concentrations,² the patients continue to absorb appreciable amounts of calcium from the gut.

Kanis *et al*³ reported recently that 24R,25-(OH)₂D₃ at low daily doses increased intestinal absorption of calcium in anephric subjects and patients with advanced chronic renal failure, as measured by total body counter. The method reflects absorption throughout the entire intestine and does not discriminate between active transport and passive diffusion. On the other hand, Walling *et al*⁴ reported that in nephrectomised rats the duodenal, largely active, transport response was equivalent for equimolar doses of either 1,25-(OH)₂D₃ or 1α,24,25-trihydroxycholecalciferol while for 24R,25-(OH)₂D₃ it was none. We decided therefore to find out whether 24R,25-(OH)₂D₃ stimulates absorption in the proximal small intestine in man.

Patients, methods and results

Twelve patients with chronic renal failure who were not undergoing dialysis were investigated. None had been treated with vitamin D. For two months six patients were each given 1.3 μg daily of 24R,25-(OH)₂D₃ and the other six 1.0 μg daily of 1α-hydroxy vitamin D₃ (1α-OHD₃). Before and immediately after treatment serum and urinary calcium, phosphorus, and creatinine were measured. Intestinal calcium absorption was measured by concurrent use of oral and intravenous calcium tracers and calculation by deconvolution, as described by Szymendera *et al*⁵ but modified in that the oral dose of the tracer was given with 198 mg of calcium carrier as glucoheptonate instead of a test breakfast. This method, whose reproducibility exceeds 94%, measures absorption in the proximal small intestine, where calcium is taken up largely by active transport.

The table summarises the results. After small doses of 24R,25-(OH)₂D₃ the absorption increased in two patients, remained unchanged in two, and fell in two patients. Thus, the observed differences of paired results represented the natural variability, and the mean change (±SD), 2.20 ± 3.56% of the test dose, was not significantly different from zero.

The other agent, 1α-OHD₃, failed to act in one patient with polycystic kidneys but increased the intestinal absorption of calcium in the remaining five patients, who had chronic glomerulonephritis. This response was significant by the Wilcoxon signed rank test ($P < 0.05$, one tail). The increased absorption was accompanied by a rise in the serum concentration and urinary excretion of calcium. These related changes were significant ($P < 0.05$).

Comment

Our results show that treatment of uraemic patients with small doses of 1α-OHD₃ increased calcium absorption in the proximal small intestine and in turn raised serum calcium concentrations and the urinary excretion of calcium. These results are presented merely to show that the applied test showed changes that occurred after administration of an agent known to be active in chronic renal failure.

On the other hand, 24R,25-(OH)₂D₃ had no demonstrable effect on calcium absorption tested in this way. Thus, our results agree with those of Walling *et al*⁴ in that 24R,25-(OH)₂D₃ does not stimulate active calcium transfer in duodenum and proximal jejunum. The mode of action of this vitamin D₃ metabolite on calcium absorption therefore remains to be elucidated.

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Social class, smoking, and obesity

Previous studies of the effects of smoking on obesity in British men have been based on surveys of either predominantly social classes III, IV, and V¹ or classes I and II.^{2,3} In the former, smokers were consistently less obese than the non-smokers, though the smallest difference between smokers and non-smokers was in the small proportion of the sample in classes I and II.¹ In the surveys of mainly upper class men there was no difference between smokers and non-smokers.^{2,3} We have studied the relationship between smoking and obesity in working populations in North-west London with an adequate proportion of members of classes I and II as well as of III, IV, and V. Data on women as well as on men are available.

Methods and results

Information on age, social class, and smoking habits was obtained from 1339 men (aged 18-64) and 582 women (aged 18-59) interviewed during a study of ischaemic heart disease.⁴ Smokers were defined as those regularly smoking at least one cigarette, cigar, or pipe a day. The obesity index of weight/height² (kg/m²) was used (weight in standard light gown; height without shoes). Skinfold thicknesses were measured at forearm, triceps, subscapular, and suprailiac sites. In both sexes there was a lower proportion of smokers and higher proportion of non-smokers in classes I/II than in IV/V.

