overlying enamel soon followed, simulating, but only in end-effect, coronal caries in man. In no instance could primary coronal cavitation be established. The animal cavities here, as in the cereal experiments, were invariably associated with progress of calculus-like material beyond the amelo-cemental junction, arousing inflammatory or other disturbances in the periodontal membrane and further facilitating the impaction of food debris. The most severe cavitation was generally found in those parts of the denture neighbouring on the openings of the salivary ducts, and excavation of an adjacent tooth root appeared to be largely dependent on extension of parodontal disease to that area. So far these findings have been confirmed in a further series of 146 sugar-fed hamsters by radiographic examination of all and by serial sections of 266 representative teeth. The precise mechanism of the cemental and dentinal breaches is now under active investigation.

Comment

It is of interest that root cavities may also result from calculus-induced parodontal disease in *ferrets* given diets containing relatively large amounts of bread or oatmeal (King, 1944; King and Glover, 1945), and in these animals, at least, identification of the calculus presents no difficulty. The amount of "calculus" obtainable by gently scraping teeth of affected hamsters is relatively small and determinations of its chemical composition have not yet been made. However, the presence of calcium in such scrapings has been shown histologically by Lillie's (1948) modification of the alizarin-red technique of Langeron (1933): the alizarin-positive hamster specimens compare well with similar preparations of human and ferret calculus. These observations—together with the manner in which the material builds up on the hamster's enamel cuticle, burrows into the gingival crest, pushes out the subgingival epithelium and forms a parodontal pocket, invades the periodontal membrane, and progresses along the cementum of the tooth root—strongly suggest the accretions' similarity to calculus in the ferret.

From these results and from others to be reported later it would seem that extreme caution should be exercised in interpreting tooth cavitation in the hamster as being analogous to human coronal caries arising in the enamel. This is not to decry the use of the hamster for dental research purposes, since for parodontal studies alone it is an animal of great promise. Indeed, it may be that some of the cervical and interstitial tooth cavities assumed to be of carious origin in man in fact result from parodontal disease, but much further investigation is necessary before this suggestion can be seriously entertained.

Summary

The relative incidence and distribution of dental cavities in hamsters are described, following experimental feeding of diets containing high proportions of refined and raw sugar.

In contrast to the findings of other workers, it was observed that the lesions arose in the cementum of the molar tooth roots, whence they progressed through the dentine to the pulp. Disintegration of the coronal dentine and enamel occurred as a secondary extension of the root cavities, and in no instance could primary cavitation of the enamel be established.

The lesions were associated with irritation and other disturbances due to penetration by calculus-like material and impacted food debris, and similar phenomena have been encountered in ferrets.

The differences between the hamster syndrome and enamel caries in man are discussed.

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HYPERCALCAEMIA DURING VITAMIN D TREATMENT OF RHEUMATOID ARTHRITIS

BY

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That excessive administration of vitamin D gives rise to toxic symptoms has been known since 1928, when their occurrence was reported in a baby treated with irradiated ergosterol (Hess and Lewis, 1928). Since that date many other reports have been published (Anning, Dawson, Dolby, and Ingram, 1948). The purpose of the present communication is to stress the dangers inherent in the employment of massive doses of vitamin D, the inadequacy of purely clinical control, and the absolute necessity for repeated laboratory control of such treatment. Two cases seen at the Rheumatism Clinic of the Manchester Royal Infirmary are reported in illustration of these points.

Case 1

A single woman aged 61 was admitted to the infirmary on September 8, 1949. She was extremely pale and apathetic, and complained of pain in the neck and knees with marked lack of energy.

After an attack of tonsillitis and erysipelas in 1942 she had developed a generalized polyarthritis accompanied by anorexia and loss of weight. Several courses of gold produced no improvement, and her condition remained unchanged until 1946. At this time some subjective improvement occurred following treatment from her doctor. Eighteen months before admission she first developed pain in the neck, which steadily increased in severity until it became her principal complaint. About this time she began to tire easily and to lose her appetite. These symptoms persisted up to the time of her admission to hospital, and were accompanied by loss of weight and by nocturnal frequency of micturition. The only significant point in the past history was "Bright's disease" at the age of 5 years.

