alkyl group	Bp (Alc) °C	MP (deriv.) °C	Density (deriv.)	Refractive index (91° C)
Methyl	66	47	1.15	1.5235
Ethyl	78	52	0.92	1.5105
Propyl	97	58	1.06	1.5056
Isopropyl	83	90	1.09	1.4989
Butyl	116	57	1.03	1.4987
Sec-butyl	99	30	1.70	1.4957
Isobutyl	108	80	1.60	1.4955
Amyl	138	46	1.01	1.4926
Isoamyl	130	55	0.98	1.4939

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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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