turned on to his back. May 17th: Urine passed voluntarily. Blisters on inner side of first metatarsophalangeal joint on both feet; these were cut and dressed with picric acid. Marked spasmodic jerkings of flexion of thighs. These are more frequent than before operation. May 24th: Wound quite healed. A quantity of serum came away from the lower end of incision and firm pads were placed along whole length of wound. May 26th: Some movement of toes of right foot noticed and can voluntarily invert foot. No movement of left limb. The spasmodic jerkings are less than formerly. Sensation roughly tested and agrees fairly well with the condition prior to operation but pin prick now recognised as such on the right limb. Knee-jerks present both sides, right and left. May 28th: Voluntary flexion of right thigh. Power in toes greater. Bowels acted naturally for the first time. June 1st: Still some collection of serum under the wound, horse-hair drain inserted. More power in right limb, and left thigh can occasionally be moved. June 6th: Power in both limbs slightly greater, the knee-jerks are brisker and an extensor toe response can be obtained on both sides. Sores on the toes healing. June 13th: Power still improving, spasmodic contraction of muscles marked, especially of peroneal muscles. Action of bowel and bladder occasionally involuntary. June 15th: Plaster jacket applied from iliac crests to axillæ. June 26th: Can stand when supported; walked a few steps with help. July 1st: Patient went home.

Result of examination on Sept. 26th.—The patient has continually improved; he can now, with the help of crutches, walk 40 yards without a rest, the limbs being slowly advanced, and he states that improvement still continues. The right limb is much stronger than the left, the leg muscles, quadriceps, and psoas groups acting with fair strength. The same muscles act on the left side but slightly. He is able to rise from the sitting to the erect position. The nutrition of the muscles is good but the feet are still blue and cold, there are no sores, and the wound has perfectly healed and left a healthy scar. With regard to the reflexes both knee-jerks are exaggerated; there is ankle clonus on the right side and the ankle-jerk is brisk on the left. There is plantar extensor response on both sides. The abdominal, epigastric, and cremasteric responses are absent. There is no bladder trouble. Aperients are required for the bowels and spasmodic movements of the limbs readily occur on peripheral stimulation. As to sensation, this has altered to this extent, that on the right side over the leg and thigh there is but little deficiency. A light touch by cotton-wool, a pin prick as sharp, a pin head, hot and cold water tubes, and passive movements of the joints are fairly well recognised. The localisation of touch, "spot naming," is inaccurate. On the left side these forms of sensibility are very deficient but there is still some power of appreciating pressure by the head of a pin from that of the point but no pain arises. The upper limit of loss of sensation is at the original level and there is now a zone on the trunk and outer sides of right thigh corresponding to representation of the seventh dorsal to second lumbar segment, on which light touch is not recognised nor a prick appreciated as such. Thus sensation has greatly improved in the right leg and thigh but has diminished in degree over an area which corresponds to the extent of the surgical procedure.

Liverpool.

FURTHER OBSERVATIONS ON SALTS OF THE ALKALINE EARTHS WHICH AFFECT THE COAGULABILITY OF THE BLOOD.

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IN previous papers which have appeared in THE LANCET¹ it has been shown by Sir Almroth Wright and Dr. W. E. Paramore, Dr. G. W. Ross and myself that the carbonates and lactates of calcium, magnesium, and strontium are potent agents for increasing the coagulability of the blood when administered by the mouth to the human subject in doses ranging from 30 to 60 grains. It seemed desirable to extend this investigation by ascertaining to what extent the same property is possessed by the other salts of the alkaline earths which are available for pharmaceutical purposes and the present paper presents a further instalment of observations directed to this end. For liberty to continue this research in his laboratory my best thanks are due to Sir Almroth Wright.

