Experimental: Preliminary experiments were carried out by the serial dilution method[4] using a stock strain of *E. typhosus* as the test organism. Plain beef infusion broth was used throughout.

One hundred and seventeen crude liquors, prepared by the cultivation of *P. notatum* or *P. chrysogenum* in a medium suitable for penicillin production, and eighty-six partially purified penicillin solutions were tested. The potency of these liquids ranged from 35 to 49,000 Oxford Units per cc. All the crude liquors showed some degree of bacteriostatic activity when tested in low dilutions against *E. typhosus.* The partially purified fractions, containing higher concentrations of penicillin, inhibited growth of *E. typhosus* in dilutions from 1:400 to 1:32,000.

In subsequent experiments the crystalline sodium salt of penicillin (G) was tested by the double serial dilution method for bacteriostatic action against both *Staphylococcus aureus* and *E. typhosus.* It was found that this preparation of penicillin was 64 times more potent against *Staphylococcus aureus* than against *E. typhosus.* On this basis crystalline penicillin sodium, having a potency of 1,650 Oxford Units per mg against *Staphylococcus aureus,* was chosen as standard and a value of 26 Typhoid Units per mg assigned to it. All subsequent tests for activity against *E. typhosus* were carried out by the Oxford cup method[7] using a substandard, established at 7 Typhoid Units per mg by titration against the crystalline penicillin sodium. Plain beef infusion agar containing neither glucose nor cerelose was used throughout. Table 1 shows the results on a number of fractions tested.

TABLE 1

BACTERIOSTATIC ACTION OF PENICILLIN AGAINST E. TYPHOSUS

Preparation of penicillin*	Potency against *Staphylococcus aureus*	Potency against *E. typhosus*
	Oxford Units/cc	Typhoid Units/cc
Crude liquors	> 35	0.5–2.0
Partially purified fractions	5,970–13,980	74–92
Liquid concentrates	32,000–49,000	50–800
	Oxford Units/mg	Typhoid Units/mg
Dried penicillin "Commercial"	620–993	7–20
Crystalline penicillin sodium	1,650	26

* All penicillin tested was prepared by Chas. Pfizer and Company, Brooklyn, N. Y.

A variety of Gram negative organisms,[8] in addition to *E. typhosus,* were tested for sensitivity. Table 2 shows the relative susceptibility of the organisms tested. Only two strains of Gram negative organisms, a strain of *E. coli* which produces large amounts of penicillinase and a freshly isolated strain of *Ps. pyocyaneus* were completely resistant.

[7] W. H. Schmidt and A. J. Moyer, *Jour. Bact.,* 47: 199, 1944.

[8] These cultures were received through the kindness of Dr. Hattie Alexander, Babies Hospital, New York, N. Y.

TABLE 2

RELATIVE SUSCEPTIBILITY OF GRAM NEGATIVE ORGANISMS TO ACTION OF PENICILLIN

Strain	Typhoid units per cc causing inhibition
E. typhosus (3 strains)	0.016
Sh. dysenteriae Flexner (V)	0.031
S. paratyphi B*	0.125
Sh. dysenteriae Flexner (W)*	0.125
*S. panama**	0.125
Sh. dysenteriae Flexner (Y)*	0.250
Sh. dysenteriae Flexner (X)*	0.250
Sh. dysenteriae Flexner (Z)*	0.500
Proteus vulgaris	0.500
Br. abortus	0.700
Klebsiella pneumoniae	> 1.400†
Serratia marcescens	> 1.400†
Ps. aeruginosa	> 1.400
E. coli	> 1.400

† Complete inhibition of growth was observed with 62 T.U./cc.

* Cultures were typed by the Salmonella Center, Beth Israel Hospital, New York, N. Y.

The antibacterial action of penicillin against *E. typhosus* is destroyed by clarase, which contains penicillinase, and is partially or completely destroyed at 100° C. for 1½ hours.

Summary: It is apparent that penicillin exerts an antibacterial action against Gram negative as well as Gram positive organisms. This property of penicillin becomes more apparent in high potency preparations. It is possible that a form of penicillin showing greater activity against Gram negative organisms may exist. Studies on the nature of such a substance and on the *in vivo* action of penicillin against Gram negative organisms are in progress.

GLADYS L. HOBBY

RELATION OF DOSAGE TO SURVIVAL TIME OF ARSENITE-INJECTED ROACHES

IN a study, carried on during the last several years, of the mode of action of sodium metarsenite on the American cockroach, *Periplaneta americana* (L.), various concentrations of the poison in volumes of saline proportional to body weight of the insect were injected into the roaches and the survival times determined. When the survival times were plotted against concentrations, hyperbolic curves were obtained. A portion of one of these is shown in Fig. 1. These curves are characterized by a region of inflection (*i,* Fig. 1) and a critical zone, both of which are reproducible in repeated experiments. The critical zone is a region, usually associated with long survival times, in which insects injected with equal doses of the poison have survival times that fall into a bimodal frequency distribution or actually into two separate groups. In the region of inflection, injection of slightly different concentrations of the poison may

cause the same survival time or the lower dosage may cause the shorter survival time. This anomaly, that the lower dosage may be more toxic than the higher dosage, receives a rational explanation in terms of a proposed hypothesis regarding the role of dissociation[1] in the mode of action of the poison.

