fact that under laboratory conditions the weight of frogs may fluctuate rapidly and extensively; and further, to emphasize the importance of adequate precautions to prevent such changes in physiological and pharmacological studies on frogs, especially when it is particularly important to preserve normal physiological reaction in the highest degree or in determining pharmacological dosage in relation to body weight.

89 (906)

The sensory effect of local application of hypertonic salt solutions.

By **C. C. GUTHRIE** and **M. E. LEE** (by invitation).

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While engaged in an investigation of certain effects of local application of salt solutions to exposed nerve trunks, and to nerve terminations exposed by abrading the skin, a paper appeared by Wiki,[1] in which results are presented and interpreted as showing that local anesthesia followed intracutaneous injections of solutions of various substances into guinea-pigs. A number of the salts employed by him were included among those used by us. Since the interpretation of an anesthetic action by him is at such variance with our results, it seems advisable to make a brief statement at this time.

Wiki states that strong solutions of magnesium chloride or sulphate when injected intracutaneously in the back of a guinea-pig produce marked anesthesia, as evidenced by decreased reflexes upon stimulating the affected skin area; while in our experiments, direct application of strong solutions of these salts to exposed nerve trunks (frog and turtle), abraded skin areas (human), or to the unabraded skin (frog), have resulted in very positive evidence of an irritant action. In the case of nerve trunks thoroughly isolated from surrounding tissue, a block may be produced by keeping the nerve bathed in a strong solution; but in the case of application to abraded or unabraded skin, though such applications have been continuously applied for twenty minutes or more, not one symptom of anesthetic action could be

[1] *Jr. de Phy. et Path. Gen.*, 1913, XV, 845.

detected. A number of other solutions and substances were tested in the same way and all, with the exception of cocain, gave similar results, the only difference being either a difference in the time of onset of evidence of irritant action or in the degree of such action.

Among the substances investigated by application to abraded skin areas, magnesium salts were among those that gave rise to very severely painful sensations which persisted for twenty minutes or more, at which time the solutions were removed. Tested in this way, cocain solutions were but slightly if at all irritating, and within a few minutes their application was followed by distinct evidence of anesthesia; for example, to application of normally painful mechanical stimuli, the area showed a diminished sensibility. We, therefore, cannot accept Wiki's conclusions upon the evidence he has presented.

He states that isotonic solutions of the magnesium salts are not without anesthetic action, but stronger solutions give more intense effects. These results would speak against an infiltration anesthesia such as we know can be produced by distilled water or even isotonic sodium chloride solutions. But in view of our results which demonstrate so clearly the pronounced irritating action of hypertonic magnesium salt solutions applied to abraded skin areas and complete absence of anesthetic symptoms, we are inclined to interpret Wiki's observations as evidence of infiltration anesthesia or inhibition of the reflexes through sensory stimulation.

Though aware that such experiments conducted by application of the agents to human cutaneous abrasions have been criticized especially from the psychological standpoint, yet we would emphasize their importance when carefully conducted and controlled, for not only is it possible to conduct a large series of observations in a relatively short time, but the evidence secured, being direct, is final.

Since all of the inorganic salt solutions employed (which include the chlorides and sulphates of Na, K, NH_4, Mg, and the chlorides of Ca and Ba) have similar actions, the difference being, so far as has been observed, a quantitative one, the action would seem to be more of a physical or physical chemical than of a chemical or specific nature. With hypertonic solutions the differences ob-

served in action correspond to the difference in concentration. Also, for a given degree of action the molecular concentration is not the same for all substances, and though the evidence has not yet been completely analyzed, it seems to be in general agreement at least, with the views of Meltzer and his pupils,[1] that the toxicity of solutions of salts that naturally occur in the blood varies inversely with the amount in which they are thus present.

90 (907)

The blood in "shock."

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It has been stated that in conditions of "shock" concentration of the morphological elements of the blood may take place through outward passage of liquid from the blood vessels.[2]

This point was investigated in a rather comprehensive experimental study of "shock" in etherized dogs. This condition was induced by rhythmical Faradic stimulation of the brachial plexuses and moderate hemorrhage. In general, death occurred within one or two hours. Small samples of the blood were withdrawn at regular intervals and defibrinated. The specific gravities and freezing points of the blood specimens were measured in eight experiments. The results are practically the same in all cases, and show that under the conditions of the experiments, physical alterations in the blood are not greater than may be accounted for by the loss of blood and certainly are not such as could affect the circulation sufficiently to account for the phenomena observed.

Relative to the total mass of blood, the amount withdrawn was, in round numbers, between 15 and 30 per cent., the average being 25 per cent.—estimated on the total blood being 1/15 of the body weight.

The average arterial blood-pressure at the time the first blood sample was taken was 180.5; at the time of taking the last sample

[1] *Jr. Pharm. and Exp. Ther.*, 1909, I, 1.

[2] Malcolm, *Lancet*, 1905, II, 573; 1907, I, 497.