

bottom phase. After shaking, the two solutions are allowed to separate in the cold for 48 hr. The new dextran-rich bottom phase will be of about half the original volume, and accordingly will have a double titre. (All phage titres are determined with the agar layer technique⁹.)

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G. FRICK
P. Å. ALBERTSSON

Institute of Biochemistry,
Uppsala. Jan. 8.

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Chloramphenicol and the Survival of Airborne Bacteria

IN recent years the large increase of staphylococcal infections in hospitals has resulted in much research into the sanitation and disinfection of hospital wards; but little work appears to have been conducted on the airborne survival of the causative agents. In the course of studies on the viability of airborne bacteria, certain observations were made which may, in part, explain the spread of these cells, especially the antibiotic-resistant strains.

Cells from each of a 24-hr. broth culture of *Staphylococcus albus*, *Serratia marcescens* and *Escherichia coli* were harvested by centrifugation, washed once and resuspended in distilled water. These suspensions were then aerosolized, by means of a Collision spray¹ into a stainless-steel rotating drum² of 1,100-litre capacity. Samples were collected in liquid impingers immediately after aerosolization and at subsequent hourly intervals up to 5 hr. The initial concentration in the drum was approximately 1×10^6 cells/l. of air. Loss due to physical fall-out was calculated using a modification of the radioactive tracer technique described by Harper *et al.*³

Viable decay-rates were calculated for the 5-hr. air suspension from the equation:

$$K = 1/t \times \ln N_0/N_t$$

where t is time of air suspension in minutes, N_0 is initial concentration of viable cells/l. of air, and N_t is concentration of cells/l. of air at time t .

The decay-rates of the antibiotic-sensitive cells were compared with (a) those of a resistant strain obtained from the parent strain by growth on chloramphenicol gradient plates and (b) with those of sensitive cells aerosolized from a suspension in a solution of 0.25 per cent chloramphenicol. In the course of study, cells were aerosolized from solutions of other bacteriostatic substances and vitamins and the results of two of these with chloramphenicol are shown in Table 1.

It can be seen that the *Staphylococci* are far more resistant to aerosol death than the two other genera, and it would appear that resistance to chloramphenicol affords considerable stability to the cells. More

Table 1. DEATH-RATES OF SOME BACTERIA AEROSOLIZED FROM VARIOUS MEDIA

Organism		Suspending medium			
		Water	Chloramphenicol (0.25 per cent)*	o-Amino phenol (0.5 per cent)*	Inositol (6.0 per cent)*
<i>Staphylococcus albus</i>	S	0.007	0.002	0.001	0.001
	R	0.002	0.003	0.002	0.002
<i>Serratia marcescens</i>	S	0.034	0.010	0.007	0.001
	R	0.012	0.008	0.008	0.002
<i>Escherichia coli</i>	S	0.029	0.013	0.006	0.001
	R	0.011	0.010	0.007	0.002

Relative humidity, 30-32 per cent; temperature, 25° C. S, sensitive to chloramphenicol; R, resistant to chloramphenicol.

* The concentrations of added compounds shown are those found to give optimal aerosol survival.

surprising, however, was the suggestion that a like stability could be afforded the cells by suspension in the antibiotic prior to aerosolization, and that aminophenolic compounds were also protective. Far greater stability was afforded the cells by inositol, but considerably higher concentrations were required. In the presence of chloramphenicol, however, the quantity of inositol could be reduced by half without decreasing the stability of the cells. Thus there appeared a synergistic action between the drug and the vitamin. The observed increase in survival of cells by these compounds was found to depend on the relative humidity of the air, chloramphenicol affording greater protection to the cells at high relative humidity while inositol was more effective at low relative humidity-levels.

In more recent experiments other bacteriostatic drugs, such as some of the sulpha drugs, and cyclohexane substituted with hydroxyl- or amino-groups have been found to enhance bacterial aerosol survival, and the position of the substituents on the ring appears important. As a result of this work a hypothesis has been formulated that airborne cells die as a direct result of the loss of bonded water from their protein with the subsequent collapse of protein structure. It is felt (a) that the compounds affording increased stability to the cells are able to preserve protein structure by taking the place of water molecules during desiccation, and (b) that the type of bonding between protein-water and protein-compound is weak, reversible and dependent on the relative concentrations of compound and water. It is thus possible that chloramphenicol enhances bacterial aerosol survival by the same mechanism as it inhibits protein synthesis, that is, it takes the place of water molecules or blocks the water-bonding sites of the protein but does not destroy its structure, thus enzymatic action and synthesis is prevented. When, however, the drug is diluted by body fluids or water the reverse reaction occurs, water molecules displace chloramphenicol molecules and cellular metabolism is resumed.

The fact that bacteriostasis, by several organic compounds, normally used in chemotherapy and disinfection, may preserve airborne cells might, in part, explain why some measures of sanitation have failed in hospitals.

S. J. WEBB

Suffield Experimental Station,
Ralston, Alberta. Jan. 9.

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