In one case of unsuspected twin pregnancy one fetus was left behind at hysterotomy and it continued to thrive and was subsequently born by normal delivery (Sood, 1970).

Five patients were found not to be pregnant and in one of these the uterus was perforated at the site of a scar due to a previous lower segment caesarean section and a laparotomy was undertaken to repair the damage to the uterus.

Comment

The overall morbidity of this series was 16·8%, excluding urinary tract infection. This often occurred in conjunction with other complications and is therefore considered separately. The complication rate of abdominal surgery was higher (19·3%) compared with vaginal termination (15·3%). There were some outstanding differences between certain types of complications that followed abdominal and vaginal termination. Chest infection was much commoner after abdominal surgery and the reasons for this would seem to be due to longer periods of anaesthesia and shallow breathing due to postoperative pain. Venous thrombosis was exclusively confined to abdominal surgery and would seem to be related to longer anaesthesia and restriction in postoperative activity. Whether there is a differential change in the constituents of blood is not known. The urinary tract infection rate was very high after abdominal surgery but this pronounced difference was due to the fact that while routine preoperative catheterization was performed in abdominal surgery, this was not the case before vaginal terminations. Re-evacuation of the uterus after hysterotomy was required in 2·3% of cases, and in all of them irregular bleeding due to retained products of conception occurred. Thorough evacuation of uterine cavity is obviously most essential to prevent this complication.

There was one case of maternal death, which followed termination by Utus paste.

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PRELIMINARY COMMUNICATIONS

Aluminium in Bone from Patients with Renal Failure

VICTOR PARSONS, CHRISTINE DAVIES, CLIFFORD GOODE, CHISHOLM OGG, J. SIDDIQUI

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Summary

Some samples of bone from patients with renal failure contained more aluminium than others, and the concentration tended to be highest in patients who had been uraemic or on dialysis longest. The significance of the association of raised concentrations of aluminium in bone with renal failure is discussed.

Introduction

During a study of the concentration of various ions in bone in patients with renal failure (Prosser *et al.*, 1970) some samples were found on neutron activation analysis to contain more aluminium than others. The results of the complete analysis will be reported elsewhere, but in view of the recent interest in the absorption of aluminium during the treatment of hyperphosphataemia of renal failure (Berlyne *et al.*, 1970) we are making a preliminary report of our findings.

King's College Hospital, London S.E.5
VICTOR PARSONS, D.M., M.R.C.P., Physician
CHRISTINE DAVIES, Research Assistant

Atomic Weapons Research Establishment, Aldermaston, Berks
CLIFFORD GOODE, B.SC., A.R.I.C., Principal Scientific Officer

Guy's Hospital, London S.E.1
CHISHOLM OGG, M.D., M.R.C.P., Nephrologist

Wellcome Research Laboratory, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP
J. SIDDIQUI, M.B., B.S., Research Fellow

Methods

The bone samples had been obtained for biopsy or at necropsy from the iliac crests, lumbar vertebrae, or ribs of patients who had no evidence of renal disease and of patients with terminal renal failure sustained by either dietary restriction or regular dialysis therapy. Each of the samples was divided. One part was fixed for microscopical examination and the other part was weighed wet, dried at 100°C for 12 hours, and then ashed for similar periods at 200°, 400°, and 600°C in a muffle furnace. After each period of ashing the samples were weighed again. Samples of 10-100 mg were subjected to neutron activation analysis. For the determination of fluorine, firstly, 14 MeV neutrons from a Cockcroft-Walton generator (using positron counting for the ^{18}F produced) were used, and, secondly, thermal neutrons in a Herald reactor. In the latter method the induced activity is measured by sequential counting using γ-spectometry, which enables the concentrations of calcium, sodium, aluminium, and chloride to be determined (England *et al.*, 1968; Goode *et al.*, 1971).

Results

Because of variations in the amount of cancellous and cortical bone in the samples and the non-representative nature of solitary iliac crest biopsy specimens, a simple expression of the content of aluminium in wet or ashed bone gave very variable results. We were surprised at the constancy of the calcium

content, particularly when ashed at 400° or 600°C, in all the patients studied, whether suffering from renal failure or not.