On examination she was extremely pale and wasted. The skin was lax but the tongue moist. Subconjunctival calcification was present in both eyes. Pubic and axillary hair was scanty. Symmetrical tenderness and swelling were present in

the joints of the hands, wrists, and feet. Both knee-joints were painful and contained a moderate amount of fluid. Movement was restricted in the knees and cervical spine. There was slight enlargement of the heart, and a harsh systolic murmur was heard over the whole of the praecordium. The blood pressure was 220/90. Generalized muscle-wasting and weakness was accompanied by hypotonia. The deep reflexes and plantar responses were all present and normal. Tortuosity of the retinal arteries was seen on ophthalmoscopic examination. Routine urine examination showed a normal urine of low specific gravity.

Investigations revealed a normochromic anaemia, R.B.C. 3,490,000, haemoglobin 68%, and C.I. 0.97. The total white cell count was 10,600, the differential count being normal. The sedimentation rate was 82/100 mm. in the first hour. The excretion of 17-ketosteroids was 3.9 mg. in 24 hours. The urea clearance was 21% of the average normal. Radiographs of the hands and feet showed narrowing of the joint spaces and a diffuse osteoporosis. The combination of anorexia, hypotonia, and renal impairment suggested that the osteoporosis might be associated with hypercalcaemia.

Among other possibilities hypervitaminosis D was considered as a cause. Further inquiry disclosed that the patient had been taking calciferol in a dose of 200,000 i.u. daily for at least a year previously. On October 2 the serum calcium was 14.8 mg. per 100 ml., serum phosphorus 2.2 mg. per 100 ml., and the alkaline phosphatase 24 units. The latter finding did not, however, fit into the picture of hypervitaminosis D, and further radiographs were ordered so as to exclude hyperparathyroidism.

Even though she had ceased to take calciferol since her admission, her condition continued to deteriorate steadily, and it became impossible to maintain an adequate fluid intake by mouth. She became confused, disorientated, and progressively dehydrated. On October 6 the blood pressure had fallen to 140/65, the serum calcium being 15.3 mg. per 100 ml. and phosphorus 2.4 mg. per 100 ml. Radiographs of the skull and pelvis now revealed the changes typical of Paget's disease. For the next four days intravenous fluids were given, with the addition of 250 ml. of sodium citrate twice a day to combat the hypercalcaemia. After this it became possible, by special nursing, to maintain a fluid intake of 4 to 5 pints (2.3 to 2.8 litres) a day.

The serum calcium fell from 15 mg. per 100 ml. on October 12 to 12 mg. on the 17th. By this time, in view of the Paget's disease, the patient had been made to get up and sit in a chair, and was encouraged to start walking in the next few days, since Reifensstein and Albright (1944) have shown that the serum calcium rises to high levels in cases of Paget's disease immobilized for the treatment of a fracture.

A high fluid intake was maintained during the next month and the patient was kept ambulant; during this time her general condition improved considerably, particularly as regards her mental state. The urea clearance remained low.

She was discharged home, where her condition remained stationary during the next month, after which she was admitted to a bed in the chronic ward of another hospital.

Case 2

A man aged 68 was seen in the Rheumatism Clinic at the Manchester Royal Infirmary. He stated that since 1945 he had had intermittent pain and swelling of the hands, knees, ankles, and elbows, with pain in the neck, shoulders, and feet. He had had many different treatments, but no improvement. During the preceding year his appetite had become poor and he had lost weight. Six months previously he had had two attacks of diarrhoea lasting a few weeks. In the last month he had developed scalding on micturition and nocturnal frequency. He gave no relevant history of any previous illness.

On examination he was seen to be an elderly thin man, rather pale, who did not appear to be acutely ill. He had the typical clinical changes of an advanced rheumatoid arthritis in the neck, shoulders, elbows, hands, knees, and ankles. Arteriosclerosis was present in the peripheral arteries. The heart was not clinically enlarged, and the blood pressure was 240/120.

