degrees of heart-block, and in two cases, our own and that of Stephen (1954), dyspnoea was associated with chest pain so as strongly to mimic myocardial infarction.

On clinical examination cardiac enlargement and some degree of congestive failure were often found. Five patients (25%), including our own, had persistent hypotension throughout their illness. Almost three-quarters of this group developed arrhythmias at some stage, and 19 of the 20 were classed as electrocardiographically abnormal. A wide range of E.C.G. abnormalities was reported, but no single abnormality can be said to be diagnostic. There was a wide variation in the degree of cardiac infiltration necessary to cause death. In every case, however, the heart was involved as part of a disseminated process, though in two cases granulomata were discovered in only two other sites in the body. The case reported in this paper is almost unique in that, while the myocardium was so extensively involved, almost no evidence of the presence of the disease was forthcoming from a histological examination of the remaining organs.

Summary

A case is reported of fatal myocardial sarcoidosis and the literature is briefly reviewed. About one-third of cases of this condition are seen in congestive heart failure, and occasionally the presentation resembles myocardial infarction. Three-quarters of the patients die suddenly—about one-fifth without premonitory symptoms—and at necropsy disseminated sarcoidosis is commonly found. In the case reported here the disease was virtually confined to the myocardium and mediastinal lymph-nodes.

It is a pleasure to record our thanks to C. L. Blenkinsop, Esq., H.M. Coroner for the Borough of Rotherham, for permission to publish this case; to Dr. R. S. Weetch for details of the clinical history and for the electrocardiographic reports; and to Mr. R. T. Clegg for technical assistance.

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Preliminary Communications

Movement of Strontium in the Human Body

Irradiation of tissue from internally deposited radioactivity may under certain circumstances be the limiting hazard. The occupational hazard to luminizers from radium is a classical example. Irradiation of bone and bone-marrow from strontium-90 in world-wide fall-out is thought to be another. Since strontium-90, unlike radium with its decay products, does not emit γ -rays, the estimation of the body burden has to be made by indirect means rather than directly with a whole-body counter. Knowledge of the rate of turnover of bone salt and replacement of pre-existing strontium by new strontium (and strontium-90) from the diet is for this purpose essential.

Turnover and Replacement.—In this paper the terms “turnover” and “replacement” are not used interchangeably. For instance, a unit of bone may turn over—that is, be resorbed and re-formed each year. If all the old building blocks are re-utilized the replacement is nil. Only if none of the pre-existing material is re-utilized is the rate of replacement equal to the rate of turnover.

TURNOVER OF CALCIUM

Strontium, which has no accepted physiological function, is usually considered together with its chemical analogue, calcium, which is known to be essential for bone and soft tissue.

Bauer *et al.* (1957) have calculated the rate of turnover of calcium in bone. Their method was to inject radioactive calcium intravenously and to analyse the rate of loss of the radioactive calcium from plasma. An essential requirement of the method is that the marker labels all the calcium fractions of the exchangeable pool uniformly; and this seems to be true for calcium. From the second to tenth day after the injection this loss was exponential, and was attributed to the combined effect of excretion and incorporation into bone. Since the excretion was measured, the rate of incorporation into bone could be calculated as about 0.5 g. of calcium per day from an exchangeable pool of about 5 g. of calcium. If all the bone so formed were long-lived, this would be equivalent in a standard skeleton containing 1 kg. of calcium to nearly 20% turnover per year.

Bluhm *et al.* (1960) noted that the exponential rate of loss of radioactive calcium from plasma became slower after about 10 days. To explain this they postulated that there was additional loss from the exchangeable pool by diffusion into some larger space, so they deduced a rate of turnover about one-half to one-third of that

of Bauer *et al.*—say 8% per year. An alternative explanation for change of rate is that some newly formed bone is very labile and soon resorbed.

REPLACEMENT OF STRONTIUM: SINGLE-DOSE EXPERIMENT

Previously we (Bishop *et al.*, 1960) have injected strontium-85 (0.5 μC), a γ -emitter, intravenously into two normal subjects and were able to follow its loss from plasma for two days, its excretion for three to four months, and with a whole-body counter its retention for a year. Retention, which must equal the injected less the excreted, was not a simple exponential function but presumably the sum of many. After a few weeks it could be expressed as a power-function.

