THE BLOOD CALCIUM IN 'IDIOPATHIC' EPILEPSY

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INTRODUCTION

IN view of the suggestions^{1 2} that the convulsions of epilepsy may be due to pathological variations in the blood calcium level it was decided to investigate the blood calcium of a series of epileptics and at the same time examine the evidence in recent literature that might throw light on the possibility of hypocalcæmia being an ætiological factor in this condition.

The close resemblance between the convulsions seen in spasmophilia and after parathyroidectomy in experimental animals, and that type of epileptic fit which Collier³ and others have described as 'myoclonic' is so obvious that it was natural that observations in the variations of blood calcium in epilepsy should be made.

In favour of the hypothesis of a hypocalcæmic factor in fit-causation has been the known fact that bouts of fits are particularly common in females at the time of menstruation, when it has been shown that there are marked variations in the blood calcium level.^{4 5 6 7} Pathological findings have also been in favour of the hypothesis, for Schon and Susman⁸ have reported abnormalities in the histological structure of the parathyroids of epileptics, and areas of hypofunction associated with sclerosis have been noted by Schmiegeld.⁹ From the experimental aspect support has also been given to the hypothesis by the work of Brodski,¹⁰ who reported beneficial results in certain cases of epilepsy from transplanting parathyroid gland tissue into the patients. From the comparative aspect the work of Dryerre and Greig¹¹ on the convulsions of milk fever in cattle, and of Greig¹² on the lambing sickness in sheep—both conditions in which a definite hypocalcæmia has been demonstrated—naturally again has suggested the possibility of a low blood calcium being of importance in the fits of 'idiopathic' epilepsy. On the other hand, the convulsions of eclampsia¹³ and in beriberi¹⁴ have been shown conclusively to be unassociated with a low concentration of calcium in the blood.

The largest series of epileptics subjected to calcium investigations was that reported by Lennox and Allen,¹⁵ who examined 77 cases and found the blood calcium level to be normal, though the calcium level in the cerebrospinal fluid was slightly low. Armstrong and Hood¹⁶ reported normal blood figures, and normal figures in smaller numbers of cases have also been ruled

by Osnato, Killian, Garcia and Mattice,¹⁷ Patterson,¹⁸ Stewart and Percival,¹⁹ and Hepburn and Neibaum.²⁰

PERSONAL STUDIES

For the purpose of this investigation typical epileptic cases were taken, and for the time being all medicinal and dietetic treatment was stopped. As certain observers have suggested that varying degrees of activity of the autonomic nervous system^{21 22 23} and alterations in the sugar level^{24 25} have an influence on the blood calcium, all specimens were taken when the patients were under similar basic conditions, and the period chosen was that of fasting before breakfast. The serum calcium was estimated by the Pincussen and Schimmelpfing²⁶ modification of the method of Kramer and Tisdall, i.e. the serum calcium was precipitated by potassium oxalate, and allowed to stand for 24 hours instead of the 30 minutes originally recommended, the precipitate being then washed, dissolved in dilute sulphuric acid and titrated against standard potassium permanganate solution.

Fifty-four cases (24 female and 30 male) were examined. The values found were within fairly definite limits, though the variations were far greater than those noted by observers in normal subjects. Thus though the average value for the female cases was 10.6 mg. per 100 c.cm. serum, the figures obtained varied between 9.6 and as high as 12.2. While the male average value of 10.5 mg. per 100 c.cm. was obtained from figures varying from 8.5 and 13.3 mg. per 100 c.cm., the vast majority of the values certainly lay between 9.5 and 12.

The average figures obtained, it will be noticed, are slightly higher than these recorded in healthy subjects. Although Watehorn²⁷ gives 10 to 10.8 as the normal figures, most observers, using the method of Kramer and Tisdall, give figures between 9.6 and 9.9. Di Foutsin²⁸ has, however, noticed that persons in bed for long periods tend to have a raised serum calcium; and it may be that the slightly high figure is due to this factor, for though the majority of the patients were not permanently in bed, they were all liable to long periods there, after a severe bout of fits.

Attempts were made to collect specimens of blood from patients immediately before or in the fits, but owing to the fact that the moment of the onset of the fit can never be known and that during the fit the convulsions make venepuncture impossible, only three specimens were obtained, two of which gave normal readings and one the high figure of 13.1 mg. Specimens of blood withdrawn from a case of status epilepticus in the twentieth fit, after the twenty-second fit, and one hour after the fits had been stopped by injection of luminal, all gave normal readings. As one would expect from these figures, an intravenous injection of 20 c.cm. of 10 per cent. calcium glucolate into one patient during a short bout of fits yielded no beneficial result. Similarly Klein and Forcrone²⁹ have reported that they obtained no benefit from intravenous injection of calcium chloride.

As mentioned above, it has been stated that alterations in blood sugar level influence the blood calcium figure.^{24 25} Since blood sugar investigations were being undertaken in the hospital, it was decided to withdraw blood specimens at the same time for calcium estimation. A fasting specimen was first withdrawn, and then 50 gm. glucose given and further specimens withdrawn at half-hourly intervals. Twenty-eight cases were investigated in this manner. No regular curve was obtained corresponding to the rise and subsequent fall of the blood sugar, and although the calcium readings were not constant in individual cases, the values found were all within the limits of normal physiological variation and experimental error.