The ratios of the dry weight to the wet weight and of the ash weight to the dry weight for the three groups are shown in Fig. 1, and by using these ratios an attempt can be made to project the content of bone prepared in different ways. The results suggest that the ratios of inorganic mineral are not disturbed in renal failure, though the content may vary widely according to the type of bone disease in renal failure. For non-uraemic patients the calcium concentration expressed as a percentage (±S.D.) of ashed weight at 400° and 600°C is 32·2 ± 2·4, for those with acute renal failure 35·2 ± 2·0, for those with chronic renal failure 32·8 ± 2·4, and for those on regular dialysis 33·2 ± 2·7 (Fig. 2), There is no significant difference between the groups.

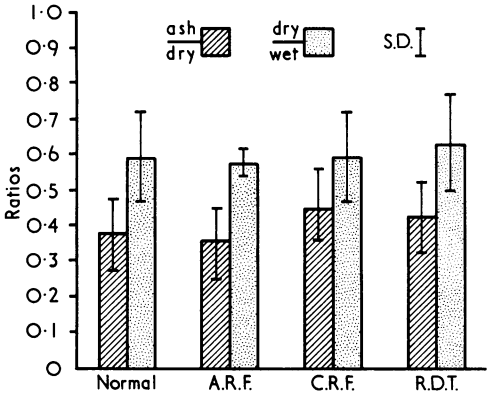

FIG. 1—Wet weight to dry weight, and dry weight (100 and 200°C) to ash weight (400 and 600°C) ratios for bone samples from normal patients, those with acute renal failure (A.R.F.), chronic renal failure (C.R.F.), and those on regular dialysis therapy (R.D.T.).

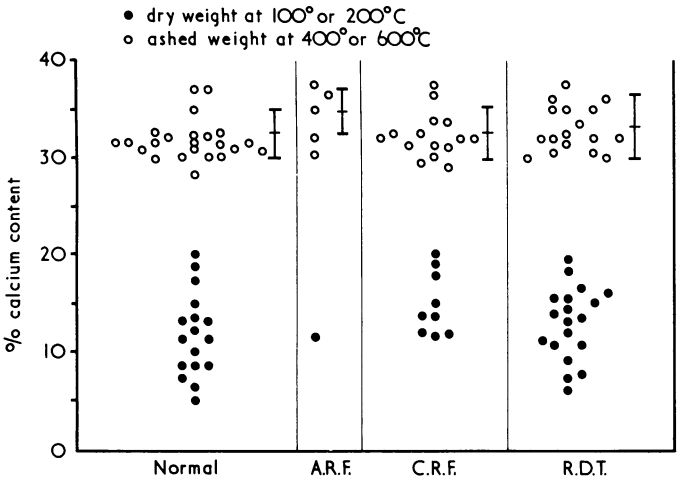

FIG. 2—Calcium content of dried and ashed bone from patients with no renal failure (Normal), acute renal failure, and those on regular dialysis (R.D.T.).

The concentration of aluminium, expressed as mg of aluminium/kg of calcium, is shown in Fig. 3. All the patients were grouped together regardless of how much aluminium hydroxide they had received, because in retrospect this was not always easy to estimate. The patients with most aluminium in bone were collected and special note was made of a history of aluminium intake, the presence or absence of bone disease, the duration of renal disease, and the severity of the polyneuropathy which is often found in these patients (see Table).

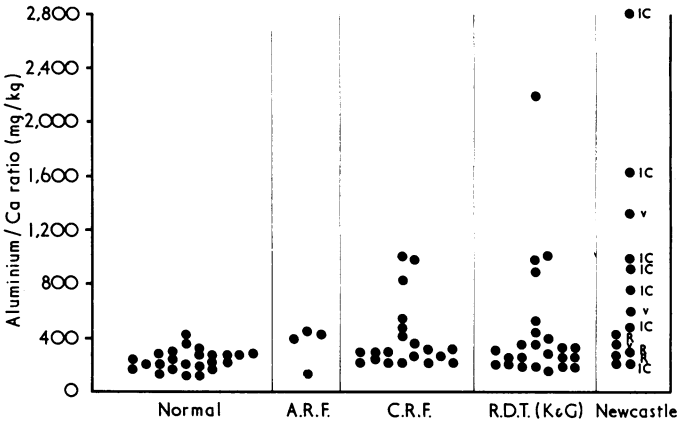

FIG. 3—Aluminium content of ashed bone from patients with no renal failure (Normals), acute renal failure (A.R.F.), and those on regular dialysis therapy (R.D.T.) from King's and Guy's Hospital (K. & G.) and Royal Victoria Infirmary (Newcastle). IC = Illiac crest. V = Vertebrae. R = rib samples.

