PHYSICAL ASPECTS OF AIR DISINFECTION

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(With 9 Figures in the Text)

CONTENTS

I. INTRODUCTION

Air disinfection may be defined as the killing of bacteria in small particles or droplets suspended in air. Such particles fall out of suspension in a time which is short compared with that usually allowed for disinfection *in vitro*, and they cannot be assumed to retain bactericide after settling. An effective air disinfectant must therefore act quickly, and this requirement gives rise to most of the problems of the subject. Moreover, air-borne bacteria, under most natural and experimental conditions, have a protective coating of partially dried organic matter which impedes the disinfectant. Since the concentration of bactericide in this coating, at the surface of the bacteria, governs the rate at which they are killed, any delay in penetration may result in the failure of the bactericide to act during the relatively short time for which the particles are air-borne.

In theory there are some special conditions in which air disinfection would have to be treated altogether differently from disinfection *in vitro*; for instance, single naked bacteria might be attacked by a disinfectant vapour by direct condensation on their surface. However, in this paper I shall deal only with the killing of bacteria found inside the nucleus derived from a natural salivary particle. The

condition of these salivary bacteria-carrying particles appears to be analogous to those obtaining *in vitro*, except that the volumes of suspending material and bacteria are not so grossly disparate. As a result it is possible to consider the condensation of bactericide from the vapour on to the particle, and then to use the terms 'concentration' and 'mole fraction' with reference to bactericide in the particle, in the same manner as they would be used in describing disinfection *in vitro*. Lidwell (1948) has analysed the physical factors in the attainment of bactericidal concentrations in air-borne particles, with particular reference to the dynamics of condensation. In this paper, on the other hand, the general treatment will be confined to the equilibrium conditions resulting from the process of condensation. Particular cases are later discussed on their own merits, as it is shown that the ideal behaviour, though it should be considered for a proper understanding of the subject, is not directly applicable to any particular set of real conditions.

It will be taken as proved that air disinfectants reach the bacteria only by condensation of the vapour on to the bacteria-carrying particles. The difficulties of the collision theory were recognized by Finn & Powell in Twort, Baker, Finn & Powell (1940), who, nevertheless, regarded it as the most realistic one in view of the experimental evidence available at the time. Since then it has been shown by Swinbank (1947) that liquid droplets, even when charged, do not coalesce on collision unless they are larger than 50μ in diameter. The theoretical evidence against the theory was reiterated by Puck (1947) and was confirmed by experiments carried out both by Puck and by Lovelock (1948a) with sprays of non-volatile bactericides which proved ineffective against air-borne organisms.

II. THE COMPOSITION OF A SALIVARY PARTICLE SUSPENDED IN AIR CONTAINING WATER VAPOUR AND THE WATER-SOLUBLE VAPOUR OF ONE OTHER SUBSTANCE

Definitions

Relative humidity, r, will throughout be understood to be expressed as a fraction of saturation. This fraction refers to measurements taken in the absence of any other vapour, and depends only on the mass of water per unit volume of air, and the temperature. In the presence of another vapour with an affinity for water, saturation will occur at some value of r less than unity.

Relative saturation b of a vapour other than water will similarly be understood to mean the fraction of the saturation concentration of the substance measured in dry air, at the same temperature. In the presence of water vapour there will exist a maximum value of b, less than unity, for a stable system. The interaction of highly polar substances, such as water and air disinfectants, is complicated, and no general conclusions can be derived theoretically for their non-ideal behaviour, but it would be expected that intermolecular attraction would result in the sum of the two separate relative saturations, $b+r$, being less than unity for any saturated system.

Mole fractions in solution will be conventionally indicated by square brackets round the letter representing the substance, e.g. $[W]$ for mole fraction of water.

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(1) *The necessity for treatment as a three-component system*

If a salivary particle is taking up two different vapours at the same time, its composition can be conventionally represented on what is known as the 'ternary diagram' (Fig. 1). It is neither valid nor sufficient to consider the equilibrium condensate alone, as this implies limiting conditions of vapour saturation and vanishing particle size, which are usually far from being realized. As this aspect of the problem has been neglected in the past, the physico-chemical treatment appropriate to a three-component system, two of whose components are in equilibrium with vapour, is outlined below. Before that can be done an approximation is necessary. This is because a salivary particle is not a simple substance, and should strictly be considered as consisting of a large number of components. I believe this strict treatment to be unnecessary, and shall approximate as follows.

(2) *The apparent 'molecular weight' of a salivary particle*

If the salivary particle material is imagined to be replaced by a single suitably hygroscopic substance the simple ternary diagram would be sufficient to describe the system. The unknown quantity in this substitution is the molecular weight of the hypothetical substance. I shall define the 'apparent molecular weight', or A.M.W., of a salivary particle as the molecular weight that this substance should have in order to resemble the material of the particle most closely in physical behaviour. The numerical value of the A.M.W. will be deduced later from published data; the regularity of the results is a measure of the validity of the approximation.

(3) *The ternary diagram*

Such approximation leads to a formal homogeneity necessary for theoretical treatment. The ternary diagram can then be constructed by labelling the corners of an equilateral triangle P, W and B (particle, water and bactericide) and repre-
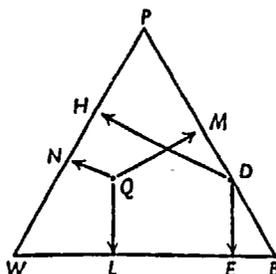
Fig. 1. Ternary diagram of salivary particle composition in air containing water and bactericide vapours. QL, QN and QM represent mole fractions of particle P, bactericide B and water W respectively. If the triangle is of unit height $QL+QM+QN$ is unity for any position of Q.

senting the relative molecular proportions, or mole fractions, of the three components in the usual manner by the perpendicular distances from a point inside the triangle to the side opposite the corresponding apex. Such a point is Q in Fig. 1, and the mole fractions of particle, water and bactericide are represented by QL, QM and QN, where $QL+QM+QN=1$ by simple geometry, if the height

of the triangle is unity. Any point such as D on one of the sides will represent the absence of one of the components, but the mole fractions of the other two will still be given by DE and DH.