Examination of the lungs, abdomen, and C.N.S. revealed nothing abnormal. The prostate was not enlarged. The B.S.R. was 39/200 mm., albuminuria was present, and the blood urea was 76 mg. per 100 ml. A radiograph of the hands showed advanced changes of rheumatoid arthritis in both hands.

The patient was considered to have uraemia, and was referred by his doctor to Professor R. Platt, at the Manchester Royal Infirmary, where the serum calcium was found to be raised to 12.8 mg. per 100 ml. and the blood urea to 94 mg. per 100 ml. As he had been taking calciferol in a dosage of 600,000 i.u. twice a week for about a year he was considered to be suffering from the effects of calciferol intoxication. No conclusion concerning the presence of previous renal impairment was arrived at.

Calciferol was discontinued and copious fluids were administered, but the patient died three weeks later.

Discussion

Vitamin D affects the absorption of calcium, its deposition in growing bone, and its excretion. The administration of large doses is followed, though not invariably, by a significant rise in the serum calcium level, and metastatic calcification is apt to occur in the kidneys, arteries, and elsewhere.

Among the earliest toxic symptoms of hypervitaminosis D are loss of appetite, fatigue, and pallor. As these are common constitutional manifestations of rheumatoid arthritis their significance when due to vitamin D may readily escape notice. Other common symptoms include thirst, nausea, vomiting, epigastric discomfort, headache, constipation or diarrhoea, and frequency of micturition. The tongue becomes dry, and the patient appears dehydrated, drowsy, and apathetic, finally sinking into coma.

Anning *et al.* (1948) pointed out that the total dose at the onset of symptoms varied from 1.4 to 35 million i.u. of vitamin D. There is also evidence to show that susceptibility may vary from time to time and in different seasons (McCance and Widdowson, 1942-3, 1943-4). Age is also a factor, children having a higher requirement than adults (McCance, 1947). Reed, Struck, and Steck (1939) have shown that there is an increased susceptibility to the toxic effects of calciferol in the presence of renal disease.

The detection of hypercalcaemia seems to be the best available indication of toxicity. Anning *et al.* (1948) suggest a level of diffusible serum calcium of 7.5 mg. or over per 100 ml. as indicating the "imminence of a toxic state." Although a significant rise of the total serum calcium usually occurs, many authorities doubt its reliability as a test (Reed, 1934; Slocumb, 1942). Furthermore, hypercalcaemia occurs in hyperparathyroidism, myeloma in about 50% of cases, skeletal neoplasia, and in conditions in which large parts of the skeleton are suddenly immobilized, as in anterior poliomyelitis (Duncan, 1947). In Paget's disease immobilization after a fracture may lead to dangerously high levels being reached (Reifensstein and Albright, 1944). This may explain why, in Case 1, in spite of the fact that the vitamin D was stopped, the patient continued to deteriorate while in bed and improved when she was made to do exercises and walk.

Consideration of published case records (Anning *et al.*, 1948) suggests that immediate withdrawal of vitamin D on the first indication of toxicity will, as a rule, result in a rapid disappearance of symptoms, though the blood calcium may remain high for several weeks. Similarly, though renal damage may occur before toxicity can be diagnosed, it is probably reversible if withdrawal is prompt (Slocumb, 1942). Frequent renal-function tests are therefore necessary.

Examination of the urine for albumin (Anning *et al.*, 1948) is an unreliable indication of renal impairment, being inconstant or absent in some cases.

Treatment consists in forcing fluids by mouth. Herrmann, Kirsten, and Krakauer (1949) have suggested the use of 250 ml. of sodium citrate 2.5% given intravenously four-hourly.

In view of the necessity for laboratory control the question arises whether the results of treatment of rheumatoid arthritis with massive doses of vitamin D are justified. In 1935 Dreyer and Reed reported improvement in the arthritic condition of two patients receiving massive dosage of vitamin D for hay-fever. This was followed by numerous reports, principally in the United States, of its use in rheumatoid arthritis. Though many claims for its curative value have been made, most observers have doubted its efficacy. The Council on Pharmacy and Chemistry of the American Medical Association (1939) concluded that "clinical evidence does not warrant the claim that massive doses of vitamin D are of benefit in chronic arthritis, in allergic conditions, or in psoriasis."