Discussion

Aluminium is the second most common mineral element in the biosphere. It is found in the ash of all plants, mainly in trace amounts. It seems to be of no nutritional value, since no deficiency diseases have been reported when it is lacking (Gilbert, 1957). Most of the aluminium taken by mouth is excreted in the faeces. Mammalian muscle is low in the element, while the viscera may contain as much as 1 mg/kg wet weight.

Normal individuals maintain a serum aluminium concentration of 0·3 mg/l. or less, while patients with renal failure taking aluminium resins attain concentrations of up to 110 mg/l. (Berlyne *et al.*, 1970). Berlyne *et al.* also report the case of a patient with renal failure being dialysed against aluminium-free dialysate and not on aluminium therapy who reached a concentration of 14 mg/l., presumably owing to the normal excretory function of the kidney failing over a long period of time to keep pace with dietary sources.

Our results show that patients with renal failure occasionally accumulate 10 times more aluminium in bone than normal subjects. Our normal or non-uraemic bone concentration of aluminium (238 mg/kg calcium) is higher than the 98 mg/kg reported by Kehoe *et al.* (1948) in an adult skeleton, but extrapolations from solitary samples may be unreliable.

Patients with High Bone Aluminium Contents Showing Type of Renal Disease, Incidence of Neuropathy, Bone Disease, and Aluminium Administered

Case No.	Age and Sex	Renal Disease	Duration (Months)	Dialysis (hours/week)	Neuropathy	Mineralization	Osteomalacia	Resorption	Plasma Creatinine (mg/100 ml)		Aluminium Administration	Bone Aluminium (mg/kg/Ca)
									High	Low		
1	43 M.	Polycystic	20	20	0	Low normal	Nil	Trace	13·5	6·6	Nil	2,920
2	36 F.	Glomerulonephritis	24	28	+	Low	Nil	Nil	9·2	2·6	Nil	2,260
3	32 F.	Pyelonephritis	40	28	+	Low	++	±	10·2	3·1	Nil	1,640
4	21 F.	Postpartum renal failure	37	20	−	Low	Nil	Nil	10·1	2·6	High	1,340
5	46 F.	Glomerulonephritis	24	28	++	Low	++	+	15·0	6·4	High	1,150
6	49 M.	Nephrosclerosis	44	20	−	Low	++	+	15·8	6·7	Nil	1,060
7	40 M.	Glomerulonephritis	36	28	+	Normal	Nil	Nil	11·3	6·3	High	1,006
8	29 M.	Nephrosclerosis	38	20	−	Low	++	±	14·4	4·8	Nil	940
9	18 M.	Glomerulonephritis	24	28	+++	Normal	Nil	Nil	16·0	4·0	Nil	930
10	28 M.	Pyelonephritis	30	P.D.	++	Normal	Nil	++			Nil	806

P.D. = Peritoneal Dialysis

Little is known about the part that aluminium might play in pathological processes, but there is evidence that it need not be as inert as Wrong (1970) has argued. Gelfant (1963) used aluminium salts, especially chloride, as inhibitors of mitosis, while several workers have used aluminium salts in vitro to induce neurofibrillary spheroids and tangles in central and peripheral neurones (Klatzo *et al.*, 1965; Seil *et al.*, 1969). It is interesting to note that several patients with a high aluminium content in bone have also severe neuropathy, and studies of the deposition of aluminium in nervous tissue are under way.

Aluminium salts may also interfere with the orderly deposition of bone (Bachra and Van Harskamp, 1970) in that aluminium at concentrations of 1 μm or less can, by forming insoluble phosphates, initiate the precipitation of calcium apatite. Other clinical evidence (Nassim and Connolly, 1970) suggests that in the treatment of widespread soft-tissue calcification with aluminium hydroxide there is not only inhibition of further calcification but, over a period of two years, radiological evidence of a decrease in calcification with no evidence of the development of osteomalacia, though this can occur on such therapy.