This manner of representation has the advantage of generality, in that the same diagram can apply to any three substances under corresponding conditions of fractional vapour saturation, and certain simple relations are expressed as straight lines.

(4) *Ideal equilibrium concentrations: representation on the ternary diagram of systems with one independent variable*

A single point on the ternary diagram represents one particular composition. A line represents a series of compositions which for the present purpose correspond to a continuous change in the environment of the particle. If r and b represent the fractional saturations of water vapour and bactericide respectively, as previously defined, then there are three systems that are of interest.

(i) r is constant while b varies;

(ii) b is constant while r varies;

(iii) r and b both vary but not independently, so that the amount of bactericide present is a constant fraction of the maximum (saturation) amount at any given
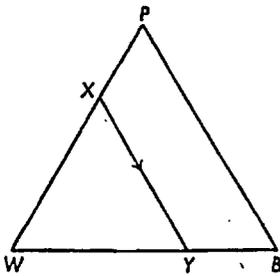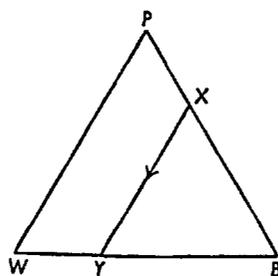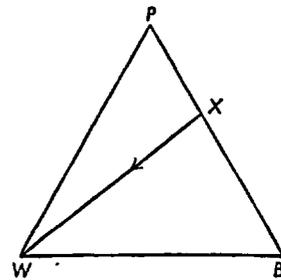

Fig. 2.   Fig. 3.   Fig. 4.

Figs. 2–4. Ideal ternary diagrams for systems with one independent variable.

Fig. 2. Constant relative humidity while bactericide concentration varies.

Fig. 3. Constant aerial concentration of bactericide while relative humidity varies.

Fig. 4. Bactericide concentration is maintained at a constant fraction of the maximum aerial saturation value at each relative humidity.

relative humidity. This is a relation of practical importance, and the glycostat (Puck & Chaney, 1946) was designed to supply a concentration of triethylene glycol satisfying it:

(i) If the relative humidity (R.H.) is kept constant while the bactericide concentration is varied, by Raoult's law, $[W]/[B] = r/b$, and the ternary diagram is of the form shown in Fig. 2. The point X represents conditions with no bactericide. As the fractional saturation increases from zero to $(1-r)$ the line is traced out to Y, where total saturation is indicated by a vanishing particle concentration, as the quantity of condensate increases without limit. The dew-point would indicate 100% R.H. (see Kreuger (1944) for experimental evidence for this).

(ii) If the aerial concentration of bactericide is kept constant while the R.H. is varied, the diagram is complementary to Fig. 2 with one difference (Fig. 3). The

line XY is now parallel to PW but the composition of the condensate does not remain stationary at Y as the R.H. is carried to saturation $(r = 1 - b)$. Owing to the limited quantity of bactericide present, assuming a very low vapour pressure, its aerial concentration will gradually decrease by condensation and will be represented by a point moving along YW. At W there will be no bactericide vapour left.

(iii) If b varies with r such that $b = \text{constant} \times (1 - r)$, b will be maximal at zero R.H. and decrease to zero at $r = 1$. As P is also zero at $r = 1$ the line will start somewhere along PB and end at W (Fig. 4).

(5) Possible causes of departure from the ideal composition

(i) *The bactericide is almost insoluble in the dry particle*, so that concentrations are lower than the ideal at low R.H.'s. This has been considered with reference to triethylene glycol by Puck (1947) and Lester *et al.* (1949), and is probably a general feature of air disinfection. (See also § IV (2), below, on the behaviour of the hydroxy acids.)

(ii) *Chemical combination with the particle material occurs*, so that little or no re-evaporation takes place. The particle concentration can eventually be higher than the ideal, though this may not be significant for bactericidal purposes owing to inactivation of the substance by the combination.

(iii) *Supersaturation.* This is not very likely in normal air owing to the nuclei present, but may occur locally near the point of vaporization, if the bactericide is vaporized by heat.

(iv) *Very low aerial concentration of bactericide*, so that equilibrium is attained slowly compared with the settling rate of the particles. The application of the laws of diffusion to the non-equilibrium state has been considered by Lidwell (1948), who concluded that the rate of diffusion of the bactericide either in air or in the particle could limit the rate of kill. Owing to the extremely small distances involved I shall assume, on the other hand, that equilibrium between various layers in the particle is attained sufficiently rapidly for the equilibrium state to be important. The diffusion barrier in air is more doubtful, but it must not be forgotten that all air-borne particles of the size of bacteria or larger are continually moving into a fresh atmosphere by gravitational action, the faster rate of fall of the larger particles allowing them to take up vapour faster and thus partly compensating for the larger amount needed for equilibrium. In the following sections I shall amplify the view that the main factor causing departures from the ideal equilibrium is limited solubility rather than low diffusion rates. There will, of course, be a lower limit of concentration beyond which this will no longer hold, and the air-diffusion barrier will be the more important.

