have previously been recorded (Symington *et al.*, 1958; Symington, 1959). The microscopical appearances in fact resembled those found in the adrenogenital syndrome, in which condition there is an excess of corticotrophin. It has been suggested that Cushing's syndrome may be due to hypersensitivity of the adrenals to corticotrophin, which is not present in excessive amounts (Christy, Wallace, and Jailer, 1955).

A raised urinary pregnanetriol is characteristic of adrenal hyperplasia due to the adrenogenital syndrome. In this case, however, the mean ratio of the 11-desoxy/11-oxygenated ketogenic steroids was 0.35 (Table II), which is normal. The ratio of these fractions in the adrenogenital syndrome is much higher and averages 2.3 (Hill, 1960).

The responses to 9α-fluoro-16α-hydroxyprednisolone and A.C.T.H., together with the negative Patterson test for dehydroisoandrosterone, indicated that this boy was suffering from adrenocortical hyperplasia and not from an adrenal adenoma or carcinoma.

The prognosis in Cushing's syndrome due to adrenocortical hyperplasia recorded in adults is bad and the average expectation of life without treatment is about five years (Bishop, 1954). Bilateral total adrenalectomy is the treatment of choice, and in our opinion the anterior transverse upper abdominal approach is a highly satisfactory one for this procedure (Aird and Helman, 1955). Partial adrenalectomy is unreliable, as the patients are apt either to relapse or to require maintenance cortisone, anyway, in order to prevent adrenal crises.

The results of total adrenalectomy on this boy have been most satisfactory and he has been very well for the past 20 months on small maintenance doses of cortisone and fludrocortisone. He now has the normal appearances and vigour of a boy of 12. His genitalia are developing with puberty, which seems to be taking place normally. He started to grow four months after adrenalectomy and he now shows a pubertal spurt of growth.

Summary

A case of Cushing's syndrome due to adrenocortical hyperplasia developing in a 9-year-old boy is described, in which the presenting symptoms were obesity and arrested growth.

He was treated successfully by total bilateral adrenalectomy through a transabdominal incision.

The diagnostic tests differentiating this condition from adrenal tumour are described, and the results compared with those found in the adrenogenital syndrome. A follow-up report is given over two years, with particular reference to growth and development.

We thank Professor D. V. Hubble for his help and encouragement in presenting this case, and Professor T. Symington for his report and explanation of histological sections. We are grateful to Dr. E. C. Butterworth, of the Biochemistry Department of the North Staffordshire Royal Infirmary, for the urinary steroid estimations, and to Dr. E. E. Hill and the Department of Clinical Endocrinology, Birmingham, for the fractionation of 17-ketogenic steroids. We also acknowledge the help of Dr. W. E. C. Astle and Dr. G. Anderson with the radiology, and Dr. L. Bowcock for the photographs.

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Preliminary Communications

An Isotope Test of Calcium Absorption *

At the present time the measurement of calcium absorption requires full calcium balance procedures. A valid calcium balance takes at least three or four weeks to perform and the determination of the state of calcium absorption in any individual subject is therefore time-consuming and costly. It is probably fair to say that many of the problems of calcium absorption remain unsolved largely because of the technical difficulties involved in their study.

The availability of radioisotopes of calcium and strontium, and in particular the availability of calcium-47, which is a γ-emitting isotope with a relatively short half-life, suggested the possibility that a simple isotopic procedure might be developed for the measurement of calcium absorption. The fate of ingested isotopes of calcium and strontium has been studied (Staub, 1954; Blau *et al.*, 1954; Bronner and Harris, 1956; Samachson, 1960), but no standardized test procedure has been established. The present paper describes a simple isotopic procedure for estimating calcium absorption based on plasma activity two hours after oral administration of the isotope.

