found to be of the order of 0.08 cc per 100 g rat. From the administration of 2-ethyl hexanol by stomach tube to 85 rats, the LD 50 has been shown to be of the order of 0.39 cc per 100 g rat.

2. A marked anesthetic quality of 2-ethyl hexanol was observed.

3. 2-ethyl hexyl phthalate given by stomach tube to 50 rats in doses of 1 to 34 g per kg body weight produced no deaths. 2-ethyl hexyl phthalate has a very low order of toxicity in rats.

4. 2-ethyl hexyl phthalate given intraperitoneally in doses of 1, 2, and 3 cc respectively, to 65 mice resulted in the death of 7. However, only one mouse in a group of 20 was killed by the largest dose (128 g per kg body weight). 2-ethyl hexyl phthalate has a very low order of toxicity in mice.

14168 P

Probable Mechanism by Which Somatic Changes in Certain Emotional States Are Mediated.*

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Somatic changes commonly occur as the result of emotional reactions such as fear, tension and anxiety. Among the somatic changes are sweating, tachycardia, elevation of blood pressure, leucocytosis, increased intestinal peristalsis and alterations in metabolism of glucose and in skin temperature. Results of investigations on certain of these changes were reported by Diethelm[1] on glucose metabolism, Mittelmann and Wolff[2] on skin temperature, and Milhorat, Small and Diethelm[3] on leucocytosis.

In the present investigations an attempt was made to understand the mechanism or mechanisms by which these somatic changes are mediated. Many of the changes resemble those induced by the administration of adrenalergic and cholinergic drugs. In fact, Cannon and de la Paz[4] observed that blood withdrawn from the suprarenal veins of cats during periods of fear had adrenalergic effects on a surviving strip of rabbit intestine, whereas blood drawn while the animals were quiet had no such effect. The method used in the present studies represents a modification of the procedure of Cannon and is described below. The method of determination of adrenalin in the blood by colorimetric means,[5] was found unsatisfactory for our purposes.

Methods and Materials. Healthy adult rabbits were killed by a blow on the head. The intestines were removed immediately and with careful handling were washed in saline. A loop of intestine was suspended in Ringer-Tyrode's solution, attached to a recording lever and the contractions were recorded on a kymograph. The solution was gently agitated throughout the experiment by means of a stream of air bubbles. The bottle containing the muscle strip and Ringer-Tyrode's solution was suspended in a water bath at 37°C.

The blood was drawn from the patient's cubital vein, mixed immediately with heparin in a small Erlenmyer flask and within a period

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2 Mittelmann, B., and Wolff, H. G., *Psychosomatic Med.*, 1939, **1**, 271.

3 Milhorat, A. T., Small, S. M., and Diethelm, O., *Arch. Neurol. and Psychiat.*, 1942, **47**, 779.

4 Cannon, W. B., and de la Paz, D., *Am. J. Physiol.*, 1911, **28**, 64.

5 Bloor, W. R., and Bullen, S. S., *J. Biol. Chem.*, 1941, **138**, 727.

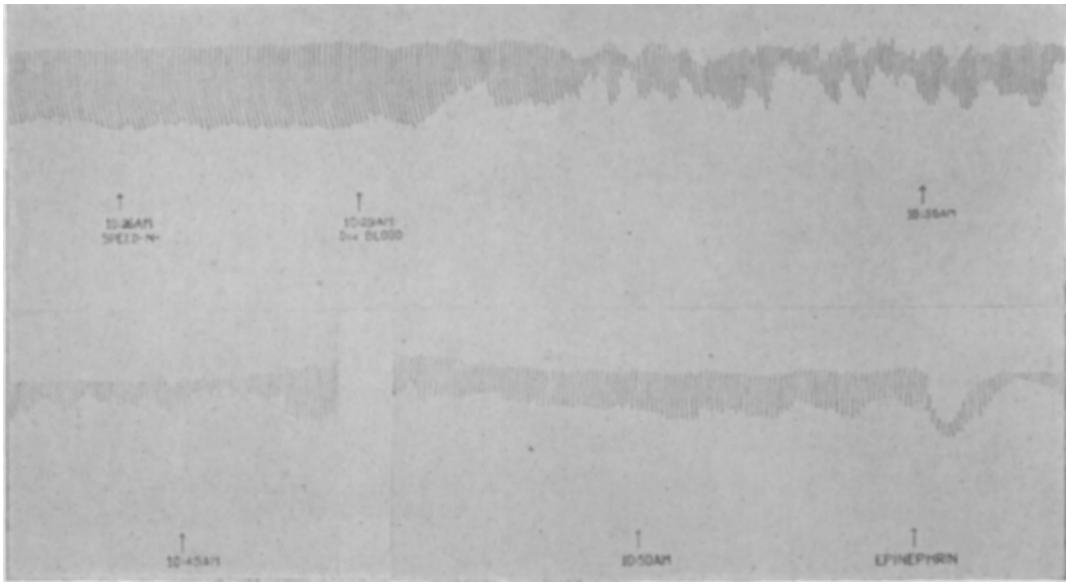

FIG. 1.

of 3 minutes, 5 cc were added to the Ringer-Tyrode's solution. At the conclusion of every experiment the muscle was tested by adding acetylcholine or adrenalin to the solution. The amounts of heparin used were found to be without influence on the spontaneous activity of the muscle or on the response to the pharmacologic agents used.