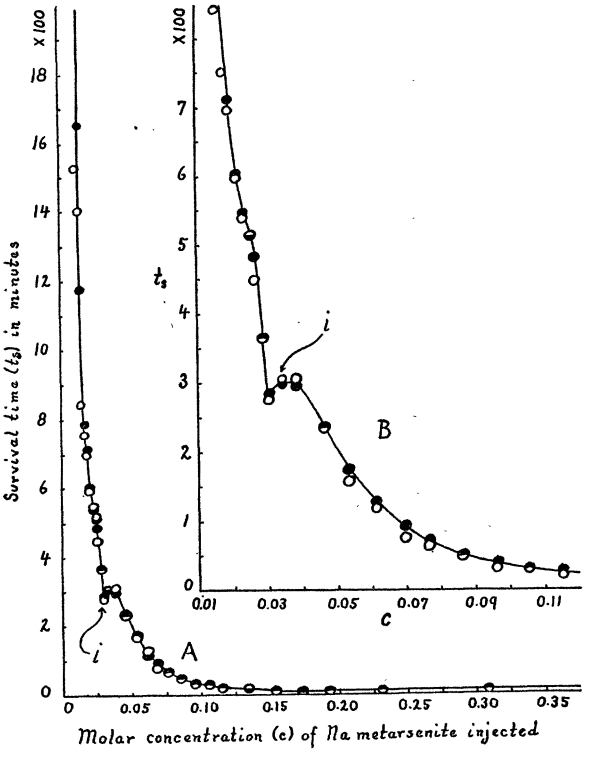

FIG. 1. A concentration-survival time curve of *Periplaneta americana* injected with Na metarsenite. Curve *B* is part of curve *A* on a larger scale to show better the region of inflection, *i*. Circles: Harmonic means of observed t_s. Solid dots: Survival times calculated by equation (2).

It is postulated that the toxic action is dependent upon the degree of ionization of the poison; that the arsenical ion thus formed, or a secondary material itself dependent upon the formation of the arsenical ion, combines with certain vital tissue components in what is here designated a fundamental lethal reaction; that the fundamental lethal reaction leads to the death of the insect; and that the death of the insect takes place as a result of a certain minimum quantity of the arsenic combining with a unit quantity of the tissue component.

An examination of the literature shows that hyperbolic dosage-survival time curves are sometimes described by use of equations of the type $ct = k$ and $(c - c_o)\ (t - a) = k$. Such relatively simple expressions have not yielded good fits to our experimental data. Good fits can be obtained by use of equations developed by the authors and which are essentially the well-known equation $(c - c_o)^n\ (t - a) = k$ so modified that the influence of dissociation is taken into account.

In accordance with the above postulates, let it be assumed that the sodium metarsenite dissociates with the formation of an arsenical ion and suppose (tentatively) that this ion combines with the tissue component to cause the death of the insect. If t_s = survival time, c' = concentration of the arsenical ions, c_o = the highest concentration of the poison that fails to kill and a = the shortest survival time theoretically possible, it may be postulated in accordance with the data that the rate of change of survival time with respect to the effective concentration of the poison is inversely related to a power, n', of the effective concentration, *i.e.*, $-d(t_s - a)/d(c' - c_o) = k'(c' - c_o)^{-n'}$. When integrated this becomes $t_s - a = K\ (c' - c_o)^{-n}$, where $K = k'/n$ and $n = n' - 1$. The concentration corrected for dissociation is $c' = pc + c(1-p)\left(\frac{c_d}{c}\right)^m$, where p is the proportional ionization of the poison at the highest concentration that can be used, c is the concentration of poison injected, c_d is the highest concentration at which complete dissociation of the poison takes place, and m is a constant. Fully expressed, the equation is

$$t_s = \frac{K}{\left(\left[pc + c(1-p)\left(\frac{c_d}{c}\right)^m\right] - c_o\right)^n} + a. \qquad (1)$$

In equation (1), pc is the concentration of ions and $c(1-p)$ that of the undissociated molecules proportional to that in the highest total concentration of the poison, and $\left(\frac{c_d}{c}\right)^m$ is a factor that determines the rate at which additional ions are formed from the molecules as c decreases and as ions are removed from the body fluid in the fundamental lethal reaction. The factor $\left(\frac{c_d}{c}\right)^m$ may attain but not exceed 1.