METHODS

The isotope was usually given with 250 mg. of calcium as calcium chloride not less than one hour after the last meal; no further food was allowed for at least one hour after the oral dose had been given. Some concentrated orange juice was also given to render the mixture more palatable. Samples of venous blood were taken at intervals after the administration of the dose, and the plasma activity was determined and expressed as a percentage of the dose per litre of plasma. In a few cases the isotope was given with calcium carbonate carrier. The isotope was equilibrated for 24 hours with the carrier before administration, and filtration of the material showed that only about 10% of the radioactivity was filterable.

The dose used was 7.5 μc of calcium-47 (half-life 4.7 days) or 5 μc of calcium-45 (half-life 152 days). The calcium-45 was given only to subjects over the age of 40.

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With calcium-47, 10 ml. of plasma was counted in a well-type scintillation counter (Harshaw NaI(Tl) crystal type 8F8) under such conditions that any contribution to the count rate by scandium-47 was excluded. When the count rates were low the calcium was precipitated from 20 ml. of plasma with an equal volume of saturated ammonium oxalate, and the precipitate was redissolved in concentrated hydrochloric acid and made up to 10 ml. With calcium-45, 10 ml. of plasma was mixed with saturated ammonium oxalate and left to stand for 12 hours. The mixture was then drawn through a filter-paper disk by vacuum filtration and the precipitate washed with saturated ammonium oxalate. The activity in the precipitated film was determined with an automatic end-window Geiger counter (Nuclear Chicago gas-flow detector type D 47 with " micromil " window).

There were 34 normal subjects who were given only calcium-47. They consisted mainly of members of the laboratory and medical staff, but also included a few patients convalescing from acute illnesses. There were 27 cases of osteoporosis as defined by the radiological procedure of Barnett and Nordin (1960); 21 cases of steatorrhoea (11 idiopathic, 8 post-gastrectomy, and 2 pancreatic); and 12 patients receiving steroid therapy for various clinical conditions. The steroid used was prednisolone (7.5–30 mg. daily) or dexamethasone (3–6 mg. daily). There was also one case of Cushing's syndrome.

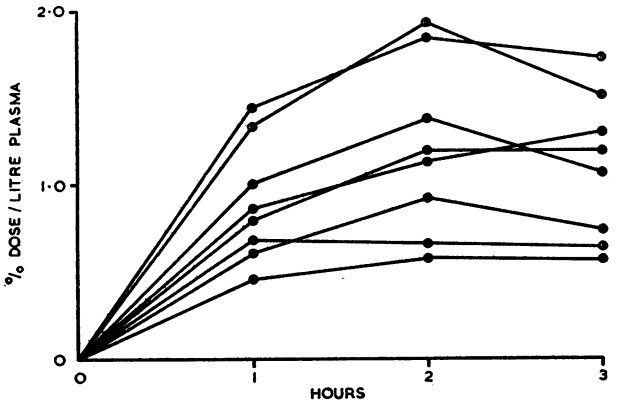

FIG. 1.—Plasma activities in eight subjects at one, two, and three hours after oral administration of calcium-47 chloride.

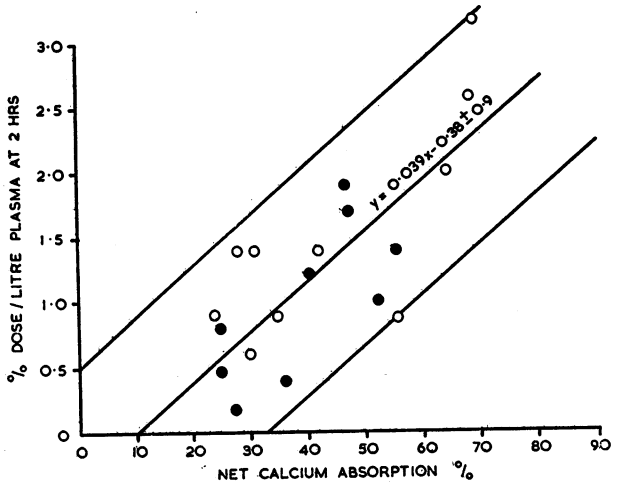

FIG. 2.—Relation between two-hour plasma activity and net calcium absorption on calcium balance in 19 cases. Black dots represent cases in which balance and test were simultaneous. Circles represent cases in which the balance had been performed some time before the isotope test.

