The actions of compound 98 on heart rate, blood pressure, respiration, and nictitating membrane responses were, in general, the same as for compound 99, except that minimal effects were first seen at about 0.5 to 1 mg/kg, and death from respiratory arrest occurred at from 10 to 20 mg/kg. The effect of dibenamine on the blood pressure response to compound 98 is shown in Fig. 2.

Neither compounds 98 nor 99 exhibited tachyphylaxis or potentiation as a result of repeated doses given over a period of a few hours, and neither modified the control response to test doses of epinephrine or acetylcholine.

The mechanism of action of compounds 98 and 99 remains to be determined, but certain presumptions may be made on the evidence available about the effects observed in the cat. Since they are quaternary ammonium compounds, they are in all probability excluded from the central nervous system. For the same reason, action on sympathetic nerve endings is unlikely. Hence their pressor effect would appear to be due to a nicotinic action on autonomic ganglia. A relative predilection for sympathetic ganglia is suggested by the absence of marked parasympathetic phenomena. It is of interest that there was no evidence of depression of ganglia after repeated doses. Rapid destruction of these phosphate esters seems likely because of their short duration of action and lack of cumulative effects. The pharmacologic actions observed do not appear to have been reported previously among phosphate esters and specificity of any degree for sympathetic ganglia is rare. Further study of this class of compounds would therefore seem to be indicated.

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References and Notes

1. The compounds described were prepared in these laboratories by Dr. H. M. Fitch from the appropriate phenols and chlorophosphates, using conventional methods.
2. A. S. V. Burgen and F. Hobbiger, *Brit. J. Pharmacol.* **6**, 593 (1951).
3. O. A. Rose and A. Ebel, *J. Am. Geriatrics Soc.* **4**, 142 (1956).

4 March 1960

Self-Absorption Correction for Carbon-14 Assay

R. W. Hendler has proposed a method to derive self-absorption corrections for carbon-14 assay [*Science* **130**, 772 (1959)]. His method consists in the determination of the apparent specific activities for various weights of the radioactive compound. An apparent specific activity at a convenient arbitrary weight is taken as the reference activity, and the ratio of the apparent specific activities at any weight to the reference activity is designated as the conversion (or correction) factor F. By multiplying by F, the apparent specific activity at any weight can be converted into the standard specific activity. The novel aspect of Hendler's paper is the finding that when F is plotted against weight of sample, a straight line results.

Table 1. Slopes and intercepts of tangents to the initial and final part of the self-absorption correction curves F. The tangents were constructed by drawing a line connecting the two lowest and two highest integer values on the curve. (Thus for No. 1, 5 and 6 mg, and 21 and 22 mg.)

No.	Source	Preparation	Area (cm^2)	Range (mg)	Tangents of F			
					Initial		Final	
					Slope	Intercept	Slope	Intercept
1	J. Katz	$BaC^{14}O_3$ on filter paper	3.14	5–22	0.018	0.68	0.049	0.17
2	J. Katz	$BaC^{14}O_3$ on filter paper	2.55	6–18	0.023	0.65	0.071	0.04
3	Veterans Administration Hospital, Los Angeles, California	$BaC^{14}O_3$ on filter paper	4.50	8–38	0.016	0.58	0.035	0.30
4	Department of Physiology, Univ. of California, Berkeley	$BaC^{14}O_3$ on filter paper	19.5	10–85	0.011	0.60	0.013	0.37
5	Department of Biology, California Institute of Technology, Pasadena	C^{14} protein on steel	2.85	5–21	0.027	0.91	0.046	0.61
6	Katz and Golden [*J. Lab. Clin. Med.* 53, 658 (1959)]	$BaS^{35}O_4$ on glass filter paper	3.14	4–25	0.032	0.59	0.048	0.35

The empirical procedure described by Hendler has been in common use in many laboratories to determine self-absorption corrections for $BaC^{14}O_3$ and other C^{14} compounds, and it has also been described in detail for $BaS^{35}O_4$ [J. Katz and S. Golden, *J. Lab. Clin. Med.* **53**, 658 (1959)]. However, as far as I am aware, F has never been found to be a linear function of sample weight.

I have at hand six conversion tables (summarized in Table 1); four tables are for $BaC^{14}O_3$, one for $BaS^{35}O_4$, and one for C^{14}-protein. Two of the tables for $BaC^{14}O_3$ and the one for $BaS^{35}O_4$ were prepared by myself; the rest have been in use for many years in three other laboratories. The $BaCO_3$ and $BaSO_4$ were prepared by collecting the precipitate with suction on filter paper; the C^{14}-protein, by evaporating aliquots in planchets. The diameter of the samples ranges from 18 to 48 mm, and the weight ranges from 5 to 85 mg. For radioassay mica end-window and gas-flow Geiger tubes of several types were used, one of the tubes (the Micromil gas-flow counter) being identical with one used by Hendler.

When the values of the conversion factor for all six tables were plotted against sample weight, the resulting curves were not linear, but increased continuously in slope. The tangent to the upper portion of these curves tended to pass through the origin. While it was difficult to extrapolate to zero mass, it seemed that, at least with two curves, the curve tends to become parallel to the abscissa.

An elementary consideration of the character of self-absorption explains the nature of the curves described above. When the region of "infinite thickness" is approached the count becomes maximal and constant, and the apparent specific activity, when the weight increases, becomes simply inversely proportional to the sample weight. F then becomes directly proportional to weight. (For instance, take the count rate at infinite thickness, at 50 mg, as 500 count/min and the reference specific activity as 20 count/min per milligram. Then F at 50, 100, 200, and 400 mg would be 2, 4, 8, and 16). Obviously, then, in this region the plot of F is a linear function of weight and when extrapolated will pass through the origin.

