Protective Action of Antipneumococcus Serum against B. Friedländer (K).

B. Friedländer Strain "K" (Type E)	Antipneumococcus Sera		Anti-Friedländer Serum	Virulence Controls
	Type I 0.2 cc.	Type II 0.2 cc.	Rabbit, "E" Type 0.2 cc.	
0.1		D 42	D 18	
0.01		D 18	S	
0.001	D 18	S	S	
0.0001	D 18	S	S	
0.00001	D 42	S	S	D 21
0.000001	D 18			D 42
0.0000001				D 19

Protective Action of Anti-Friedländer Serum against Pneumococcus Type II.

Culture Pneumococcus Type II cc.	Virulence Controls	Anti-Friedländer Serum. Rabbit immunized with Strain "E" 0.2 cc.	Antipneumococcus Serum Type II Horse 0.2 cc.
0.2		D 46	D 42
0.1		D 46	D 72
0.01		S	S
0.001		S	S
0.0001		S	S
0.00001	D 36		
0.000001	D 46		
0.0000001	D 46		

The phenomena described appear analogous to those of heterogenetic specificity among animal species.[1]

[1] Cf. Forsman, *Biochem, Zeitsch.*, 1911, xxxvii, 78.

2801

On variants of B. pestis caviae resistant to lysis by the bacteriophage.

J. BRONFENBRENNER and C. KORB.

[*From the Laboratories of the Rockefeller Institute for Medical Research, New York City.*

In preliminary experiments last year we found that bacteriophage therapy did not influence the course of experimental mouse typhoid, produced by the feeding of *B. pestis caviæ* to mice. We

were led, therefore, to inquire into the tendency of this organism to develop resistance to lysis, and to compare the virulence of such resistant strains with that of the original culture.

It was found that therapeutic administration of bacteriophage did not lead to production of resistants *in vivo* during the ten days period. Nevertheless, the mortality of animals treated during this period was the same as that among the untreated, infected controls.

Moreover, when the resistants were produced from the culture of *B. pestis caviæ in vitro,* it was found that such resistants are avirulent. When fed to or injected into mice these resistants did not recover their susceptibility to lysis, and when recovered from animals killed for this purpose they were found to remain resistant and avirulent.

These findings indicate, therefore, that the failure of bacteriophage therapy in experimental mouse typhoid is due not to production of resistants, but to failure on the part of the bacteriophage to destroy all the susceptible bacteria.

It was found that resistants isolated from the lysed cultures of *B. pestis caviæ* maintained their resistance to lysis during twenty-five passages on agar, at frequent intervals. When transferred to broth, however, one group of resistants (namely, those which yielded an agglutinated growth upon first transfer to broth) became susceptible to lysis after 5 to 7 daily passages. The other group of resistants (yielding a diffuse growth in broth) failed to become susceptible to lysis even after 120 daily passages in broth.

Simultaneously with the recovery of susceptibility, the cultures of the first group regained the degree of virulence comparable to that of the parent culture of *B. pestis caviæ.* The cultures of the second group of resistants failed to recover virulence thus far (four months after isolation). These latter cultures, apart from their lack of both virulence and susceptibility to lysis, are identical with the parent culture of *B. pestis caviæ* as indicated by their biochemical reactions, and by their antigenic properties.

The findings reported above are of interest for two reasons: In the first place they indicate that in the case of *B. pestis caviæ* there seems to exist some interdependence between the susceptibility to lysis and the virulence. Secondly they offer evidence in favor of the view that production of resistant strains is the result of selection of variants already existing in the parent culture. If

resistance to lysis were to be considered the result of development in bacteria of specific resistance to the bacteriophage, it would to explain our findings, be necessary to assume (in addition to d'Herelle's hypothesis, that individual bacteria may develop immunity) that this acquired immunity is inheritable, and has been transmitted in our experiments for countless generations in the absence of bacteriophage.

2802

On the nature of inactivation of the bacteriophage by alcohol.

J. BRONFENBRENNER and C. KORB.

[*From the Laboratories of the Rockefeller Institute for Medical Research, New York City.*]

Lytic filtrates are rendered inactive by the addition of an excess of alcohol.[1] If this reaction is carried out at low temperature, it becomes evident that the rate at which this inactivation proceeds is not uniform, but becomes very slow after the first few minutes. The phase of rapid initial inactivation apparently coincides with the precipitation of the filtrate by alcohol.[2] Addition of salts to the filtrate increases the rate of inactivation of the lytic principle when alcohol is added subsequently, and the higher the valency of the cation, the greater is the effect of the salt. Reduction of the salt content of the filtrate by dialysis results in the reduction of the destructive effect of alcohol upon it. It appears that in reducing the activity of the lytic agent alcohol acts not directly by virtue of its virucidal action, as assumed by d'Herelle, but indirectly by causing precipitation of the medium which, in turn, results in adsorption of the lytic principle.

[1] d'Herelle, F., The Bacteriophage, English translation, Williams and Wilkins Co., 1922, 123.

[2] Bronfenbrenner, J., and Korb, C., PROC. SOC. EXP. BIOL. AND MED., 1923-1924, xxi, 177; *J. Exp. Med.*, 1925, xlii, 419.