III. DEDUCTIONS FROM PUBLISHED WORK

(1) Particle composition: determination of the 'apparent molecular weight' of a salivary particle from the water content at various relative humidities

If a salivary particle is suspended in air containing water vapour only, the binary diagram is sufficient to describe its composition. Fig. 5 shows the simple form which this takes for pure substances if Raoult's law is obeyed and the mole fraction

of water in the particle is equal to r, the relative humidity. Without a knowledge of the molecular weight of the particle the diagram can tell us nothing about the relative proportions by weight of the two components at any R.H. However, the problem may be approached indirectly by means of Lidwell's (1948) observations on the settling rate of salivary particles at different humidities. Fig. 6 shows the form of the graph obtained by plotting settling rate against R.H. By using Stokes's law one can convert these figures into what should theoretically be a linear form (Fig. 7). If the experimental points are not in fact amenable to this treatment it means that the material of the particle cannot be treated even approximately as having one molecular weight.
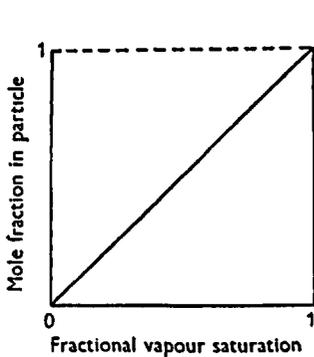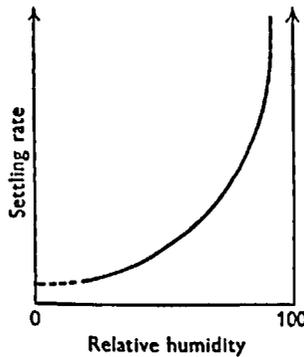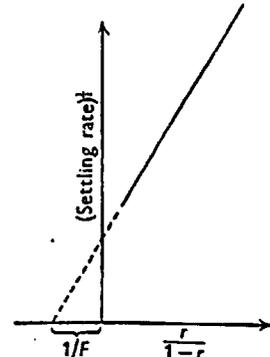

Fig. 5.   Fig. 6.   Fig. 7.

Figs. 5–7. Stages in the determination of the 'equivalent molecular weight' of a salivary particle from the settling rate at various relative humidities.

Fig. 5. The ideal binary diagram for water in the particle at any humidity.
Fig. 6. Form of the settling rate/relative humidity graph (O. M. Lidwell).
Fig. 7. Data of Fig. 6 converted to theoretically linear form from which the 'equivalent molecular weight' may be deduced.

The data are transformed as follows:

By Raoult's law, if P is the dry particle mass, M its A.M.W. and W the mass of water in it at any relative humidity $r-1$,

$$r = \frac{[W]}{[W]+[P]} = \frac{W/18}{W/18+P/M},$$

where 18 is the molecular weight of water. Rearranging this equation and putting $S = r/(1-r)$ and $F = 18/M$, we have

$$P + W = P + FPS = P(1+FS).$$

Also, since the total particle mass $(P+W)$ is, by Stokes's law, proportional to (settling rate)$^{\frac{1}{2}}$ and P is constant, it follows that

$$(\text{settling rate})^{\frac{1}{2}} = \text{constant} \times (1+FS).$$

Instead of finding $P+W$ for each experimental observation it is sufficient to plot (settling rate)$^{\frac{1}{2}}$ against S; the intercept on the negative S axis will then give $F = 1/S = 18/M$, from which M follows. The form of the graph is shown in Fig. 7. The scatter of points on the original graph had no obvious trend away from a straight line. More extensive observations might show a significant curvature,

but those given are sufficient to show that the procedure is valid to a first approximation. The value of the intercept, calculated by fitting a straight line to the points and extrapolating, gives $M = 3 \cdot 38 \times 18$, with a standard error of the estimate of $1 \cdot 7 \times 18$, where 18 is the molecular weight of water.

(2) *Particle composition and killing rate: dependence on relative humidity*

If a salivary particle is suspended in air containing both water and bactericide vapours in known concentrations, and if we know the saturated vapour concentration of the bactericide, the molecular weight of the bactericide and the molecular weight of the particle, we can estimate the particle concentrations at any R.H. from the simple relations represented in Fig. 3. This, however, would imply ideal behaviour throughout, and it would seem advisable to have an experimental check using less sweeping assumptions. Lidwell (1948) gives figures for the masses of salivary particles exposed to hydroxy acid vapours that enable this check to be made. It is still necessary to assume that Raoult's law applies throughout to

Table 1. *Particle composition at various relative humidities for a constant concentration of hydroxy acid vapour (masses in 10^{-12} g.)*

	A1				A2			
Relative humidity (R.H.)	0·26	0·48	0·64	0·88	0·35	0·685	0·81	0·87
Mass of particle at given R.H. (M_0)	620	860	1000	2800	730	860	2450	2150
Mass of same particle when acid is also present (M_1)	730	1420	2450	4460	860	1730	4050	3620
Dry particle mass, no water or bactericide (P)	530	590	530	600	575	410	780	500
Mass of bactericide in particle (B)	100	490	1140	790	105	670	1010	760
Percentage of bactericide in particle ($B\%$)	14	35	46·5	18	12	39	25	21
Killing rate in equivalent air changes per hour (K_d)	15	42	85	30	32	70	53	37

the water, i.e. that the relative humidity r is equal to the mole fraction of the water in the particle, whatever the amount of bactericide present. This is much more plausible than the corresponding assumption for bactericide owing to the small size of the water molecule and its relatively high aerial concentration at all but the lowest humidities.