Elsewhere Loutit (1961) analysed the loss of strontium-85 from plasma in the first week or so, and deduced an exchangeable pool of about 2.75 mg. of strontium and clearance into bone of 0.4 mg. of strontium a day. This calculation was based on an assumption that the urinary specific activity would be the same as in plasma, as appears to be the case with calcium (Blau *et al.*, 1954; Bauer *et al.*, 1957). (Recent work by ourselves shows that this is not true for strontium (see below)). However, the statistic of 0.4 mg. a day was not used to calculate turnover, because while the calculation is valid for exchange mechanisms it may not be applicable to osteogenesis. Instead the following argument was adduced. Something like 85% of the injected isotope was excreted within the year. The remaining 15% was retained in definitive as distinct from temporary bone. Normally about 20% of dietary strontium (about 2 mg./day in the United Kingdom) is absorbed. Therefore replacement of strontium in bone is about:

$$0.2 \times 2 \times 365 \times 0.15 \approx 22 \text{ mg./year.}$$

The skeleton with 1 kg. of calcium and an average Sr:Ca ratio of 320 $\mu\text{g./g.}$ (Bryant and Loutit, 1961) should contain 320 mg. of strontium. Thus the replacement is $22/320 \times 100 = \text{about } 7\% \text{ a year.}$

DAILY-DOSE EXPERIMENT

More recently we (Carr *et al.*, 1962a) have reported results showing that strontium-90 built into grain in biological processes of plant growth is equally available for absorption by man as strontium-85 incorporated into milk by a cow. Three subjects on constant diet drank 0.5 μC of ^{85}Sr daily for a month, which can be taken as four weekly periods. An equilibrium was set up within a week, when (a) plasma levels were constant: 3, 7, and 3 m $\mu\text{C/L.}$ respectively; (b) daily urine excretions were constant: 25, 60, and 50 m $\mu\text{C/day}$ respectively, so that renal clearances from plasma were approximately:

$$\frac{25}{3}, \frac{60}{7}, \frac{50}{3}, \text{—i.e., } 8, 8, 17 \text{ l./day.}$$

The balances in the second to fourth periods for the three subjects combined indicated a final retention of 6% of ingested isotope. These values were in accord with direct measurements made by Dr. J. Rundo with a whole-body counter. If 30 m μC —that is, 6% of 0.5 μC —was being transferred daily to bone in each case, the bone clearance for this ^{85}Sr was 5–10 l./day according to the subject.

These diets, being based on milk, were in fact low in stable strontium (1 mg./day), so that the subjects were in the first week in negative balance for stable strontium.

In the later weeks of approximate balance the numbers suggest that up to 60 $\mu\text{g.}$ —that is $6/100 \times 1,000$ —of dietary strontium were entering bone by replacement per day.

However, though the level of ^{85}Sr in plasma was then constant there is still a disequilibrium of this marker between the various compartments. The specific activity of diet (500 m $\mu\text{C/mg. Sr}$) was far higher than that of plasma 3–7 m $\mu\text{C/l.}$: $\sim 50 \mu\text{g./l.}$ —that is 60–140 m $\mu\text{C/mg. Sr}$. The plasma must be fed from at least two sources—the diet and resorbing unlabelled bone. Since the plasma specific activity was 3.5 to 8 times less than that of the dietary source, the bone must be contributing 2.5 to 7 times more stable strontium than diet.

Calculations suggest that our three subjects were absorbing from the gut one-eighth to one-fifth of the dietary ^{85}Sr and thus 120 to 200 $\mu\text{g.}$ of strontium per day, since three-quarters of the dietary strontium was accountable to bread and milk, equally available. Resorbed bone consequently must be supplying 500 to 900 $\mu\text{g./day.}$

Further calculations from the data, which it would take too long to detail, indicate that whereas more than half the absorbed dietary strontium is excreted daily a much smaller fraction of the 500 to 900 $\mu\text{g.}$ of “osteogenous” strontium is excreted per day. These calculations are based on the observation that the specific activity of urine was several times higher than that of plasma (Carr *et al.*, 1962b). Thus about 0.5 mg. of osteogenous strontium is recycled each day back to bone along with 60 $\mu\text{g.}$ replaced from the exogenous dietary source.

The replacement of bone strontium over this short period was $\frac{60 \times 100}{320,000} \approx 0.02\%$ per day (equivalent to a maximum of $\sim 6\%$ per year. However, if some 0.5 mg. of strontium is re-utilized in addition, total turnover is some 10 times greater than replacement.

OBSERVATION FROM FALL-OUT STRONTIUM

Strontium-90 has been a contaminant of diet in the United Kingdom since testing of megaton devices started in 1952. Bryant and Loutit (1961) assume that the average specific activity ($^{90}\text{Sr/Sr}$) of diet was 1.5, 3.1, and 3.9 in the three years 1954–6. Measurements indicate that it was 4.2, 4.6, 6.9, 4.9, and 4.9 in 1957–61.

From these figures one can calculate what the specific activity should be in bone in any year if bone replace-

The lines indicate the calculated specific activity of bone, in $\mu\text{C } ^{90}\text{Sr}$ per mg. Sr, at the end of each year 1954–60 for 1, 2, 5, and 10% random replacement per year. The values assumed for the specific activities of diet are given in the text. The circles indicate observed mean values of specific activities in different bones.

ment is a random process. The Chart shows the increase in specific activity with time for replacement at 1, 2, 5, and 10% per year. It also shows observed specific activities for various bones (femora, ribs, vertebrae, ilia, calvaria, patellae). The observations for 1959 and 1961 are for normal subjects killed in accidents. The plots suggest that replacement is 1–2% per year for calvaria, 2–5% for femora, ribs, and patellae, and 7–10% for ilia and vertebrae. Kulp and Schulert (1961) calculate a figure of 2.5% per year for the whole skeleton.