Whether aluminium can influence the calcification processes in uraemic bone other than by phosphate depletion is unknown, but its deposition in uraemic patients could just be explained as the simple incorporation of an ion in excess as an "innocent bystander." But, in view of possible toxic effects, it is interesting to note that the aluminium concentrations found in one centre familiar with renal bone disease are among some of the highest reported, suggesting that there might be some causal effect.

There was no correlation between aluminium content and the amount of aluminium hydroxide taken, but on the whole the longer the patient had been uraemic and on dialysis the higher the concentration of aluminium. The rapid lowering of serum phosphate when aluminium hydroxide is given may partly be explained by the deposition of aluminium phosphate in tissue, including bone, rather than just the loss of phosphate in the gut as suggested by recent work at Charing Cross Hospital (Bailey *et al.*, 1971).

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MEDICAL MEMORANDA

Thyrotoxicosis Developing During Cyclophosphamide Therapy

I. R. McDOUGALL, W. R. GREIG, H. W. GRAY, J. F. B. SMITH

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We report here the case of a woman who developed typical Graves's disease (thyrotoxicosis with goitre and ophthalmopathy) during a continuous five-month course of oral cyclophosphamide given for ovarian adenocarcinoma not radically removed by surgery. The evolution of thyrotoxicosis, a presumed autoimmune disorder, during systemic immunosuppressive therapy is of interest; an alternative possibility is that the tumour tissue was producing a humoral thyroid stimulant.

Case History

A 46-year-old woman was referred to the thyroid clinic at the Royal Infirmary, Glasgow, in August 1968 with a two-month history of 4 kg weight loss despite a good appetite. She disliked heat and sweated continuously. In addition she had developed exertional dysponea and palpitations and had become excessively nervous. There was no family history of thyroid disease.

She looked distinctly thyrotoxic, with bilateral lid retraction, exophthalmos, and periorbital puffiness. Her skin was warm and moist and she was hyperkinetic and had digital tremor. The thyroid gland was diffusely enlarged (40 g), with a systolic bruit. She had no pretibial myxoedema.

There was also pronounced capital alopecia due to oral cyclophosphamide therapy, which she had been taking continuously since February 1968 (6 months), when she had undergone a laparotomy for lower abdominal pain and palpable ovarian swellings. This operation had disclosed large bilateral ovarian neoplasms; the one on the right had ruptured, resulting in the deposition of malignant tissue in the pouch of Douglas, the anterior abdominal wall, and the posterior uterine wall. Subtotal hysterectomy, bilateral salpingo-oophorectomy, and removal of as much of the neoplastic tissue as was technically possible was undertaken. Histological examination of the surgical specimen showed that both ovaries were replaced by poorly differentiated adenocarcinoma with extensive necrotic and haemorrhagic areas. The metastases consisted of similar material. There was no evidence of struma ovarii or of teratomatous tissue.

The operation was not curative (since not all of the neoplastic tissue could be removed), and for this reason 600 mg of cyclophosphamide was instilled into the peritoneal cavity. In the immediate postoperative period she received 100 mg of cyclophosphamide intravenously; this was changed to 200 mg of cyclophosphamide by mouth by the second postoperative day. The dose of oral cyclophosphamide was reduced during her three weeks in hospital, and at the time of discharge she was taking 50 mg a day, which she took continuously till seen by us because of thyrotoxicosis.

Investigations carried out at the thyroid clinic in August confirmed the clinical diagnosis of thyrotoxicosis; the serum protein-bound iodine concentration was 10·4 μg/100 ml (normal 4-8 μg/100 ml). The uptake of a tracer dose of ^{131}I 24 hours after administration was 48% (normal 20-45%), and the 48-hour serum protein-bound ^{131}I was 3·83% of the dose per litre (normal less than

University Department of Medicine and Nuclear Medicine, Glasgow Royal Infirmary, Glasgow C4
I. R. McDOUGALL, M.B., M.R.C.P., (U.K.), Lecturer
W. R. GREIG, M.D., PH.D., M.R.C.P.(ED.GLAS.), Senior Lecturer
H. W. GRAY, M.B., M.R.C.P., Lecturer
J. F. B. SMITH, M.B., M.R.C.P., Senior Medical Registrar