The results (figure) showed that in men in classes I/II smokers were significantly more obese than non-smokers (smokers mean (±SD) W/H² = 25.1 ± 2.77; non-smokers mean W/H² = 23.8 ± 2.73). In classes IV/V the reverse was seen (smokers mean W/H² = 24.7 ± 3.46; non-smokers mean W/H² = 26.3 ± 3.76). There was no difference in class III (smokers mean W/H² = 24.8 ± 3.15; non-smokers mean W/H² = 24.8 ± 3.40). Ex-smokers (not shown in figure) were significantly more obese than smokers in all classes ($P < 0.05$). In women there were no significant differences in W/H² between smokers and non-smokers in classes I/II (smokers mean W/H² = 23.1 ± 2.77; non-smokers mean W/H² = 24.0 ± 3.48) or class III (smokers mean W/H² = 24.4 ± 4.00; non-smokers mean W/H² = 24.5 ± 4.04). In classes IV/V, however, non-smokers were more obese than smokers (smokers mean W/H² = 24.1 ± 3.86; non-smokers mean W/H² = 25.8 ± 2.37). Ex-smokers (not shown in figure) were significantly more obese than smokers

Responses of uraemic patients to two-months' treatment with 24R,25-(OH)₂D₃ or 1α-OHD₃

Case No	Plasma creatinine (μmol/l)		Calcium absorption (% oral dose)			Plasma calcium (mmol/l)			Urinary calcium (mmol/day)		
	Before	After	Before	After	Difference	Before	After	Difference	Before	After	Difference
Responses to 24R,25-(OH) ₂ D ₃											
1	1255	1361	8.25	8.24	0	1.82	1.77	-0.05	1.9	1.7	-0.2
2	1273	1202	23.07	24.28	0	2.02	2.02	0	2.6	2.7	+0.1
3	884	1140	12.34	7.55	-4.8	2.42	2.52	+0.10	2.0	2.9	+0.9
4	1096	1052	5.72	14.34	+8.6	2.12	2.37	+0.25	2.0	2.8	+0.8
5	707	1008	14.06	3.80	-10.3	2.40	1.97	-0.43	1.6	1.5	-0.1
6	583	610	9.76	28.19	+18.4	2.10	2.25	+0.15	3.6	4.1	+0.5
Responses to 1α-OHD ₃											
7	707	884	9.90	15.00	+5.1	1.80	2.02	+0.22	2.7	3.3	+0.6
8	619	716	19.21	83.15	+63.9	2.40	2.52	+0.12	1.9	3.2	+1.3
9	566	619	14.59	19.18	+4.6	2.25	2.40	+0.15	1.6	2.1	+0.5
10	469	513	26.01	40.51	+14.5	1.92	2.22	+0.30	2.4	2.9	+0.5
11	380	495	13.65	51.00	+37.4	2.50	2.64	+0.14	2.4	4.0	+1.6
12	318	283	23.30	23.09	0	2.25	2.45	+0.20	1.8	1.8	0

Conversion: SI to traditional units—Creatinine: 100 μmol/l = 1.13 mg/100 ml. Calcium: 1 mmol/l = 4 mg/100 ml; 1 mmol/day = 40 mg/day.

(a) Obesity index (W/H²); (b) sum of skinfold thicknesses for smokers and non-smokers according to social class for men. (c) and (d) Corresponding data for women. The standard error of each mean is indicated on all graphs. ●—● Men smokers (classes I/II n=171; III n=344; IV/V n=191). ○—○ Men non-smokers (classes I/II n=146; III n=126; IV/V n=61). ■—■ Women smokers (classes I/II n=41; III n=143; IV/V n=37). □—□ Women non-smokers (classes I/II n=84; III n=161; IV/V n=26).