Table 1 shows particle compositions calculated from Lidwell's data. The first three rows and the seventh are as published, showing respectively the R.H.; M_0, the particle mass before introduction of bactericide vapour; M_1, the mass afterwards; and K, the killing rate in equivalent air changes per hour. The other rows are calculated as follows:

Let P be the dry particle mass, and m its A.M.W. Let B be the mass of bactericide and A its molecular weight. Let W be the mass of free water in the particle before the introduction of bactericide and z the mass of water after its introduction (not the same as W even at the same R.H. owing to mutual condensation of water and bactericide). For convenience I shall introduce the variable $S = r/(1-r)$ from the

last section. Then the value of m can be found exactly as in the last section by plotting S against M_0 for all the points. The most probable value comes to be nearly twice that of water, or 36. P can then be calculated from M_0 (row 4).

When bactericide is present we have $M_1 = P + B + z$ and by Raoult's law

$$r = \frac{[W]}{[W] + [P] + [B]} = \frac{z/18}{z/18 + P/m + B/A},$$

from which by simple algebra and putting $m = 36$

$$B = \frac{M_1 - P(1 + \tfrac{1}{2}S)}{1 + 18 \cdot S/A} \quad \text{(fifth row).}$$

The sixth row gives the percentage by weight of bactericide in the particle, which should be compared with the killing rate shown next to it. The maximum in the killing rate approximately coincides with that in the calculated concentration.

A_1 was α-hydroxy-α-methyl butyric acid (mol. wt. 118) and A_2 was cyclopentanol carboxylic acid (mol. wt. 130). The mass of water z is not given explicitly in the table but is easily found by subtraction. The weight proportions were converted to molecular proportions, which are not tabulated but shown directly on the ternary diagrams of Fig. 8 for A_1 and Fig. 9 for A_2. These are to be compared with the ideal diagram of Fig. 3. The distortion is pronounced, and at the lower R.H.'s
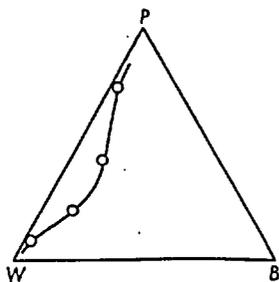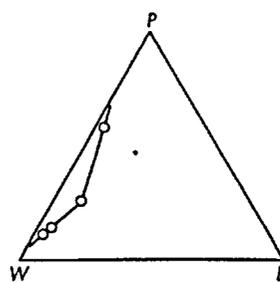
Fig. 8.　　　　　　　　Fig. 9.

Figs. 8, 9. Ternary diagrams deduced from published data (O. M. Lidwell) of particle compositions at various relative humidities with a constant aerial concentration of hydroxy acid. To be compared with Fig. 3.

it appears that much less acid was in or on the particle than is indicated by theory. There are two possible explanations; either the acid could not diffuse through to the centre of the particle and therefore re-evaporated from the surface, or it diffused rapidly but soon reached saturation and subsequent condensation was again balanced by evaporation.

From the next section it would appear that the second explanation is more likely to be true.

(3) *Water solubility and effective aerial concentration*

For ionizable substances like the hydroxy acids it is reasonable to assume that re-evaporation of condensed molecules from the surface of a salivary particle is unlikely until a layer of almost pure acid is beginning to be built up on its surface. In any case ideal equilibrium relations do not apply, and we are free to look for any kind of empirical relation that, if found, would help in assessing the relative

importance of factors such as solubility, vapour pressure and dissociation constant. Lovelock (1948b) tabulates results of tests on hydroxy acids which indicate a rough correlation between solubility and actual aerial concentration required for half the maximum killing rate. This relation is of practical significance because the concentration at which a maximum killing rate is reached is not easily determined owing to asymptotic behaviour of the curve relating aerial concentration and killing rate, and is often too high to be tolerable. The concentration for half the maximum rate, on the other hand, is easier to determine accurately, since in this region the rate is usually varying rapidly with concentration.

From Lovelock's table on p. 94 the average aerial concentration required for half the maximum killing rate with the seven hydroxy acids listed as of 80% or greater solubility in water was $3\cdot1\mu g./l$. That for the four acids with solubilities from 20 to 0·4% was only $0\cdot3\mu g./l$. It may be provisionally concluded that some process is at work whereby the more soluble a hydroxy acid is in water the higher its fractional vapour saturation has to be before its killing rate on salivary particles reaches a useful value. The situation is complicated by the differing vapour pressures, so that the following comparison, from the same table, may carry more

Table 2. *Effective aerial concentrations of 2-hexenoic acid* (i) *and α-hydroxy n-hexoic acid* (ii), *compared with their water solubilities*

	(i)	(ii)
Maximum killing rate	59	92
Aerial concentration at half maximum killing rate ($\mu g./l$.)	0·6	0·6
Solubility (g./100 ml. of water)	1 to 2	100
Vapour pressure in vacuum at 20° C. ($\times 10^{-4}$ mm. Hg)	About 100	1·88
Vacuum vapour pressure expressed as $\mu g./l$.	About 350 ·	7·4
Percentage vapour saturation	0·17	8·0

weight. Two acids have been chosen with similar bactericidal properties, reaching half the maximum killing rate at the same low aerial concentration, but differing widely in solubility and vapour pressure (Table 2). The figure given for the vapour pressure of 2-hexenoic acid is approximate, being based on the vapour pressure of n-hexoic acid from the tables, while that for the vapour pressure of α-hydroxy hexoic acid was from a direct measurement with the N. K. Adam apparatus. The substances were chosen because of the similarity of their maximum killing rates and were compared at the same aerial concentration, so that air-diffusion effects should have been similar. The effect of differing solubility may therefore be taken as a real one, and from the table it can be seen that the ratio of percentage air saturation for the two acids is about the same as the ratio of the solubilities. The interpretation of this effect will not be attempted here, as no simple physico-chemical explanation appears to be possible. This result should be considered, for example, in relation to the work of Ferguson (1939) on chemical potentials as an index of toxicity.