The method uniformly followed in this investigation has

been to administer at a fixed period of the day either to myself or others, usually patients suffering from urticaria or hæmophilia, a definite dose of the drug under trial, and then to test the resulting variation in the coagulability of the blood during a period of two or more hours. The apparatus used consisted of Sir Almroth Wright's well-known calibrated capillary tubes, into which a definite quantity (5 cubic millimetres) of blood is sucked, the tube being then immersed in water at blood heat, and the contents expelled after a measured interval of time on to blotting paper to see if coagulation has taken place. In spite of criticisms which have appeared as to the sufficiency of this method it has proved itself amply adequate for the purpose in hand, very consistent results having been obtained. In a paper on the subject in the *Biochemical Journal*, vol. ii., part 4, p. 184, C. J. Coleman rightly points out that there is a diurnal fluctuation in the coagulability of the blood of which note must be taken, and that it is particularly affected by the taking of food and drink. I have been careful from the outset to avoid this source of fallacy by limiting the period of observation to the hours from 3 to 7 P.M., the intervening time being employed in quiet sedentary work, the same rule being observed in the case of patients. The results obtained with the different salts available are given below seriatim.

Magnesium lactate.—This salt is only mentioned to say that further experience with it convinces me that it is a valuable drug for combating the accidents of hæmophilia in cases when as sometimes happens the calcium salts do not seem to act. I detailed in a former paper the case of a patient of Sir Almroth Wright who being a sufferer from hæmophilia is liable to periodical oozing of blood from his gums. This symptom has been very effectively treated during the last 12 months by doses of from 40 to 60 grains once or twice repeated either of this lactate or that of strontium. The magnesium salt has the advantage for cases of this kind in that it can easily be prepared extemporaneously by the dispenser by saturating lactic acid with magnesia, which is always available. The large dose unfits the compound for delivery in a mixture; it should be dissolved in hot water by the patient himself. The lactate is a good standard for judging other salts by, a dose of 30 grains generally producing a reduction of 30 per cent. in the time of coagulation either from 3 minutes to 2, or from 2 to 1½.

Boro-citrate of magnesium.—This is a soluble salt said by Martindale and Westcott to have been introduced for the purpose of conveying boric acid into the bladder in cases of cystitis. Its efficiency in this respect I am unable to state, but the drug undoubtedly undergoes some dissociation in the body. It is not without effect as a hæmostatic, but I should class it as inferior to the lactate for this purpose. The following are particulars of some trials with this drug, which were repeated more than once with similar results. On one occasion 30 grains given to the patient before mentioned reduced the coagulation time of the blood from 2¾ minutes to 2 minutes and 20 seconds in the course of 2 hours, a relatively poor result. On another occasion the same dose procured a reduction in the course of 1 hour from 2½ to 1¾ minutes, at which figure the time remained until the conclusion of the experiment 1 hour later. Simultaneously the same dose was taken by myself after the coagulability of my blood had been purposely lowered by the free consumption of fruit; a reduction was obtained from 2½ minutes to 2 minutes and 10 seconds in the course of 50 minutes and to 1¾ minutes at the end of 20 minutes more, no further reduction taking place. The boro-citrate of magnesium is, therefore, not altogether inefficacious in affecting the blood but seems to present no obvious advantage; in this case, also, the bulk of the dose requires dispensing in powder form.

Magnesium carbonate.—Although the doses given by Sir Almroth Wright and Dr. Paramore amounted to 60 grains of the carbonate the usual medicinal dose of 10 grains contains magnesium equal to 23 grains of the lactate, so that the latter quantity, if suitably dissolved in the acids of the alimentary canal, is sufficient to produce a characteristic effect upon the blood. Now it is interesting to note that for a long time past it has been the custom in the treatment of urticaria and other allied affections to associate the carbonate of magnesium with the bicarbonate of sodium and potassium together with bitter infusions, remedies which undoubtedly stimulate the secretion of gastric juice. The supposition that magnesia is beneficial by saturating acids suggested to be in excess in the alimentary canal seems untenable in view of our present knowledge as to the action of these associated remedies. There can be little doubt that urticaria, for example, depends

