applying Langmuir's[3] "principle of independent surface action," according to which the distribution and orientation of polar organic molecules at an interface are determined by the character and number of the more active and the less active portions of the molecules. Throughout the alcohol series the potential of the polar group remains practically constant; *i. e.*, the effect of the OH group is constant, so that the increasing stimulating effect is determined by the non-polar group. The non-polar groups in the alcohol series differ in the number of CH_2 units, or in the length of the carbon chain. It is assumed that each additional CH_2 unit exerts an exponentially increasing effect on the shift of molecular equilibria at the receptive surface. This disturbance of the previously existing equilibria is the initial process of a catenary series of events which culminates in the discharge of a nervous impulse. Details as to the nature of the first effect are as yet unknown.

From our point of view it should be possible to secure data on the stimulating efficiency of the members of various homologous series of compounds, and by a study of the data from the different series, to formulate a generalized statement concerning the nature of the initial process in chemical stimulation.

Studies are now in progress on the effects of normal primary aliphatic aldehyde and acid series. A complete report of the whole work will be presented later.

4917

Hemorrhagic Reactions in Tuberculous Lesions and Skin Tests During Protracted Anaphylactic Shock.

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The method which gives the best result for reproducing the observations which we will describe is as follows: Guinea pigs are injected intraperitoneally with a large dose (10-20 mgm.) of the slightly virulent tubercle bacillus strain R.1, or with killed tubercle bacilli. The infection is followed 3 to 8 days later by the intraperitoneal injection of 0.1 to 1.0 mgm. egg white (dry weight). After this treatment the guinea pigs usually develop a strong skin sensitiveness to egg white,[1] often giving large necrotic skin reactions with 0.01 mgm. egg white.

[3] Langmuir, I., *Chem. Reviews*, 1929, vi, 451.

[1] Dienes, L., *J. Immunol.*, 1929, xvii, 531.

When the guinea pigs, 9 to 14 days after the treatment, are injected with somewhat larger doses of egg white intraperitoneally (10-30 mgm. dry weight) they die in 4-12 hours, the symptoms showing great similarity to the tuberculin shock. The most striking finding at the autopsy—beside an abundant exudate in the peritoneal cavity—is that in the peritoneum and the tuberculous lesions (in the omentum, mesenterium, and peritoneal walls) large hemorrhagic areas are present. Sometimes the hemorrhages extend almost over the entire peritoneum. When the reaction is slight it corresponds entirely to the usual reaction of tuberculous animals killed by the injection of tuberculin around the tuberculous lesions. From 93 tuberculous guinea pigs sensitized with egg white, tested with intraperitoneal injections during the last year, 30 died with the above described symptoms. In these guinea pigs the method of treatment and sensitization and also the interval between the treatment and the testing was variable. Of the guinea pigs which were infected and treated intraperitoneally, with few exceptions all died with the characteristic symptoms when tested in the third week after the treatment.

If the guinea pigs live somewhat longer or survive a severe shock we often observe that the formerly made skin tests with egg white and tuberculin show a bluish purple discoloration, and also extensive hemorrhages often occur in them. The hemorrhagic skin areas or a part of them might become necrotic during the following days. We observed extensive hemorrhages also in recently healed operation sites. In one guinea pig a strong reaction was present in skin areas where the hairs had been pulled out during the shock. In an experiment which might serve as an illustration 8 guinea pigs were injected intraperitoneally with egg white 23 days after sensitization. These guinea pigs were infected in the groins. All developed a severe protracted shock, 5 dying between 2 hrs. 20 minutes and 20 hrs. The guinea pigs were skin tested the day before in 4 different sites with tuberculin preparations. In 5 guinea pigs, 2 of which survived, smaller or larger hemorrhagic areas developed in the skin tests. Since our attention has been called by the paper of Shwartzman[2] to this phenomenon we observed it accidentally in 3 guinea pigs after tuberculin injection among a large number of tuberculin-tested guinea pigs. Two experiments in which we tried to reproduce this phenomenon with tuberculin in guinea pigs remained unsuccessful.

The hemorrhagic reaction in our observations was specific neither

[2] Shwartzman, G., PROC. SOC. EXP. BIOL. AND MED., 1928, xxv, 560; 1928, xxvi, 207.

to the tuberculous lesions nor to the inflammatory reaction (skin test) produced with egg white. The readiness to form hemorrhages in inflammatory areas of various origin is very probably a symptom of the severe illness caused in the sensitive animals by the egg white or tuberculin, which is present in varying degree in the different animals.

There are 2 reasons why we publish these observations before the completion of the work—concerning the general reactions of the tuberculous animals sensitized with egg white—in connection with which they were made. The first is that the observations in their present form make it very probable that the focal reactions which we observe around the tuberculous lesions in the animals killed in tuberculin shock are not the result of a special sensitiveness of the lesions to the tuberculin. There is no reason to doubt the specificity of the tuberculin reaction, but the focal reaction, at least in part, seems to be a non-specific symptom of a certain type of intoxication of the organism. It is well known that focal reactions in tuberculous patients are often caused by various non-specific influences. The other reason for the publication of these observations is that they are in close analogy with the intensification of skin reactions in rabbits after the intravenous injection of bacterial filtrates, as described by Shwartzman[2] and Hanger.[3] The doses of the bacterial filtrate which produced this effect are toxic, (a large percent of the rabbits die after the intravenous injection) and it is possible that the hemorrhagic reaction in the formerly injected skin areas is a result of the intoxication, as seems to be the case in our observations.

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Average Valence of the Gelatin Ion Determined by a Modified Theory of Membrane Equilibrium.

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From Donnan's theory[1] we can calculate the depression of the osmotic pressure of a gelatin solution, by the addition of a salt like NaCl. According to this theory this depression should never exceed 50% of the pressure of the colloid electrolyte in complete absence of a diffusible electrolyte. Experimental observations show

[3] Hanger, F. M., PROC. SOC. EXP. BIOL. AND MED., 1928, xxv, 775.

[1] Donnan, F. G., *Z. f. Elektrochem.*, 1911, xvii, 572.