(4) *Propylene glycol*

Lidwell, Lovelock & Raymond (1948a) found that the killing rate on salivary particles during the vaporization of propylene glycol was proportional to its rate of vaporization, and bore no simple relation to the total quantity vaporized. They also found that successive 'spraying spits' into a room in which propylene glycol had just been vaporized gave killing rates that decreased rapidly with time after vaporization. These observations may be explained on the basis of the conclusion of Robertson, Appel, Puck, Lemon & Ritter (1948) that weak solutions of propylene glycol show a very slow rate of kill *in vitro*, but that if the solution is strong enough the rate of kill is very rapid, so that most organisms are killed in a few seconds. If, therefore, air-borne bacteria are introduced into a uniform atmosphere considerably undersaturated with glycol the killing rate will be very small. If, instead, the quantity of glycol required to reach the same final concentration is gradually vaporized into the bacteria-laden air the effect will be different. Before complete mixing of the vapour there will be regions of high concentration, or possibly supersaturation, where the killing rate will be high even if the high concentration lasts for only a few seconds. Clearly the killing rate will depend mainly on the rate at which these regions are formed, that is, on the rate of vaporization of the glycol. This argument can be quantitatively tested as follows: in the experiments of Lidwell *et al.* (1948a) already quoted, the volume of the chamber was 810 cu.ft. or 23,000 l. At the 60 % R.H. at which most of the killing rate determinations were carried out, the saturation concentration of propylene glycol is 0·1 mg./l. (Jennings & Bigg, 1944; Puck, 1947). Hence if X g. of glycol are vaporized per minute they could saturate a volume of $10,000X$ l. in 1 min. or, using minutes as the time units, $10,000X\,dt$ l. in the infinitesimal time dt. If we assume that the bacteria in this volume are killed, the fraction left alive after a time dt will be $1 - \dfrac{10,000X\,dt}{23,000}$. By definition the rate of kill in equivalent air changes per minute is then

$$-\frac{1}{dt}\ln\text{ (fraction left alive after time } dt\text{) or } 0\cdot43X.$$

The rate of kill actually found by Lidwell *et al.* (1948a) was $0\cdot75X$, and the discrepancy can be accounted for if we assume that the undersaturated regions make some contribution to the killing rate, which must clearly be true. In view of the complexity of the process, this can be considered as experimental evidence in favour of the preceding argument.

IV. TRIETHYLENE GLYCOL

(1) *The saturated vapour concentration of triethylene glycol*

The vapour-pressure-temperature relation of triethylene glycol has been determined in vacuum in the range 140–200° by Gallaugher & Hibbert (1937) and at room temperature and pressure by Wise & Puck (1947). Their respective equations are:

$$\log p = 9\cdot6396 - 3726\cdot2/T \text{ at } 180°, \tag{1}$$

$$\log p = 8\cdot758 \ - 3170/T \quad \text{at} \quad 20°. \tag{2}$$

Although, if (1) is used to calculate the vapour pressure at 20°, almost exact agreement is obtained with (2), extrapolation over such a wide range is hardly permissible with such a highly associated substance. Rather, the coincidence obtained by crude extrapolation indicates some disagreement. This can also be seen by comparison of the coefficients of $1/T$ in the equations; the latent heat apparently decreases with the temperature—a most unusual effect. Since the determination at the higher temperature was easier and less likely to be subject to systematic error, it was of interest to extrapolate equation (1) to 20° in a more accurate manner for comparison. The method of extrapolation was based on that of Thomas (1949) but differs from his suggested best method owing to the absence of information on a suitable standard substance. Instead, the relation $L = a(T_c - T)^{0.4}$ was used to give the differential equation for the vapour pressure. T_c, the critical temperature, was calculated from Thomas's figures for atomic and constitutional constants (analogous to the parachor) and came to 680° K. The vapour-pressure equation was then

$$\log p = A + \frac{a}{R} \int \frac{(680 - T)^{0.4}}{T^2} dT.$$

The difference between this integral and the value of $\log p$ from a direct extrapolation of equation (1) was found graphically by assuming that the graph of equation (1) was tangential at 180° C. to the curve represented by a complete solution of the integral. The simple equation for the vapour pressure at 293° K. (20° C.) was found to be

$$\log p = 12.400 - 4613/T, \tag{3}$$

from which the saturation concentration at 20° C. was about $4\mu g./l.$ Comparing equations (2) and (3), it is clear that the calculated temperature coefficients of the vapour pressure are widely different. The molar heats of vaporization calculated from the two equations are 14,600 and 21,200 cal. respectively.

This discrepancy may be due to the fact that Wise & Puck's results were obtained by vaporizing the glycol at some (unspecified) higher temperature, with the possibility of mist formation. This mist would be glycol in excess of that required for saturation, and would cause the apparent vapour pressure to be higher than it really was. In addition, mist formation would be less at the higher air temperature so that the error would decrease with rising air temperature, making the temperature coefficient of the vapour pressure seem lower than if the error had been constant, or non-existent.