Summary

Two cases of toxicity due to massive dosage of vitamin D are described. The dangers of this form of therapy, particularly in rheumatoid arthritis, are pointed out, and the necessity for laboratory control is stressed.

We would like to thank Dr. J. H. Kellgren for permission to publish these cases and for his constant help and encouragement. Our thanks are also due to Professor R. Platt for allowing us to quote some of his findings in Case 2, and to Dr. M. D. Milne for helpful criticism.

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The Staff Side of the Nurses and Midwives Whitley Council states that the Council is referring to the Ministry of Labour and National Service, for consideration by the Industrial Court, the question of revised salaries for public health and domiciliary district nurses and midwives, the Staff and Management Sides having failed to agree on the matter. In June last year increased salaries were agreed for the lower grades of hospital nurses, and in July the Staff Side put forward proposals for public health and domiciliary nurses which would have had the effect of maintaining the existing relationship between the salaries of the public health nurses and those of the hospital nurses, on which those of the public health nurses had previously been based. Similar proposals on behalf of domiciliary midwives were submitted in September, 1949. In February this year the Staff Side was informed by the Management Side that it was unable to agree to any revision of the salaries of public health and domiciliary nurses and midwives. In view of the serious anomalies which the Management Side's decision created the Staff Side asked that the matter should be referred to the Industrial Court for arbitration.

POLIOMYELITIS IN CORNWALL IN 1949

BY

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During 1949, 110 cases of poliomyelitis occurred in Cornwall, giving an incidence of 0.3 per 1,000 of the population, a little less than double the rate for England and Wales in 1947. The age distribution over the county as a whole was normal—namely, approximately one-third under school age, one-third 5 to 14, and one-third 15 and over. Distribution of the first 100 cases is shown in Fig. 1.

It will be noted that there are four main centres of infection in the county, Camborne-Redruth, Penzance, Fowey, and Truro. It is interesting to compare this distribution with that of 1947 and to note that areas most affected in that year were relatively free of the disease in 1949.

The Camborne-Redruth outbreak was the first in the county; indeed, other than Newhaven, it was the first group of cases in the country. On June 21 three cases of paralysis were notified in Illogan, a village some four miles from Redruth. During the subsequent two months 21 further cases occurred in the Camborne-Redruth Urban District, and one at Truro School. An interesting feature of this small outbreak was the age group affected, 56% being under 5 years old.

The outbreak was for some time confined to the village of Illogan, and it seemed certain that the source of infection was close at hand. Of the three initial cases, two were pupils at the Illogan Infants' School, and the other, a child of 3, had an elder sister there. Careful investigation of the food supply and hygiene of the school together with the movements of staff and pupils failed to uncover any possible origin of the outbreak.

Consideration was given to the possibility of the importation of the virus from outside, but no visitors had stayed in any of the affected houses during the previous six weeks, nor had the occupants been away on holiday. Two old cases of poliomyelitis were known to be present in the district, but as it was two years since they contracted the disease the possibility of their still carrying the virus seemed remote.

Five more cases occurred in Illogan, all intimately connected with the school, four being pupils; the fifth, a child of 2½, had a brother at the school.

From Illogan the disease spread to Camborne and Redruth, Truro, and St. Day. When peripheral spreading occurs it is usually fairly easy to trace the origin of the first case. In Redruth, for instance, a case was notified on June 29, and on June 30 two boys in an adjoining house developed paralysis. The two families had gone by bus to Portreath beach on June 20 and again on June 21. The bus route is through Illogan, and many children from the village had joined the bus.

The first case in Camborne was admitted to the Isolation Hospital on July 8. The patient was a cousin of an Illogan case, and his aunt, in spite of warnings, had visited his home on two occasions, the last being eight days previously.

One solitary case was reported from Truro School; the boy developed paralysis on July 12, the infection being possibly contracted on June 25, when he went to a large religious meeting at Gwennap Pit, near St. Day, and subsequently spent the evening in Redruth.

Two cases occurred in St. Day; both had had indirect contact with Illogan.