CXXII. THE CALCIUM CONTENT OF THE BLOOD SERUM IN CASES OF GOUT.

BY VINCENT COATES (*Royal Mineral Water Hospital, Bath*)
AND PERCY CHARLES RAIMENT (*Oxford*).

From the Biochemical Laboratory, Oxford.

(Received July 25th, 1924.)

THE concentration of the inorganic salts of the blood serum in cases of impaired metabolism such as gout, seems to have attracted very little attention although there have been estimations of the urinary calcium under such conditions. Thus Little [1909] examined the urine of a gouty patient both during an acute attack and in a quiescent interval with the result that he found a calcium content of 0.067 g. during the acute period which amount rose to 0.122 g. during the quiescent stage. His calculations are for CaO. He quotes no figures for normal people. Van Noorden [1907] makes no reference to the urinary calcium output in gout cases.

Of investigations of the inorganic salts of the blood sera in this disorder we can only find one recorded examination. Lyman [1917] found a calcium content of 6.0 and 5.7 mg. per 100 cc. of serum in two cases of gout. His normal cases were also approximately 6.0 mg. %. Records of investigations in pathological conditions possibly allied to gout have been made by Weil, Guillaumin and Weismann-Netter [1923]. In an extensive study of the inorganic salts not only did they estimate the calcium in rheumatic cases but at the same time recorded observations on cases of atheroma and of hypertension without atheroma. These findings appear to us so important that we have abstracted their results, taking the average readings of their examinations.

Table I.

Type of case	No. of cases	Average Ca in mg. %
1. Normal	3	10.90
2. Hypertension without atheroma	9	11.02
3. Atheroma	10	13.08
4. Chronic rheumatism	11	14.30

We have therefore thought it advisable to undertake an investigation into the inorganic salts of the blood serum in undoubted cases of gout and the present short paper deals with the calcium findings. We chose the calcium because in the first place it appears to have been almost entirely neglected, secondly because calcium has been found to be a constituent of gouty tophi, and thirdly because cases of long standing gout in some instances show gross

bony lesions. The cases investigated were carefully selected by one of us (V. C.) at the Royal Mineral Water Hospital, Bath, the greatest care being taken to ensure that they were cases of true gout. These cases fell into two classes, viz:

1. Patients from whom it was possible to obtain a clear history of typical arthritic attacks and who exhibited tophaceous deposits, but who at the time of veni-puncture were in a quiescent stage, and

2. Patients seen within thirty-six hours of an acute attack but who had received no treatment.

The blood was collected by veni-puncture from the median basilic vein and allowed to clot in sterile tubes. The resulting serum was centrifuged, kept in the ice-chest and examined as soon as possible. The method of estimating the calcium was that described by Kramer and Tisdall [1921], the amount of serum used being 1 cc. Duplicate determinations were done in all cases where it was possible. The figures we obtained are given below:

Table II.

Subject	Age	Ca content in mg. %	Remarks
A. H.	46	16.4	Interval
H. J. S.	48	22.6	"
B. P.	52	16.4	Acute
J. S.	53	20.0	Interval
W. A.	63	18.4	"
H. L.	48	16.8	Acute
		24.0	Interval
G. L. T.	51	16.0	"

Average of eight determinations = 18.87 mg. %.

An examination of the above figures will show that we have obtained a figure for the calcium of a very much higher order than either Lyman [1917] in gout or Weil [Weil *et al.* 1923] in rheumatism. This increase in the calcium might be due to several causes such as:

1. Variations from the normal of no pathological significance.
2. Increasing age.
3. Hypertension with or without atheroma, both of which conditions commonly accompany gout.
4. Decolorisation of the permanganate by bodies other than calcium, thereby obtaining a high figure.

The first cause can be dismissed in a few words. The calcium of the blood serum of mammals seems to be one of its steadiest constituents. Thus Meigs, Blatherwick and Carey [1919] found a concentration in cows of 9.7 mg. %. Rona and Takahashi [1913], working with horse serum, report 12 mg. %. Watanabe [1918] finds the percentage calcium in the rabbit to vary from 10.5 to 12.8 mg., whilst Boggs [1908] mentions 10 mg. for the dog, and Kramer and Tisdall [1921] give 9.8 to 10 mg. for the human adult. It is therefore apparent that the adult mammal keeps a very constant level of blood calcium and in face of the observations quoted above it seems to us a fair assumption

that the variation from the normal that we have observed has some biochemical significance.