(2) *Experiments on triethylene glycol*

When triethylene glycol was dropped on to a hot metal surface, it could be seen to form a mist during vaporization, though the mist often seemed to disappear when mixed with a large volume of air. A preliminary series of experiments on the variation of killing rate with concentration and with rate of vaporization showed that one of the important variables was the temperature of the evaporating surface. It was obvious that the persistence and particle size of the mist needed investigation, and such investigations are described below.

(a) *Collection of triethylene glycol droplets by impingement*

For these experiments the ethylene glycol was vaporized from a brass block maintained at a known temperature in a chamber of 810 cu.ft. capacity. A fan was kept running throughout the experiments. The air was sampled in a standard slit sampler (Bourdillon, Lidwell & Lovelock, 1948) on to a flat disk.

Collection on glass was not successful as the droplets spread and disappeared. A better technique was impingement on to stainless steel disks in the slit sampler and later on to strips of the same metal in the cascade impactor (May, 1945), which separated the droplets into four size ranges. (It was later found that glass treated with dichloro-dimethyl-silane vapour was still more convenient.) It was found that the droplets thus collected were so involatile that they could be examined and counted even several hours after collection. They were observed under the highest power dry objective (4 mm.) by using a vertical illuminator. It was also noticed that some droplets were collected, however little glycol was vaporized. The evaporation rate of some of the air-borne droplets seemed to be so small that the lifetime of a droplet of say 10^{-4} cm. radius, whether surrounded by other droplets or not, was limited by settling rather than by evaporation. In one experiment, for instance, 5 mg. of triethylene glycol were vaporized at 150° C. into 10,000 l. of air at 16° C. and 40 % R.H. The air was kept stirred by a slow large-bladed fan. Total glycol concentration was thus (initially) $0.5\,\mu g./l.$, which is only one-quarter of the saturation concentration. Droplets of all sizes from 10^{-4} cm. radius downwards were collected by the slit sampler up to 10 min. after vaporization, while a control sample just before vaporization showed no droplets. The numbers collected per 3 sec. sample, however, fell off more rapidly with time than could be accounted for by settling alone, so that evaporation was clearly going on all the time.

(b) *The killing rate on salivary particles*

A few experiments were carried out to find how the killing rate decreased with time after the dispersal of triethylene glycol as a visible mist. They were conducted in a chamber of volume 810 cu.ft., and the humidity was reduced to about 40 %. After vaporization of the glycol from the brass block at 180° C., intervals of up to half an hour were allowed before the salivary spray was put up. The glycol was collected for estimation simultaneously with the subsequent bacterial samples. Fresh saliva was sprayed from a glass concentric atomizer worked by hydrogen from a cylinder. This spray, as may be seen from the low die-away rate in the absence of disinfectant (Table 3), was finer than the 'spraying spit' (Bourdillon, Lidwell & Lovelock, 1948) and corresponds in particle size more to their sprayed broth culture. The organisms were of mixed species however, and probably better protected than in a sprayed broth culture. The air-borne bacteria were sampled at 1 cu.ft./min. in a slit sampler, on to serum agar. About twelve points, 10 sec. apart, were obtained for each killing rate (Table 3).

It was noticed that with the higher glycol concentration the sides of the slit of the bacterial sampler became heavily coated with glycol. The killing rates are thus probably rather less than those given, since the slit, originally clean, ended

up partially blocked by glycol. At the lower concentration the slit remained completely dry.

(c) *Droplet size and vaporization temperature*

Triethylene glycol was vaporized from the surface of a brass cylinder maintained at temperatures varying from 120 to 240° C. The resulting mist was collected on to stainless steel strips in the cascade impactor. The volumes of air collected in the various experiments were the same, and the same quantity of glycol was vaporized, though at the lower temperatures it took so long that losses were to be expected

Table 3. *The killing rate on salivary particles in a mist of triethylene glycol. Volume of chamber 810 cu.ft. or 23,000 l.*

Amount of triethylene glycol vaporized at time 0–½ min. (c.c.)	0·4	0·4	0·4	2	2	None
Time at which salivary spray was put up (min.)	1	5·5	9·5	12	23	1
Mean time of bacterial sample (min.)	4	8·5	12·5	15	26	4
Die-away rate in equivalent air changes per hour*	36	27	17	28·5	18	2
Total glycol concentration measured at time of bacterial sample (μg./l.)	14	8	3	—	—	
Initial concentration from amount vaporized (approx.)	20	20	20	100	100	0

* One complete air change reduces the concentration of gas, particles, etc., to a fraction $1/e$ of its initial value. Two air changes reduce it to a fraction $1/e^2$ and so on.

Table 4. *Temperature of vaporizing surface and droplet size distribution of triethylene glycol mist*

Temperature of brass block (° C.)	Average nos. of droplets with diameters within the ranges		
	1·5–3μ	3–5μ	6–12μ
120	30	6	—
150	285	160	17·5
180	240	100	27·5
210	240	100	30
240	400	42	60

before collection started. The resulting size distribution indicated that the diameter of the droplets contributing most of the mass of the mist changed from 3 to 6μ when the temperature of the block changed from 150 to 240° C. Below 150° C. only the tail of the distribution was collected, while above 240° C. there appeared to be an increase in the smaller droplets as well as the larger ones, at the expense of the droplets of intermediate size (Table 4).

It was also observed that a denser mist was produced when the air velocity over the surface was high than when it was low.