The subjects were patients with psychiatric disorders who were resident in the Payne Whitney Psychiatric Clinic; members of the hospital staff and patients without psychiatric illness were used in the control experiments.

Observations and Discussion. Blood samples of patients displaying marked anxiety and fear, which often reached the intensity of panic, altered the rhythmic contractions of the rabbit intestine. Usually the amplitude was reduced with incomplete relaxation of the muscle strip so that the base line was elevated. The uniformity and rhythmicity of the contractions was always disturbed and the frequency of contractions was often decreased. Blood that was withdrawn while the subjects showed anxiety induced alternating phases of larger and smaller contractions indicating a superimposed gross rhythm. (Fig. 1.)

These effects were not the relatively simple responses observed when adrenalin or acetylcholine was used. The changes were mixed in nature but generally tended to resemble those of the cholinergic drugs since the base-line

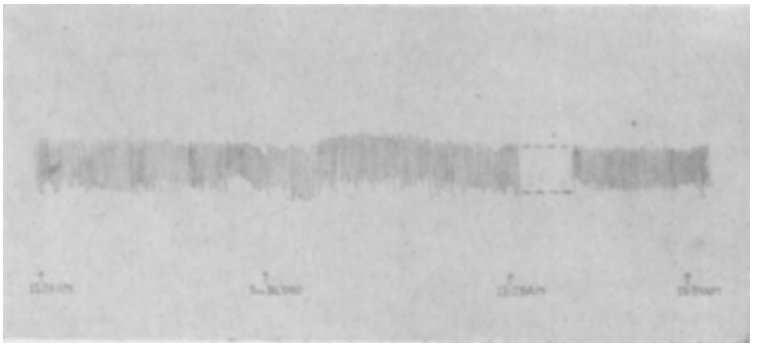

FIG. 2.

usually was elevated. Experiments repeated on patients who previously had shown anxiety or fear and whose blood had had the effects described, showed the blood to be without this pharmacologic activity after the emotional state had subsided (Fig. 2).

The nature of the substance in the blood that induces these changes is not yet known but the substance appears to be labile and disappears almost completely when the blood is allowed to stand for periods of from 15 to 20 minutes. However, the effects produced on the intestinal loop may persist for periods as long as 30 minutes when the blood has been used within 2 to 3 minutes after withdrawal. When the Ringer-Tyrode's solution containing the blood is replaced by fresh solution, normal muscular contractions return within from 5 to 8 minutes. This suggests that the substance can easily be washed out of the intestinal loop.

These observations indicate that the blood of patients showing fear and anxiety contains a substance having definite pharmacologic effects on the surviving intestinal muscle of the rabbit, and offer a possible explanation of the mechanism by which somatic changes in certain emotional states are mediated.

14169

Improved Technic for Demonstrating the Presence of *Streptococcus salivarius* on Eating Utensils.

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In a previous communication,[1] the use of a substrate containing sucrose, potassium tellurite and crystal violet for the selective isolation of "typical" strains of *Streptococcus salivarius* from washed restaurant utensils was reported. This medium demonstrated that common contaminants of drinking glasses, such as the spore-forming bacilli, coliform bacteria and staphylococci, were effectively inhibited, while streptococci apparently grew unhindered. The "typical" strains of *Streptococcus salivarius*, previously described by Niven *et al.*[2] grew by forming distinctive mucoid colonies (Plate I) and could be easily distinguished from other cocci which might occur. The number of isolations obtained during routine use of the medium were less than anticipated, indicating that the combination of potassium tellurite and crystal violet might be somewhat inhibitory to the desired organisms.[3] Such results might be expected in view of the relatively small inocula derived from glasses which have undergone washing.

Additional experiments have been undertaken to determine the selective inhibitory activity of 5 solid substrates. The media of Niven *et al.*[4] and of Stiles and Chapman[5] (minus crystal violet but with added sucrose, 1%) were compared with our previously reported basal substrate containing 3 combinations of inhibitors, *viz.*, potassium tellurite (0.03%), potassium tellurite (0.03%) + crystal violet (1:500,000), and potassium tellurite (0.02%) + sodium azide (0.02%). Twenty-four-hour broth cultures of 14 bacterial species, representative of those likely to occur on eating utensils, were streaked upon each of these media and incubated for 72 hours at 37°C. Adequate controls on non-inhibitory media were inoculated simultaneously. Results were recorded on a comparative basis using growth on the control plates as the standard of comparison. The data in

1 Rose, K. D., and Georgi, C. E., PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 344.

2 Niven, C. F., Smiley, K. L., and Sherman, J. M., *J. Bact.*, 1941, **41**, 479.

3 Unpublished data.

4 Niven, C. F., Smiley, K. L., and Sherman, J. M., *J. Bact.*, 1942, **43**, 113.

5 Stiles, M. H., and Chapman, G. H., *J. Bact.*, 1942, **43**, 64.