Significance of difference between smokers and non-smokers: *P<0.05; **P<0.01; ***P<0.001.

only in classes I/II (P<0.05). The results for men and women using the sum of skinfold thicknesses as the measure of obesity (figure b, d) were much the same as those using W/H². Obesity index (W/H²) and skinfold thickness increase with age,⁵ but multiple regression analysis did not suggest that any of the findings were due to differences in the age composition of the various social class/smoking habit groups.

Comment

Our data possibly explain why previous reports on smoking and obesity in men are conflicting. Probably the association is strongly dependent on social class, with a positive relationship between smoking and obesity in classes I/II and a negative one in classes IV/V. The results are not due to differences by social class in amounts smoked since the daily numbers of cigarettes or tobacco equivalents smoked by men in classes I/II, III, and IV/V were 16.4, 16.2, and 16.5 respectively. Differences in availability of cigarettes and in attitudes to smoking could partly account for our findings. People in classes I/II probably can afford both to smoke and eat more than they need, while those in classes IV/V may have to spend less on food if they smoke. Possibly also the fewer smokers in classes I/II reflect a greater response to health warnings in the upper than lower classes, and that those in classes I/II who have ignored warnings about smoking have also ignored the health dangers of obesity.

We found no social class crossover effect in women. Non-smokers were more obese than smokers in all three social classes. There may be differences in availability of cigarettes and attitudes to smoking between men and women that account for the contrast. Whatever the reasons for social class differences in the relationship between smoking and obesity, particularly in men, it is important to recognise that they may exist.

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Thyroglobulin concentration in neonatal blood: a possible test for neonatal hypothyroidism

Thyroglobulin (Tg) is secreted in small amounts by the thyroid gland and is measurable in the serum of most if not all adults.¹ Assay of serum Tg has been advocated as a marker for thyroid cancer.^{2,3} We suggest a possible use in screening for neonatal hypothyroidism. To test this hypothesis, it is necessary first to determine the range of serum Tg concentrations found in normal newborn infants. We present the results of assays for Tg carried out in normal neonates and compare them with those in normal adults. We include data on 12 hypothyroid subjects maintained on replacement thyroxine (T₄) and on 10 suspected hypothyroid children.

Materials, methods, and results

Human Tg was prepared from surgically removed normal thyroid tissue after separation by ultracentrifugation at 100 000 g at 0°C, column chromatography on Sephadex G200 and Sepharose 4B, and preparative polyacrylamide gel electrophoresis. Immunochemical purity was demonstrated. The preparation yielded 19S and 27S Tg; the former was more abundant and was used to raise antisera in rabbits. Radioimmunoassay was established following Van Herle⁴ with minor modifications.

Serum Tg concentration in different groups of subjects was:

(1) 60 normal non-goitrous adults 15-65 years old: range 6.5-43 µg/l (mean ± SEM 18.3 ± 1.1); values in women were slightly higher than in men.

(2) Six totally thyroidectomised adults and six athyrotic cretins, all taking adequate replacement of T₄: in all 12 subjects serum Tg was below the limit of detection of the assay (5 µg/l).

(3) 191 neonatal cord bloods: range 10-130 µg/l (mean ± SEM 57 ± 1.71). These values were significantly higher than adult concentrations (P<0.0001). Only four of the 191 samples gave values below 20 µg/l.

(4) 39 matched maternal serum and cord serum: in every case cord blood Tg was higher than maternal.

(5) Six infants (3 days to 12 months old) and four children (5-9 years old) with suspected hypothyroidism; none was on thyroid hormone treatment at the time. Results are shown in the table.

Discussion

The results of our study confirm the observation⁴ that neonatal serum Tg concentrations are higher than adult. This argues against appreciable placental transfer of Tg and suggests that neonatal serum Tg is derived from the infantile thyroid gland, perhaps because of the increased neonatal thyroid stimulating hormone (TSH) drive. In 12 hypothyroid subjects, six adult and six infantile cretins maintained on T₄, serum Tg was immeasurably low. If a "suppressed" thyroid gland secretes little or no Tg, it seems reasonable to assume that an absent or appreciably underdeveloped gland might show a similar