(d) *The saturated vapour concentration of triethylene glycol in dry air by a flow method*

It was desirable to check the saturated vapour concentration of triethylene glycol by a method which did not involve heating the substance above the tempera-

ture at which the concentration was to be determined. Accordingly a simple flow system was set up, consisting of a drying tube, a water-jacketed tube (an ordinary water condenser), two bubblers in series, a flowmeter and a pump. The tube was lined with filter paper soaked in triethylene glycol. The paper had previously been carefully dried by passing warm dry air over it. Two determinations were done at a rate of 0·2 l./min. for 50 min., one at 32° C. and one at 35° C. The connexion between the vaporizing tube and the bubblers was kept as short as possible and was warmed towards the end of each determination. The saturated vapour concentration was found to be 8 μg./l. at 32° C. and 10 μg./l. at 35° C. These figures are rather low compared to those from equation (3) of §(1), which gives values of 16 and 22 μg. respectively. This result is not surprising, however, in view of the simplicity of the apparatus and the very slow evaporation to be expected. The concentrations found are large enough to indicate that the flow method, suitably modified, would be capable of giving accurate results free from the uncertainties involved in the cooling of the vapour from a higher temperature.

(e) *The evaporation rate of triethylene glycol*

A large number of experiments were done on the exposure of small triethylene glycol droplets on stainless steel under various conditions. Most of them served for the development of the technique only, but it was concluded that evaporation in still dry air at 20° C. was at the rate of $3 \pm 1 \times 10^{-5}$ cm./hr. normal to the surface. The method used in the determination of the evaporation rate was as follows: A glass tube was drawn out to a capillary at one end such that 1 cm. of the capillary held about $2\cdot5 \times 10^{-4}$ ml. of liquid. This capillary was then allowed to absorb dry glycol from the bottle and the length of the liquid column (about 1–2 cm.) was measured. The glycol was then expelled by air pressure on to a stainless steel plate and left exposed to the appropriate conditions for periods of from a few hours to 14 days. It was then reabsorbed in the same capillary and the column length again measured. The difference in the two column lengths after a correction for the amount left in the capillary on expulsion, gave the amount of glycol that had evaporated. The area of the droplet was measured, and the evaporation rate could then be calculated in terms of loss of liquid normal to the surface per unit time, averaged over the whole surface. The desiccant used, magnesium perchlorate, was tested and found to absorb glycol strongly, so that considering the very small amount of glycol exposed, it could be assumed that at no time could an appreciable concentration be set up in the air of the exposure chamber, a screw-top jar of 200 ml. capacity. The evaporation rate of propylene glycol under similar conditions was also measured and was found to be 3×10^{-3} cm./hr., or 100 times faster by volume than that of triethylene glycol. This ratio agrees with the ratio of their saturated vapour concentrations (90 by weight or 100 by volume) calculated from the value for the saturated vapour concentration of propylene glycol of 360 μg./l. given by Puck (1947) and that of 4 μg. for triethylene glycol calculated from equation (3) of §(1).

The temperature coefficient of the evaporation rate of triethylene glycol was determined by finding the evaporation rate at 37° C. It proved to be $7\frac{1}{2}$ times faster than at 20° C., while the ratio of the vapour pressures at these two temperatures

from equation (3) was 7·4, so that the agreement can be considered as satisfactory. A large discrepancy between these two ratios would be difficult to explain theoretically.

A knowledge of the evaporation rate in still air is unfortunately not sufficient for any reliable estimate of the lifetime of a free-falling droplet of triethylene glycol. Facilities were not available for a direct determination on free-falling droplets, as was done by Finn & Powell (1940) on various other substances. The method of Bradley, Evans & Whytlaw-Gray (1946), using mass changes of droplets hanging from a quartz fibre, would give much more accurate results than the method described above, owing to the fact that the droplet curvature is controlled. There would then be no difficulty in extrapolating to small droplets by the Langmuir equation, leaving only the question of gravity effects, i.e. the movement of the droplet into a fresh atmosphere which would tend to increase its rate of evaporation. However, Finn & Powell (1940) measured the lifetime of a free-falling droplet of propylene glycol, and found it to be 4 sec. for an initial diameter of 4×10^{-4} cm. As a first approximation we may deduce that the lifetime of a similar free-falling droplet of triethylene glycol would be 100 times greater, owing to the evaporation rate being 100 times less. Taking into account the affinity of triethylene glycol for water we may guess that a droplet of diameter 4×10^{-4} cm. would have a lifetime of about 10 min. at 40 % R.H.

It therefore seemed possible that the transfer of glycol vapour from air-borne glycol droplets to the bacteria-carrying particles might, under some conditions, be the chief method by which the substance exerted its bactericidal effect.

A phenomenon supporting this suggestion was observed many times in the course of the experiments on the collection of triethylene glycol mist. It was noticed that if the film of droplets obtained by the sampling of the mist on to a stainless steel plate was kept for a few hours in a small dry closed Petri-dish, small clear areas appeared on it. On closer inspection these were seen to be around some, but not all, of the dust particles, fibres, etc., that had also been collected from the air and were contaminating the film. The proximity of these particles had caused the removal of the neighbouring glycol droplets, presumably by distillation. The observation was repeated using a film produced, not by the sampling of the mist, but by rapidly wiping dry cotton-wool over a small droplet of fresh triethylene glycol resting on the steel plate. Dust particles allowed to fall on to this film caused the disappearance of neighbouring glycol droplets, as also did salivary particles. As the metal surface was clearly glycol-repellent, it was unlikely that the removal was by any surface mechanism.