Fits obtained by use of this equation are good, except in the critical zone and when survival time is very long. The fit at this end of the curve can be improved somewhat by use of an equation which will be referred to as equation (2), and which is like equation (1) except that a bounded variable $\bar{c}_o$, directly proportional to a power of the corrected concentration and directly proportional to survival time, is substituted for the constant c_o, where

$$\bar{c}_o = k\left\{\left[pc + c(1-p)\left(\frac{c_d}{c}\right)^m\right]^b \left[pc + c(1-p)\left(\frac{c_d}{c}\right)^m\right]^{-n}\right\} = k\left[pc + c(1-p)\left(\frac{c_d}{c}\right)^m\right]^s,$$

$s = b - n$, and b is a constant. But neither equation

[1] In using "dissociation" the authors have in mind also the concept of "activity." It makes no material difference in their analysis whether the poison is considered to "dissociate" partially, or to dissociate completely into ions only a percentage of which are "active."

takes into account certain factors, such as the finite mortality of the controls, operative at this extremity of the curve.

In Fig. 1 survival times (solid dots) were calculated by equation (2) to fit the observed survival times (open circles). It should be noted that the agreement is good even in the region of inflection. A detailed analysis of the entire experimental data, a discussion of the theory underlying the development of equations (1) and (2), and a consideration of these results with respect to the literature are included in manuscripts in preparation or unpublished. It is believed that these equations are of general applicability in studies involving the action of compounds, such as sodium metarsenite, that exist in solution in two different forms related by a condition of equilibrium. The good fits obtained by use of these equations support the underlying hypothesis and indicate that the effective concentration is not necessarily the concentration of the poison that is injected into the insect. They also support the explanation that the anomaly represented by the region of inflection is the result of the rate of dissociation of the poison as concentration changes and as the fundamental lethal reaction goes on.

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SAM C. MUNSON

THE MOTION OF SMALL PARTICLES IN MAGNETIC FIELDS

As reported by Ehrenhaft[1] rotational motions have been observed in a constant vertical homogeneous magnetic field using an electromagnet with the pole pieces immersed successively in ferric chloride, copper sulfate and slightly acidulated water. The material in motion consisted of charged particles and bubbles. The speed of rotation was a function of magnetic field intensity. Polar movements of particles of iron and nickel in a gas were observed in a constant vertical homogeneous magnetic field. These movements occurred both with and against the gravitational field and took the form of spirals, parts of spirals or vertical lines.

The fact that solutions of non-uniform concentration or of different layers of concentration will rotate under the action of an inhomogeneous magnetic field has been noted by many observers. Among these is Urbasch,[2] whose work has been commented on by Drude,[3] and the more recent observations of Kendall.[4]

The authors have repeated the experiments on motions in liquids and gases reported by Ehrenhaft and have performed further experiments to study these phenomena. In these experiments the authors have used solutions of uniform concentration or single particles and a homogeneous magnetic field, as did Ehrenhaft. Unless otherwise stated, all observations were made with a microscope[5] employing dark field illumination. The various liquids were placed in a glass cell and the illumination was directed from either side perpendicularly to the line of observation, being supplied by arc lamps with suitable lenses and cooling cells (see sketch). The microscope was usually fitted with a 3X objective and a 4X ocular, though a wide variety of lenses was available and used.

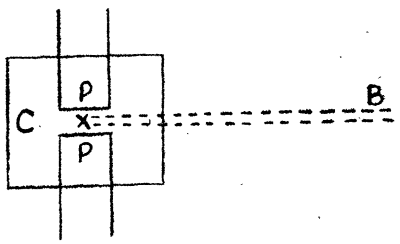

FIG. 1. C—Cell used to hold liquids; PP—Pole pieces; B—Illuminating beam; X—Point under observation. Line of observation is directed perpendicularly into plane of paper.

The electromagnet was constructed in the shape of a rectangle. Three sides of the rectangle, forming a U, had a cross-sectional area of 6 cm². The fourth side was completed by detachable pole pieces. On each leg of the U was placed a coil of 9,600 turns of No. 26 B. & S. copper wire. The field could be varied from zero up to 20,000 gausses and was reversible. The coils could be connected singly, in series or in parallel. The current could be varied from zero to two amperes. The separation between the pole pieces was ordinarily from one to two millimeters. The pole pieces were 8 millimeters in diameter. The permanent magnets used were Alnico "Blue Streak" having a total flux of 17,000 to 18,000 maxwells.

In experiments using the electromagnet rotational motions were observed in the following solutions: barium hydroxide, potassium hydroxide, sodium hydroxide, sodium chloride, potassium chloride, sodium fluoride, cupric cyanide, potassium cyanide, 1 per cent. hydrochloric acid, ferrous chloride, ferrous sulfate, ferrous ammonium chloride, ferrous ammonium sulfate, cadmium sulfate, cobalt nitrate, cobalt sulfate, nickel nitrate, nickel sulfate, a suspension of copper in copper sulfate, suspensions of iron, manganese, tungsten, zinc, aluminum, chromium, cobalt, nickel, copper, lead and brass in distilled water, a suspension

[1] F. Ehrenhaft, *Phys. Rev.*, 63: 461; 64: 43, 1943; 65: 287, 1944; *Nature*, 3909: 426, 1944.

[2, 3] O. Urbasch and P. Drude, *Zeits. f. Elektrochemie*, 7: 114, 1901; 8: 65, 150, 229, 1902.

[4] J. Kendall, *Nature*, 3587, 157, 1944.

[5] *Ibid.*, footnote 4, page 1.