CONCLUSION

The conclusion from the present paper is that strontium built into bone (as distinct from that on bone surfaces) is more tenaciously held and recycled than strontium entering the plasma from diet. Estimates of the annual rate of replacement in the adult are thus only a few per cent. per year, when calculated from long-term ingestion of strontium-90, somewhat more according to short-term experiment involving ingestion of strontium-85 for a month, and much less than the total turnover of bone mineral.

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In the July issue of *F.P.A. Journal*, the journal of the Fire Protection Association, appears the following extract: "One hundred years ago deaths from clothing burns among women presented a serious problem. The following is extracted from *Scientific American*, July, 1861: The public has been painfully startled by the sudden death of Mrs. Longfellow—wife of the distinguished poet—which took place at Cambridge, Mass., on the 10th inst. The cause of this afflicting event is thus related: Mrs. Longfellow was seated in her library, and in the act of making seals with sealing wax. A bit of paper lighted and fell upon her dress, which caught fire, and before the blaze could be extinguished she was terribly burned. She was attended by Drs. Wyman and Johnson of Cambridge, but their efforts were vain to alleviate her intense suffering or to save her life. The dresses commonly worn by ladies in warm weather are composed of muslin and such-like inflammable materials. Although we have, on several occasions, urged the preparation of ladies' dresses with non-inflammable agents, we regret to state that very little attention has been given to our admonitions. We trust that the subject of safety-clothing will hereafter receive more attention from ladies. Their safety and good sense demand this."

Medical Memoranda

Cerebral Damage in Whooping-cough

[WITH SPECIAL PLATE]

Though the occurrence of neurological complications in whooping-cough is well recognized, the mechanism of their production is not so clearly defined. The incidence of these complications ranges from less than 1% to more than 15% in the larger series in the literature (Litvak *et al.*, 1948; Berg, 1961). Hemiplegia is a frequent finding, occurring in about half the cases that develop neurological signs (Valentin, 1902; Sears, 1929; Grant and Williams, 1943). Amaurosis of cerebral origin, though rare, has been described (Lazarus and Levine, 1934; Woywitka and Riches, 1950). In the following case both hemiplegia and a visual field defect developed during the illness. Subsequent neurosurgical treatment enabled a pathological examination of the damaged cerebral hemisphere to be carried out, and the results throw some light on the controversial problem of the pathogenesis of these lesions.

CASE HISTORY

A 9-year-old girl with infantile hemiplegia and severe behaviour disorder was referred to the Neurosurgical Department of the Sheffield Royal Infirmary for investigation and treatment. She was the third child in a healthy family, being born at full term after normal delivery. Development was satisfactory till the age of 18 months, when she had a severe attack of whooping-cough, during which she became hemiplegic on the right side with a right homonymous hemianopia. This was considered at the time to be due to either encephalitis or thrombosis. Though she could say some words before the illness, afterwards she could only mumble a few sounds. At the age of 2 she started to have fits in which she cried out, turned to the left, fell down, and became incontinent. These persisted at irregular intervals, and were not controlled by phenobarbitone, phenytoin sodium, and primidone. Though she started school when 5 years of age, by the time she was 7 her speech was almost incomprehensible so that she had to be removed and given home tuition. The fits were still frequent despite anticonvulsant therapy, and her behaviour was extremely bad, with restlessness, swearing, and temper tantrums. Her behaviour gradually got worse.

Physical examination confirmed the right hemiplegia, with small, poorly developed limbs on this side and a right homonymous hemianopia. The optic fundi were normal.

An electroencephalogram (E.E.G.) showed frequent bursts of high-amplitude slow spike and wave complexes occurring bifrontally and extending posteriorly on the right. A lumbar air encephalogram revealed a dilated left lateral ventricle, while the right side was relatively normal. In view of her deteriorating behaviour and the results of the investigations a left hemispherectomy was performed.

In the subsequent five years she has gradually improved, especially in her behaviour and language, so that she can now attend a school for backward children. She is able to read and to write with her left hand. Her fits are well controlled with phenobarbitone gr. $\frac{1}{2}$ (32 mg.) and primidone 125 mg. once a day. The E.E.G. now shows a flat record on the left side and some dysrhythmia on the right.

Macroscopic Examination of Left Hemisphere.—The specimen measured 13 × 9 × 3 cm. and weighed 250 g. The lateral ventricle was grossly dilated, with marked congestion of subependymal veins and thinning of the white matter, especially in the corpus callosum. The cortical ribbon was narrowed over most of the hemisphere, and on the lateral