In combination with other observations it was decided to examine the influence of variations on the tension of the autonomic nervous system in the number of fits and the blood calcium levels. In five epileptics the parasympathetic nerves were paralysed by giving $\frac{1}{100}$ gr. atropine three times a day for a month. In all cases dilation of the pupil occurred, and towards the end of the month, when the patient was fully under the influence of the drug, blood specimens were withdrawn. No alteration in the number of fits occurred and no appreciable change in the blood calcium resulted. These results are in accordance with the findings of Lietes,²¹ who reports that division of the vagi, though giving a temporary fall in the calcium level, has no lasting effect.

A further series of five epileptics were subjected to sympathetic stimulation by giving $\frac{1}{2}$ gr. ephedrine hydrochloride three times daily. Again no improvement was found in the number of fits and the blood calcium remained approximately the same. This last finding was in accordance with these noted by Lamelas,³⁰ who reports that section of splanchnics and injection of adrenaline have no influence on the blood calcium of cats, but they do not correspond with the findings of Hetenyi and von Gaal,²³ who report a fall with stimulation of the sympathetic, or of Richter,²² who reports a rise.

CONCLUSIONS

The calcium content of the blood in epilepsy is normal, and thus the condition cannot be related to the convulsions of spasmodophilia or milk fever. The blood calcium value is independent of the blood sugar level and neither the number of fits nor the blood calcium is influenced by alterations in the tension of the autonomic nervous system.

REFERENCES

- ¹ GRAHAM, S., *Glasgow Med. Jour.*, 1932, **117**, 113.
- ² COLIN, ANDRÉ, *Convulsions et épilepsie chez les enfants*, Paris, 1927.
- ³ COLLIER, J., *Brit. Med. Jour.*, 1924, **2**, 1046.
- ⁴ BELL and HICKS, *Brit. Med. Jour.*, 1909, **1**, 517.
- ⁵ WIDDOWS, S. T., *Biochem. Jour.*, 1923, **17**, 34.
- ⁶ OKEY, STEWART and GREENWOOD, *Jour. Biol. Chem.*, 1930, **87**, 91.
- ⁷ SHARLET, H., CONSCADEN, J. H., and LYLEW, *Arch. Int. Med.*, 1927, **39**, 780.

- ⁸ SCHON, H. I., and SUSMAN, W., *Brain*, 1927, **50**, 53.
- ⁹ SCHMIERGELD, quoted by Vizioli, *Ann. di nevrol.*, 1921.
- ¹⁰ BRODSKI, J., *Wien. klin. Woch.*, 1931, **44**, 707.
- ¹¹ DRYERRE, H., and GREIG, J. R., *Vet. Record*, 1929, **9**, 509.
- ¹² GREIG, J. R., *Vet. Record*, 1929, **9**, 509.
- ¹³ BODE, R. VON, and LIEBMANN, S., *Arch. exp. Path. Pharm.*, 1925, **109**, 178.
- ¹⁴ UNGAR, A., *Biochem. Zeits.*, 1927, **120**, 357.
- ¹⁵ LENNOX, W. G., and ALLEN, M. B., *Arch. Neurol. and Psychiat.*, 1924.
- ¹⁶ ARMSTRONG, E., and HOOD, W., *Jour. Ment. Sci.*, 1927, **73**, 111.
- ¹⁷ OSNATO, M., KILLIAN, J. A., GARCIA, T., and MATTICE, M. R., *Brain*, 1927, **50**, 581.
- ¹⁸ PATTERSON, *Psychiat. Quart.*, 1929, **3**, 82.
- ¹⁹ STEWART, C. P., and PERCIVAL, G. H., *Quart. Jour. Med.*, 1926, **19**, 235.
- ²⁰ HEPBURN, J. A., and NEIBAUM, A. H., *Jour. Amer. Inst. Homeopathy*, 1931, **24**, 559.
- ²¹ LEITES, S., *Biochem. Zeits.*, 1925, **116**, 47.
- ²² RICHTER, M., *Zeits. exp. Med.*, 1926, **28**, 582.
- ²³ HETENYI, G., and VON GAAL, A., *Zeits. exp. Med.*, **75**, 516.
- ²⁴ KYLIN, E., *Acta Med. Scand.*, 1927, **66**, 197.
- ²⁵ CULHANE, K., *Biochem. Jour.*, 1927, **187**, 72.
- ²⁶ PINCUSSEN and SCHIMMELPFING, *Biochem. Zeits.*, 1927, **170**, 42.
- ²⁷ WATEHORN, G., *Quart. Jour. Med.*, 1925, **18**, 288.
- ²⁸ DI FOUTSIN, *Biochem. Zeits.*, 1926, **170**, 221.
- ²⁹ KLEIN, E., and FORCIONE, E., *Jour. Nerv. Ment. Dis.*, 1927, **65**, 372.
- ³⁰ LAMELAS, J., *Amer. Jour. Physiol.*, 1930, **95**, 111.