V. DISCUSSION

(1) The requirements of an air disinfectant are that it should be readily dispersible and that it should be rapidly lethal to air-borne organisms when these organisms are protected to a greater or less degree by an envelope of organic matter. The concentration required should be low, and usually the dispersion is required to be non-toxic, non-irritant and free from objectionable odour, as well as stable in air. As a rough generalization water solubility occupies a key position

as a characteristic of possible air disinfectants, as it is closely related to volatility, toxicity and odour for different types of chemical substances. A discussion of these matters would be out of place here, but clearly the correct approach to the problem of the selection of possible air disinfectants is by a consideration of chemical and physical properties together. However, the probable importance of water solubility has been mentioned by Lidwell (1948) and Lovelock (1948*b*), who implied that it was only the substance in solution in the bacteria-carrying particle that was actually effective. I have re-analysed some of their results in an attempt to relate solubility to air disinfectant power more quantitatively, but there are not enough vapour-pressure figures available to test the relation between water solubility and effective aerial concentration in a fully satisfactory manner. Qualitatively the implication of such a relation is that two extreme kinds of air disinfectant are to be envisaged:

(i) Substances such as the glycols completely miscible with water that are bactericidal only at very high concentration *in vitro* and which therefore must approach aerial saturation to be effective as air disinfectants. At high humidities they are inefficient owing to dilution by water in the bacteria-carrying particle.

(ii) Substances that are either partly soluble in water or, while completely miscible with pure water, are easily salted out owing to hydrophobic groups in the molecule. Solubility limits the effect of such substances as air disinfectants at low humidities, but the concentrations attained in the bacteria-carrying particles at high humidities are sufficient for rapid killing because of the lower *in vitro* concentrations needed for bactericidal action. Examples of such substances are cyclohexanol carboxylic acid (Lovelock, 1948*b*), resorcinol (Twort & Baker, 1942) and ephedrine (unpublished work).

For organic substances of low but not zero vapour pressure, the requirement of rapid bactericidal action at low concentrations *in vitro* is generally incompatible with high solubility in water. Lactic acid is one substance which is not only very soluble but is bactericidal at about 1 % strength (Robertson *et al.* 1948), though the killing rate *in vitro* at this concentration is rather small by air-disinfection standards. The substance is, however, one of the few that have been shown to be effective against dust-borne organisms (Lidwell *et al.* 1948*b*).

(2) It is improbable that propylene glycol is unique in showing a dependence of killing rate on rate of vaporization. Unless the killing rate from any particular substance is directly proportional to its aerial concentration, similar effects are bound to occur. The only way in which they may be eliminated with certainty is by producing a homogeneous atmosphere before the bacteria are introduced; such a technique is being developed in this laboratory for use in tests on air disinfectants where strict comparison between different substances is required.

(3) A germicidal aerosol may be defined as a suspension of volatile droplets or particles whose individual life is limited by settling rather than by evaporation, and whose vapour is bactericidal. Lidwell & Lovelock (1948) have shown that one of the disadvantages of some effective air disinfectants is that they condense not only on the bacteria-carrying particles but also on anything else in contact with the vapour, so that excessively large quantities are required to maintain an effective

aerial concentration in a room. A germicidal aerosol would not possess this disadvantage if its particle size were small enough to make losses by settling negligible, and if its particles everywhere acted as reservoirs of germicidal vapour. Short-range distillation might well be the main process conveying bactericide from the aerosol to the bacteria-carrying particles. Hexyl resorcinol and triethylene glycol probably act in this manner under some conditions. The solubility of hexyl resorcinol is so small that a high rate of kill cannot be expected, but its action has been detected at a lower concentration than with any other substance tested (Twort *et al.* 1940).

This activity at very low aerial concentration fits in with the relation between solubility and effective aerial concentration deduced in § III(3) from Lovelock's results on hydroxy acids, thereby suggesting that the relation may be a general one applying not only to hydroxy acids but to other types of substances also.

Hexyl resorcinol is also of interest on account of its high boiling-point, which is about 50° C. higher than that of triethylene glycol. When it is volatilized by heat the particles are of considerably smaller size than the droplets of triethylene glycol formed by vaporization at a similar temperature. It has been experimentally demonstrated by Bradley *et al.* (1946) that the evaporation rate of high-boiling organic substances such as dibutyl phthalate and butyl stearate in droplet form is in conformity with the Fuchs theory, so that particles or droplets of 10^{-5} cm. or less in diameter evaporate, at atmospheric pressure, at a rate approaching that in vacuum. In consequence, substances having boiling-points of about 350° C., which evaporate at an apparently negligible rate at room temperature, may be useful as air disinfectants, since they may yet evaporate fast enough if dispersed in sufficiently small droplets or particles.

VI. SUMMARY AND CONCLUSIONS

A consistent picture of the state of a bacteria-carrying particle in a bactericidal atmosphere is given. The particle is referred to an ideal ternary system where two of the components are volatile and in equilibrium with their respective vapours. The ideal phase diagrams for systems with one independent variable are given, and the large deviations from the ideal of an actual system are shown from calculations using published data on salivary particle masses in the presence of bactericide vapour at various relative humidities.

The importance of solubility is emphasized by the deduction of a relation, which may perhaps be general, between it and effective aerial concentration, for which no simple explanation appears possible. The anomalous behaviour of propylene glycol as an air disinfectant is deduced from the extremely non-linear relation between *in vitro* concentration and bactericidal power, and it is argued that most other air disinfectants must show similar effects, and that the measurement of killing rates can thereby be subject to error unless the correct technique is used.

Triethylene glycol, the properties of which were investigated in detail, can act as a germicidal aerosol, in the sense that glycol vapour distils over from droplets which consist mainly of glycol to those containing bacteria which originally have no glycol. The special advantages of such a mechanism are discussed.

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