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Effect of Alcoholic Intoxication and Ether Anesthesia on Resistance to Pneumococcal Infection.

KENNETH L. PICKRELL. (Introduced by Arnold R. Rich.)

From the Department of Pathology and Bacteriology, The Johns Hopkins University, Baltimore, Md.

There are numerous papers dealing with the effect of alcohol upon experimental infections, and it is rather generally agreed that infected intoxicated animals die sooner than similarly infected non-intoxicated controls. The manner in which alcohol lowers resistance has, however, not been satisfactorily explained. Numerous investigators have reported that alcohol inhibits phagocytosis but their experiments consisted in adding relatively enormous amounts of alcohol *in vitro* to the leucocyte-bacteria mixture. When small amounts of alcohol were used in such experiments there was no inhibition of phagocytosis.¹

The present experiments were carried out in order to determine whether alcoholic intoxication lowers the resistance to pneumococcal infection, and if so, to attempt to discover the mechanism by which it exerts its effect. It was decided at the outset to study the effect of intoxication on well-immunized animals in order that any resistance-lowering potentiality that might be present would be put to as severe a test as possible.

Seventy-four rabbits have been used in the experiments here reported. In every experiment the procedure has been to immunize a group of rabbits by intravenous injection of Type I antipneumococcal serum, to intoxicate some of them, and then to infect all of them and, in addition, intoxicated and non-intoxicated non-immune controls, with the same dose of virulent Type I pneumococci endermally.

To produce intoxication 40 cc. of 20% ethyl alcohol was administered by stomach tube, smaller doses being repeated when necessary. The animals were maintained in a stuporous condition throughout the experiment. Blood cultures were made from all animals at intervals of several hours. The sites of infection were followed macroscopically throughout, and at the termination of the experiment they were removed for microscopic study. A typical protocol will be presented.

Twelve rabbits were highly immunized by the intravenous injection

¹ Parkinson, P. R., *Lancet*, 1909, **2**, 1580.

tion of 10 cc. of antipneumococcal serum. Six were then intoxicated with alcohol and all, and in addition normal control animals, were infected intracutaneously with 0.1 cc. of an 8-hour pneumococcal culture. The intoxicated non-immunized rabbits and the non-intoxicated non-immunized rabbits developed a positive blood culture at 5 hours, with 5 to 10 colonies per 10 drops of blood, and death from septicemia ensued in each instance within 18 hours. The intoxicated immunized rabbits showed a positive blood culture in 9 to 10 hours with 2 to 4 colonies, and death occurred from septicemia within 24 hours. The non-intoxicated immunized rabbits did not develop a positive blood culture, and survived.

No macroscopic lesion developed in any of the intoxicated animals in contrast to the edematous, hyperemic and purpuric lesion which extended to the belly-surface in the non-intoxicated non-immunized rabbits. Microscopic examination of the sites of infection revealed a dense leucocytic infiltration in all non-intoxicated animals. In the intoxicated rabbits, in sharp contrast, there was practically no leucocytic emigration and bacteria were present in swarms in the tissues in the immunized as well as in the non-immunized group. In the non-intoxicated immunized animals there was an abundant leucocytic exudate and no bacteria could be found in the sections after 9 hours.

Experiments in which the bacteria were introduced into the lung by way of the trachea gave results quite like those of the intracutaneous experiments.

Experiments of the same type carried out on immunized rabbits kept under ether-anesthesia gave precisely the same results as those described above in the case of the intoxicated immunized animals.

Since the temperatures of the intoxicated rabbits fall to a level as low as 97°F., a series was carried out to control this factor. It was found that lowering the body temperature to the level of that of the intoxicated rabbits, by keeping rabbits flat on their backs, did not inhibit leucocytic emigration and did not affect their immunity.

Blood counts showed that the scarcity of leucocytes at the infected site in the intoxicated animals could not be attributed to leucopenia. The effect of intoxication upon the activity of the phagocytes was therefore investigated in 24 animals. Five cc. of an aleuronat-suspension was injected into the pleural cavity and 18 hours later, when there was an abundant polymorphonuclear exudate, half of the rabbits were intoxicated. After 2 hours' intoxication, 2 cc. of a concentrated culture of Type II, rough, avirulent, pneumococci was injected into the pleural cavity. Smears of the

pleural exudates made 45 minutes later showed abundant phagocytosis, and there was no difference in the phagocytic index between the normal and the intoxicated animals. Analyses at this time showed that the alcoholic content of the blood was never above 40 mg. higher than that of the pleural exudate, and both were as high or higher than the figures given in the literature for the blood level during human intoxication.

Differential counts in vital preparations of blood from both rabbits and patients in alcoholic stupor revealed no difference in the number of non-motile cells as compared with normals.

Conclusions. Alcoholic intoxication maintained at the point of stupor destroys resistance to pneumococcal infection in the rabbit. Even in animals rendered highly immune by the intravenous injection of antipneumococcal serum, intoxication deprives them of their immunity. The loss of resistance to the infection is due to the fact that intoxication profoundly inhibits the vascular inflammatory response as long as intoxication is maintained. Leucocytic emigration at the site of infection is negligible and the bacteria, therefore, proliferate uninterruptedly. Similar experiments show that ether-anesthesia has as marked an inhibitory effect on the inflammatory response as has alcoholic intoxication, and produces as marked a loss of resistance to infection.

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Pyrididium as a Source of Interference in Vitamin C Determinations.

CATHERINE F. GANNON AND TERESA MCGOVERN. (Introduced by Irving Wright.)

From the Department of Medicine, New York Post-Graduate Medical School and Hospital, Columbia University.

The method commonly employed for determination of vitamin C in the body fluids makes use of Tillmans¹ indicator, 2,6 dichlorophenol indophenol. This is not specific for the vitamin but under controlled conditions is practically so. Substances normally present in urine, namely cysteine, glutathione, and ergothioneine,² may

¹ Tillmans, J., Hirsch, P., and Jackisch, J., *Z. f. Untersuch. d. Lebensmitt.*, 1932, **63**, 241.

² Emmerie, A., and Van Eekelen, M., *Biochem. J.*, 1934, **28**, 1153.