were benefited as compared with littermate controls on the same ration without addenda. (2) The greatest growth resulting from feeding the rats 66 to 97% of their own feces was 4 gm. per week; most of the animals grew much less or declined steadily but more slowly than the control animals. (3) It would seem that vitamin B(B_1) studies, using the assay method outlined by Sherman and Chase, were not seriously encumbered with disturbing influences of coprophagy since the small amounts of feces ordinarily consumed by the animals are not sufficient to influence their growth rates appreciably.

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Bacteriophage in Experimental Staphylococcal Septicemia.

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The principles of phage therapy have been developed upon 2 cardinal assumptions: 1. That an active homologous bacteriophage introduced into a host harboring a pathogenic organism in the tissues will propagate at the expense of the disease incitant, eventually causing the latter's widespread lytic destruction and constituting as a consequence a benign *therapia sterilisans* with no danger of untoward response on the host's part such as might attend use of germicidal drugs. 2. That phage lysates contain in solution certain constituents of bacterial cells released at the time of lysis. These substances are capable of inducing antibody responses upon contact with animal tissues and may be expected effectively to produce an active immunity. With a few notable exceptions, studies on phage therapy in experimental infections have been directed largely toward evaluation of phage as a possible therapeutic modality, as is, of course, also the case with purely clinical observations. However, the primary action anticipated in the application of phage to the treatment of diseases, i. e., massive bacterial dissolution *in vivo* has not been subjected to any critical experimental analysis so far as the authors are aware. Since any accepted concept of phage action will have definite influence upon the manner in which phage is applied clinically and also upon the nature and extent of our clinical expectations, a series of experiments was undertaken to investigate whether conditions essential for bacterial lysis can develop in animal

tissues and if so just how much lytic destruction of susceptible organisms is produced. Previous work by Krueger and Northrop[1, 2, 3] on the reaction occurring between a staphylococcus and antistaphylococcus phage showed that under controlled *in vitro* conditions bacterial growth is an essential conditioning factor for phage formation and that the percentage rate of increase of phage is proportional to the percentage rate of increase of bacteria, i. e., $\frac{dP}{dt} \propto C \times \frac{dB}{dt}$. Phage accumulates within the bacteria meanwhile maintaining equilibrium with phage in the surrounding medium until a certain critical concentration of phage per bacterium is attained, when lysis ensues. There is thus a definite lytic threshold. Further, phage is distributed between susceptible cells and the medium in 2 ways; with live cells, either resting or growing, distribution is of normal type and diffusion of phage into or out of the organisms proceeds in the direction of maintaining equilibrium. With dead cells, however, phage is adsorbed irreversibly and equilibrium may be represented in terms of Freundlich's adsorption isotherm equation.

The infection chosen for the present study, an acute septicemia produced by intravenous injection of the identical strain of staphylococcus into rabbits, was selected rather than a chronic pyemic state in order to limit phage effects to actual lysis of organisms and to obviate as far as possible the antibody responses which may occur in more prolonged infections. There were available accurate methods for quantitative determination of the phage[4] and of staphylococci.[5] For each experiment 3 rabbits received intravenously a certain number of washed staphylococci per kilo of body weight. One animal was immediately given an intravenous dose of standard bacteriophage calculated on a kilogram basis as adequate to furnish a titrable concentration of phage in the blood stream. A second animal received a like amount of broth and the third animal was given nothing at all.

Blood samples were taken at intervals for the purpose of determining the concentration of bacteria and the concentration of phage per ml. of circulating blood. In no instance was it possible to detect any increase whatsoever in phage/ml of blood and there never devel-

[1] Krueger, A. P., and Northrop, J. H., *J. Gen. Physiol.*, 1930, **14**, 223.

[2] Northrop, J. H., and Krueger, A. P., *J. Gen. Physiol.*, 1931, **15**, 329.

[3] Krueger, A. P., *J. Gen. Physiol.*, 1930, **14**, 493.

[4] Krueger, A. P., *J. Gen. Physiol.*, 1929, **13**, 557.

[5] Krueger, A. P., *J. Gen. Physiol.*, 1929, **13**, 553.

oped in the blood stream a ratio of phage to bacteria adequate for initiation of lysis even when the amount of phage injected was greatly in excess of the amount required to lyse the number of bacteria used. The bacterial curves in treated animals and controls exhibited no significant differences. Bacteria recovered from the blood stream both in fatal infections and in animals who survived (because they received less than the lethal dose of organisms) showed no change as regards susceptibility to phage action. That is, exposure to phage in the circulating blood did not produce phage resistant strains.

Red cells were found to be capable of adsorbing phage in quantities sufficient to make this action a considerable factor in the failure to establish a lytic threshold *in vivo*.

Our experiments indicate that: 1. Homologous anti-staphylococcus bacteriophage introduced in large quantities into the blood stream of rabbits suffering from acute experimental staphylococcal septicemia not only does not increase in amount but is rapidly eliminated from the blood stream. 2. The phage has no influence on the course of the experimental infection nor upon the quantities of bacteria found in the blood stream. 3. In the case of the infection studied it is not possible to establish in the circulating blood those conditions shown in earlier work to be requisite for bacterial lysis. 4. Phage adsorption on red blood cells effectively operates to remove considerable quantities of phage from participation in lysis. 5. Clinical failures in the treatment of staphylococcal septicemia with bacteriophage, such therapy aiming at lytic dissolution of cocci in the blood stream, are not only explicable but are to be anticipated in light of known facts concerning the bacterium-bacteriophage reaction.

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Meningococcus Precipitinogens in the Cerebrospinal Fluid.

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The demonstration of type-specific substances for Group I-III and Type II strains of meningococcus,[1] and the production of sera

[1] Rake, G., PROC. SOC. EXP. BIOL. AND MED., 1931, **29**, 287.