Consider now the region of very low mass, where the apparent specific activity is almost independent of mass. In that region F will tend to become constant and the slope will be very small. F will intersect the ordinate above the origin (see Hendler). The curve between the two regions obviously will increase in slope, reaching a constant maximal value at the region of infinite thickness, and only then become linear, and when extrapolated will intersect the origin. Our experi-

mental curves, within their range, approximately show this type of change.

It is difficult to explain why Hendler got results so markedly different from the ones described here, and it seems doubtful whether his treatment is generally valid.

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7 December 1959

The experimental basis for Katz' objection to the straight line relation of F to sample thickness cited in my article [*Science* **130**, 772 (1959)] is essentially contained in six sets of data to which he refers, and which he has kindly supplied me. Two curves for $BaCO_3$ were obtained by Katz by plating on filter paper. These have increasing slopes. One for $BaCO_3$ on filter paper has been in use for many years at the department of physiology, Berkeley, California. These data appear to fit the straight line function perfectly over the whole range from 10 to 80 mg. The curve for the fourth set of data starts with increasing slope, is linear in the central portion, and ends with decreasing slope. Clearly the nature of the curve reflects the individual manner of preparing it. The fifth set of data is described by a curve having a gradually increasing slope which, for the experimental points provided, is adequately described by a straight line.

The last set of data mentioned in Katz' report is for $BaSO_4$ and is the only set published [J. Katz and S. Golden, *J. Lab. Clin. Med.* **53**, 658 (1959)]. I shall address all particular statements to these data which are reproduced in Fig. 1. Although no generality was claimed in my paper for the treatment of S^{35} data, it is gratifying to see that a straight line describes these data with an error which, at its greatest value, is only 2 percent (Table 1). Katz mentions his counting error as being 3 to 5 percent. It must be stressed that no rigid theoretical basis was claimed for the observed straight line relation, and its justification is in its empirical usefulness. In all of Katz' data there is a tendency to increasing slope. I would suggest that at the lower weights of material plated on filter paper certain additional factors which were absent in my preparations (on stainless steel planchets) came into play. First, there is a loss of back scattering. This has been cited by Katz and Golden in their article. Second, the filter paper, being porous and of generally rougher surface than metal, might tend to block radiation from thin samples intimately residing in the texture of this material. Third, it would be difficult, at best, to know if a thin layer of precipitate was completely and evenly spread on the surface of this material. All of these factors would decrease counts observed and hence increase F as the weight was decreased.

Table 1. Comparison of values of F obtained from straight line and from Katz' and Golden's determinations. Straight line equation $F = 0.04m + 0.54$ where m = weight of sample in milligrams.

Mg	Katz' and Golden's value	Value for straight line	Difference (%)*
10	0.93	0.94	1.1
11	0.965	0.98	1.6
12	1.00	1.02	2.0
13	1.04	1.06	1.9
14	1.08	1.10	1.8
15	1.12	1.14	1.8
16	1.16	1.18	1.7
17	1.20	1.22	1.7
18	1.245	1.26	1.6
19	1.29	1.30	1.6
20	1.335	1.34	0.4
21	1.38	1.38	0
22	1.425	1.42	0.4
23	1.47	1.46	0.7
24	1.52	1.50	1.3
25	1.57	1.54	1.9

* The straight line was drawn through all points down to 4 mg. Excluding the less certain values below 10 mg, as Katz and Golden suggest in their paper, would make this small difference tend to disappear.

The analysis of F shown in Katz' Table 1 is not at all relevant to the

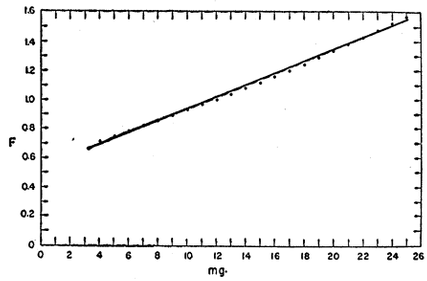

Fig. 1. F values from Katz and Golden plotted against weight of sample over a fixed area.

point in question. F is obtained from the best straight line drawn through all of the experimental values. It is easily obtained and can be used to correct experimental data with rather good accuracy. This is true also for the data from which Katz constructed his table. The analysis in Katz' table seems to support the contention that the values at small thicknesses are subject to the errors discussed above, which tend to raise their values.

No rigid theoretical basis is claimed for the straight-line treatment. The obtaining of a straight line is clearly dependent upon the particular technique employed. At the National Institutes of Health, to my knowledge, six individual investigators on a variety of counters have obtained good straight-line relationships. If Katz had known that a straight line $F = 0.04m + 0.54$ could adequately describe his data, he would have saved considerable effort by using it.

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20 April 1960

Induced Somatic Mutations Affecting Erythrocyte Antigens

Abstract. The frequency of inagglutinable erythrocytes was increased in pigeons following total body irradiation and in human polycythemic patients treated with P^{32}. Persistence of the increased levels of inagglutinable cells was observed in pigeons retested at over 200 days after irradiation and in a polycythemic patient retested at 173 days posttreatment. These data provide additional evidence for the mutational origin of the antigen-lacking cells.

Atwood and Scheinberg (*1*) have proposed that the red cells which lack the A antigen are the progeny of bone-marrow stem cells in which mutations have arisen. If these inagglutinable cells arise as a result of mutation they should be increased following irradiation. The procedure for detection of the inagglu-