¹THE LANCET, Oct. 14th (p. 1096) and 21st (p. 1164), 1905, and August 18th (p. 436), 1906.

upon an effusion of serum into the tissues connected with a deficient coagulating power in the blood, though why in this instance the effusion is determined to the skin is unexplained, and that successful treatment involves an increase in this coagulating power seems well established. Therefore in this instance old empirical practice finds a justification in modern research. Though not prompt enough for treating the emergencies of hæmophilia, the continued use of the carbonates of magnesium and lime when properly associated with other drugs which procure their solution in the alimentary canal, seems quite sufficient for the treatment of other disorders of the kind indicated.

Magnesium sulphate, in strong contrast to other salts tried, seems to be quite without effect in increasing the coagulability of blood, even in non-purgative doses. This has been previously ascertained, I believe, by Dr. Paramore.

Bromide of strontium is not a convenient drug to experiment with on account of its soporific effect but seems to share with the lactate the property of increasing coagulability. Two examples will suffice. A dose of 15 grains in my own person produced a reduction from $1\frac{3}{4}$ to $1\frac{1}{4}$ minutes in the course of $1\frac{1}{2}$ hours, and again on another occasion the same dose procured a reduction from $1\frac{3}{4}$ to $1\frac{1}{2}$ minutes in the course of one hour, a trifling effect but corresponding to an equivalent dose of lactate.

Lactophosphate and *glycerophosphate* of lime are two soluble modifications of the phosphate of calcium which have been proposed for use in medicine with a view of more effectually introducing this substance into the economy. My experience with these two drugs may therefore be read with interest. One would have thought that as the lime in milk is principally present as phosphate and is a most important factor in the phenomenon of coagulation by rennet the same substance would play an important part in the coagulation of blood; and again, that if introduced in an extra quantity into the blood some manifest effect of its presence would have been produced. I find, however, that the lactophosphate and the glycerophosphate appear most inert bodies. I have administered them both to myself and to patients in doses far exceeding those employed medicinally with little or no effect. Experiments with the lactophosphate were somewhat cursory as the salt is not very soluble, 10 grains requiring 2 to 3 ounces of hot water for solution; doses taken in the solid form, however, of 15 to 30 grains produced no perceptible result. With the glycerophosphate more extensive trials were made; as an example of which I may record the following exhaustive test. On a certain day of the present year I took 30 grains of the glycerophosphate of lime dissolved in water at 4.40 P.M., my coagulation time being then 2 minutes exactly, and at 5.40 P.M. the time was unaltered. On the next day at 5.30 P.M. the time was $1\frac{1}{4}$ minutes, showing perhaps a trifling result from the previous day; another 30 grains were then taken, and at 6.15 the time was 1 minute 50 seconds. On the third day a third dose of 30 grains was taken at 5 P.M., the coagulation time being again 1 minute and 50 seconds, and at 7 P.M. the time was exactly the same. The figures here shown exhibit the uniformity in the rate of coagulation maintained in the blood of a healthy man, and also the great exactitude obtained with practice with Wright's capillary tubes in testing this phenomenon. A clear day was then allowed to elapse and on the fifth day of the experiment the blood was again examined, and the time found to be slightly over 2 minutes. The large quantity of 90 grains of a reputedly active salt had therefore been taken without any manifestation of what one would expect to be its principal effect. An equivalent quantity of the lactate would, as I know by personal experience, have given a very different result. Four whole days were then allowed to elapse, during which the coagulability of the blood was intentionally lowered by the free consumption of oranges, and the test was then resumed. The day after this interval the coagulation time was taken and found to be 2 minutes and 40 seconds, a condition similar to what is found in urticaria; 45 grains of the glycerophosphate were then taken at the hour of 6 P.M. and by 7.30 the time had become reduced to 2 minutes. On the next day at the same hour the remarkably short period of $1\frac{1}{4}$ minutes was recorded without any more of the salt having been taken, but on the succeeding and final day of the experiment the blood had returned to the old figure of 2 minutes. The second trial, therefore, seemed to have produced an effect, though of a moderate amount compared to the dose taken.