The second cause—advancing age—appears at first sight to be a possible one, but to that view there is, in our opinion, two objections. The first is based upon two recent observations on two people whose ages were 57 and 52, but who were free from, and had never suffered from, gout. Their calcium content was 10.2 and 14.0 mg. % respectively. The second objection is based upon the figures of Weil given above. There we have quoted figures for cases of hypertension and atheroma, and although he has unfortunately omitted to give the age of the patients, yet atheroma, at least, is not usually associated with youth, and we think it a fair assumption that the ages do not differ materially from those of our own gout cases. Assuming this to be so, an inspection of his table will show that his average for hypertension is only 11.02, and for atheroma 13.08, figures far below the average of our gout cases.

The reasons above stated apply with equal force to a consideration of the point whether the rise is due to any condition of atheroma or hypertension. As both these conditions are commonly associated with gout we have given the matter considerable attention but in view of the figures quoted above we feel unable to conclude that so large a rise in the calcium content as we show can be due, entirely, to either cause.

The fourth possibility, viz. that the permanganate is decolorised by some body other than the calcium is worthy of a good deal of consideration. Uric acid and urates present in the serum might account for some of the permanganate. To test this point a determination on the serum of G. L. T. in Table II has been made. Taking the same serum 1 cc. of a solution of sodium urate, containing 0.5 g. in 500 cc. of water, was added to 1 cc. of the serum and the calcium content of the mixture ascertained by the same method. The result was 15.8 mg. % against 16.0 mg. % for the same serum without the added urate. This figure, allowing for experimental error, seems to us to be of the same value and we conclude that within moderate limits, the urates are not affecting the result.

Clark [1921] has pointed out the difficulty of removing all the adsorbed oxalates, and also the impossibility of performing unlimited washings owing to the solubility of calcium oxalate. As oxalates will decolorise permanganate there is some force in the argument that imperfect washings will produce a high calcium value. But in this connection we would like to point out that we have adhered strictly to the method of Kramer and Tisdall [1921] and that they themselves by that method arrive at a normal value of approximately 10 mg. %. If, by the same method, we arrive at a higher figure in certain pathological cases we feel justified in the assumption that any error due to adsorbed oxalates or any other cause will be of approximately the same order, and the increase that we find may justifiably be credited to the calcium.

For all these foregoing reasons we have ventured to say that the calcium

content of serum in cases of gout is considerably raised. The causes and significance of this elevation we have not presumed to discuss as the investigation is still proceeding, and we hope in the near future to be able to publish results of the concentration of other inorganic salts in cases of this obscure metabolic disorder.

It is worthy of note that in one or two recorded cases of hyperplasia of the parathyroids there has been atheroma accompanied by calcification of tendons, etc. [Barker, 1922] Also de Wesselow [1923] has noted a case considered clinically to be one of hyperplasia of the parathyroids in which the calcium content of the serum reached a very high figure.

We have to express our thanks to Dr Gibson of the Radcliffe Infirmary for kindly supplying us with the blood of two non-gouty patients.

CONCLUSIONS.

1. The examination of the calcium content of the blood serum in cases of gout shows a considerable rise from the normal.
2. A short discussion attempts to show that this rise is specifically due to the gout and not to any extraneous factor.

REFERENCES.

- Barker (1922). *Endocrinology and Metabolism*, **1**, 702.
Boggs (1908). *Bull. Johns Hopkins Hosp.* **19**, 201.
Clark (1921). *J. Biol. Chem.* **40**, 487.
Kramer and Tisdall (1921). *J. Biol. Chem.* **47**, 475.
Little (1909). *Biochem. J.* **4**, 30.
Lyman (1917). *J. Biol. Chem.* **30**, 1.
Meigs, Blatherwick and Carey (1919). *J. Biol. Chem.* **37**, 1.
Van Noorden (1907). *Metabolism and Pract. Medicine*.
Rona and Takahashi (1913). *Biochem. Z.* **40**, 370.
Watanabe (1918). *J. Biol. Chem.* **36**, 531.
de Wesselow (1923). *Quart. J. Med.* **16**, 351.
Weil, Guillaumin and Weismann-Netter (1923). *Compt. Rend. Soc. Biol.* **88**, 732.