RESULTS

In the first eight normal subjects the blood was taken hourly for three hours and the results obtained are shown in Fig. 1. The activity in the plasma rose slightly in the first and second hours and then remained steady or fell slightly in the third hour. On the basis of these results the two-hour blood activity was selected as the significant value.

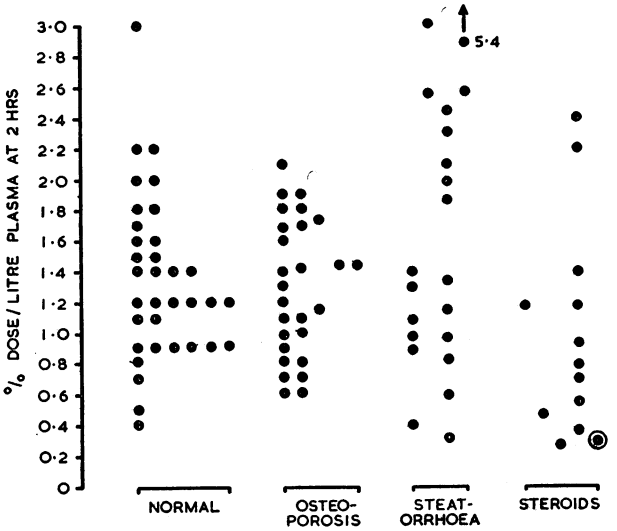

FIG. 3.—Two-hour plasma activities in various diagnostic groups.

Absorption tests were carried out on nine subjects in whom calcium balances were being performed at the same time and in 10 in whom balances had been done within the previous year. The net absorption of calcium calculated from the calcium balance is compared with the isotope test in Fig. 2, which indicates that there was a reasonably good agreement between the two procedures (correlation coefficient $=0.78$; $P<0.01$). The regression line of the plasma activity on the net absorption is: $y = 0.039x - 0.38$ and the 95% confidence limits are $\pm 0.9\%$ of the dose per litre. If only those cases are considered in which the isotope tests were carried out during the balance, the 95% confidence limits are reduced from ± 0.9 to $\pm 0.7\%$ dose per litre of plasma.

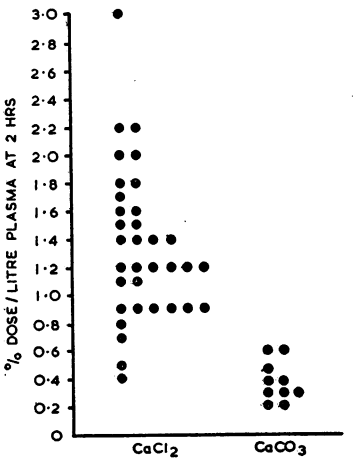

FIG. 4.—Two-hour plasma activities in normal subjects given calcium-47 in calcium chloride carrier (left) and in calcium carbonate carrier (right).

The results of absorption tests in 34 normal subjects, 27 cases of osteoporosis, 21 cases of steatorrhoea, 12 patients on steroid therapy, and one case of Cushing's syndrome are shown in Fig. 3. The two-hour plasma activity in the normal subjects extended from 0.4 to 3% of the dose per litre. The range of values observed in the cases of osteoporosis was essentially the same. In the cases of steatorrhoea the results extended right across the normal range, but there were no cases of untreated osteomalacia in this group. There was no apparent relationship between plasma activity and post-gastrectomy or idiopathic

steatorrhoea, but it may be worthy of note that the two lowest values obtained were in cases of pancreatic steatorrhoea.

In patients on steroid therapy the plasma activity ranged from 0.3 to 2.3% per litre, but all except two were below 1.4%. The two highest values were obtained in one patient who had been on steroids for only two weeks and in another on 7.5 mg. of prednisolone a day. The lowest value observed was in the case of Cushing's syndrome.