The conclusions arrived at with regard to the drugs mentioned in this paper being based on experiments carried

out with similar thoroughness to this one, though they are not all here recorded for want of space, I feel entitled to express the opinion that these two drugs, the glycerophosphate and lactophosphate of lime, though so much vaunted pharmaceutically, are drugs which in the doses in which they are usually prescribed can have little effect if they are assimilated at all. I may add that the assumption of this large quantity of glycerophosphate, amounting to 135 grains in a few days, produced no sensible effect whatever on my internal economy, neither disturbance of digestion nor of any other function resulting. At the same time I have evidence which is not yet complete that phosphoric acid and some of the soluble phosphates have an influence on the coagulating power of the blood, at any rate in bringing it up to normal, which goes to show that if these phosphates of calcium were absorbed they would be active also in the same direction. In the course of the routine testings of the hæmophilia patient so often mentioned it was found that upon half-drachm doses of Easton's syrup which had been prescribed by Sir Almroth Wright as a tonic, the coagulation time, which was generally in the neighbourhood of three minutes, came up to normal and there remained for some weeks with prevention of the usual hæmorrhages until the effect wore off, when recourse had to be had to magnesia or some other remedy. All the samples of Easton's syrup which I have been able to analyse have contained the large quantity of the equivalent of 18 minims of the dilute phosphoric acid of the Pharmacopœia in each fluid drachm which is apparently necessary to keep the other ingredients in solution—a fact perhaps not known to those who are fond of prescribing this unpalatable preparation and which makes it decidedly injurious to the teeth. Discriminating tests showed that it is the phosphoric acid which has the effect of improving the coagulability of blood, though how it acts I am not prepared to say. Certain phosphates have the same effect, but as my observations in this respect are not complete I need refer to them no further than to say that they lead me to the conclusion that the lactophosphate and glycerophosphate of lime are so comparatively inert because they are not absorbed as a matter of fact, though soluble in a test-tube. In this respect the alimentary canal would seem to be decidedly selective, as witness the case of the sulphate of magnesium.

Of the salts of the alkaline earths my conclusion is that none come up to the lactates and chlorides and carbonates if duly assimilated, and that we should rely on these for the treatment of hæmophilia. For urticaria and conditions of general debility there perhaps is a larger selection. It may be noted that the relation of lime to magnesia in the serum of blood is about that which is maintained in natural calcareo-magnesian waters—that is, the lime is to the magnesia as 2 to 1. Hammarsten's "Physiology," English edition, p. 201, gives a table which shows that the amount present in various serums is very constant, ranging from 0.06 to 0.09 per 1000 parts for the calcium, and 0.02 to 0.03 for the magnesium. In the complete blood, for which I have not been able to find any analyses distinguishing these two bases, the amounts must be larger, though doubtless in the same proportions, as they are both probably ingredients in the clot. A little more light on this subject would be useful; as anterior to the researches which have been carried on in Sir Almroth Wright's laboratory I am not aware that any one had found a use for the magnesium present in the blood in a quantity which relatively is large. Doubtless strontium is able to replace either of these bases when deficient, in a manner conformable to its chemical relations, and so is not toxic, though not a natural ingredient of the body.

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A CASE OF ECHINOCOCCUS DISEASE.

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THE patient was a Mahomedan woman, aged about 29 years, who came to the Victoria Zenana Hospital, Delhi, complaining of enlargement of the abdomen. The history of the case (as such histories generally are in India) was untrustworthy, but it appeared that she had had some enlargement for four years. A year before admission she had given birth to her fourth child. Since then the abdomen had been increasing in size up to the time when treatment at hospital was sought when it was very much enlarged and tense, the