Ten subjects were given calcium-47 carbonate instead of calcium-47 chloride. The results of these tests (Fig. 4) indicate that the absorption of isotope in calcium carbonate carrier was inferior to its absorption in calcium chloride.

DISCUSSION

The procedure we have described is simple and quite suitable for out-patient use. Its validity depends upon the relationship between the two-hour plasma activity and the net calcium absorption calculated from the balance data. The observed correlation warrants the view that the isotopic procedure provides an index of calcium absorption. The 95% confidence limits are rather wide, but we have shown that it is partly accounted for by the long interval (up to one year) between some of the tests and the balances. Even when these latter tests are included the agreement is close enough to suggest that calcium absorption is a fairly constant factor in any given individual. The relatively wide normal range is therefore presumably not a function of the isotopic procedure as such but reflects the wide range of calcium absorption in normal subjects.

The results obtained in osteoporosis are entirely compatible with the results of our balance studies in this type of case (Nordin, 1960), which have shown that the great majority of patients with osteoporosis absorb calcium normally.

The results obtained in steatorrhoea may appear surprising since lower plasma activities might have been expected. However, this is a heterogeneous group of cases, many of them on treatment, and does not include any cases of untreated osteomalacia. Our balance studies (Nordin, 1961) have shown that the faecal calcium content in cases of steatorrhoea is slightly higher than that of normal subjects at the same intake levels, but the difference is a relatively small one.

The results obtained in patients on steroid therapy are also compatible with our own previous observations and with those of other workers (Bunim *et al.*, 1958; Slater *et al.*, 1959). On moderate doses of corticosteroids the only consistent abnormality of calcium balance so far observed is an impairment of calcium absorption. It would be compatible with the view that osteoporosis is caused by negative calcium balance to suggest that this malabsorption of calcium is at least a factor in the pathogenesis of steroid osteoporosis.

The isotopic procedure lends itself to the large-scale comparison of the absorption of different calcium compounds. So far we have only tested the absorption of calcium carbonate, which is of particular interest because of its use in the fortification of bread. The results suggest that calcium carbonate may be less well absorbed than calcium chloride, but clearly further work is required.

In conclusion, we suggest that this simple procedure may lend itself to the study of calcium absorption on a much larger scale than is possible with conventional balance techniques.

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SUMMARY

Calcium-47 in 250 mg. of calcium chloride was given to 34 fasting normal subjects. The maximum plasma activity was reached about two hours later and ranged from 0.3 to 3% of the dose per litre of plasma.

There was a good correlation between the two-hour plasma activity and the net calcium absorption as determined by calcium balance in 19 subjects ($r=0.78$; $P<0.01$).

Cases of osteoporosis and of steatorrhoea and patients on steroid therapy were also studied; absorption by most of those on steroid therapy was low.

Absorption of the isotope appeared to be reduced when it was given in calcium carbonate carrier.

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Medical Memoranda

Visceral Scleroderma Without Skin Involvement

Only two reports of visceral scleroderma without skin involvement have been found in the literature. In the following case the patient presented with persistent vomiting, but there were no skin changes suggestive of scleroderma, and the diagnosis was not suspected in life or at necropsy. However, the histological examination of the heart, lungs, and alimentary tract showed changes characteristic of visceral scleroderma.

CASE REPORT

The patient, a man of 20, gave a history of persistent vomiting, almost every day for a year, with consequent loss of weight and, in the last month, generalized prostration. No other suggestive symptoms could be elicited by systematic questioning.

On examination he was grossly emaciated and too weak to sit up. His blood-pressure was 70/50 and his pulse irregular, but no abnormality was found on clinical examination in any other system.

An *x*-ray film of the chest taken at the bedside was unhelpful. An electrocardiogram showed multiple ventricular extrasystoles. Plasma electrolyte determinations gave the following results: sodium 135 mEq/l., potassium 3.5 mEq/l., chloride 71 mEq/l. Blood urea was 89 mg./100 ml. Total serum albumin was 3.4 g./100 ml., and globulin 1.6 g./