Preliminary Communications

Serum Uric Acid Levels in Hypertensive Patients Treated with Guanethidine

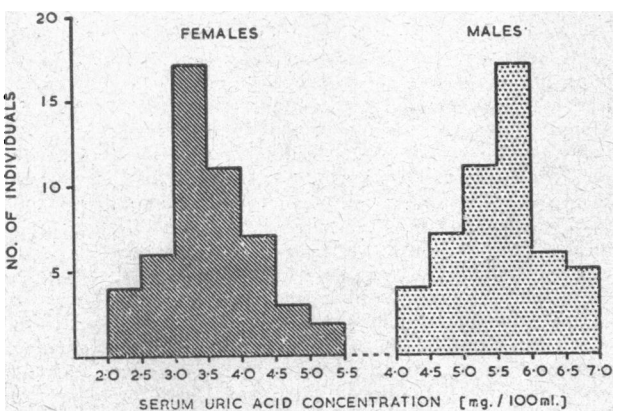
Dollery *et al.* (1960) reported that they found high levels of uric acid in the blood in over 50% of hypertensive patients who were receiving the hypotensive agents mecamylamine, pempidine, and chlorothiazide. Since patients with primary hyperuricaemia may have renal damage it is possible that drug-induced hyperuricaemia might produce further renal damage in hypertensive patients. We therefore investigated the effect on the serum uric acid level of the adrenergic blocking agent guanethidine, which is now used extensively in the treatment of hypertension.

PATIENTS AND METHODS

We studied 19 patients with essential hypertension and three with hypertension due to renal disease. All required hypotensive agents. Of these, 10 were males and 12 females, their ages ranged from 20 to 68 years, and none had a history of gout. The serum uric acid concentration and blood urea were determined at routine attendances during a six-month period. Eight of the patients were already on treatment at the beginning of the study and therefore did not have their serum uric acid concentration determined before starting guanethidine. Two were receiving chlorothiazide in addition to guanethidine on all occasions when specimens were taken, and one patient was receiving chlorothiazide on one of three occasions. Thus 20 patients were receiving guanethidine alone at the time specimens were taken.

The serum uric acid was measured by the method of Hawk *et al.* (1954) and the serum urea by the method of Marsh *et al.* (1957) and Skeggs (1957). The methods for both substances were adapted for the auto-analyser.

In 50 normal healthy male adults the mean value of the serum uric acid was 5.5 mg./100 ml., S.D. $\pm$0.75. Similarly in 50 normal healthy female adults the corresponding values were 3.5 mg./100 ml., S.D. $\pm$0.64 (see Chart). For the purposes of the present investigation hyperuricaemia was defined as a serum uric acid concentration exceeding 6.9 mg./100 ml. in a male patient and 5 mg./100 ml. in a female patient.



Serum uric acid concentrations in 50 normal healthy men and 50 normal healthy women aged 18 to 40 years.

RESULTS

There was no significant difference between the serum uric acid levels before and after treatment with guanethidine (see Table). Of the 20 patients receiving guanethidine alone at the time of uric acid estimations, three (Cases 2, 4, and 17) had hyperuricaemia. Two of these three (Nos. 2 and 4) were known to have had hyperuricaemia before treatment, but this estimation was not performed in Case 17 before treatment.

Of the three patients receiving chlorothiazide (Cases 3, 12, and 19) two had hyperuricaemia. In Case 3 hyperuricaemia was found before treatment, but the serum uric acid concentration rose still higher during chlorothiazide therapy, and when chlorothiazide was stopped the level returned to within normal limits.

Case No.	Sex and Age	Dose of Guanethidine (mg.)	Duration of Treatment (Weeks)	Blood Pressure	Serum Uric Acid (mg./100 ml.)	Blood Urea (mg./100 ml.)
1	F 37	0	0	180/110	*	22
		20	50	140/90	4·8	33
2	F 52	0	0	190/120	5·2	45
		30	1	180 100	4·7	51
		40	8	150/90	6·0	59
3	F 68	0	0	240/120	5·9	37
		30	4	120 70	7·0†	40
		30	8	180 90	4·6	36
		30	24	210 120	4·4	40
4	F 56	0	0	230 130	5·1	35
		30	2	180 100	5·2	40
		30	8	180/110	5·5	36
5	F 56	0	0	210/120	4·0	39
		20	20	180 110	4·1	44
		20	24	160/100	4·5	37
6	F 51	0	0	230/130	4·1	30
		20	4	160 100	3·8	31
		30	8	160 100	4·3	30
7	F 60	0	0	220 110	*	39
		40	4	190/100	4·8	46
8	F 65	0	0	220 115	4·0	49
		30	2	250/120	3·4	44
		40	20	240 100	3·6	34
		40	26	220 100	4·4	50
9	F 29	0	0	190 120	4·1	36
		50	20	190 120	4·1	41
10	F 50	0	0	210 125	4·1	48
		40	16	180 120	4·4	52
11	F 49	0	0	220 130	4·2	23
		20	2	150 110	4·1	43
		30	8	160 100	4·0	37
		40	16	120 80	4·0	38
		40	28	110 80	4·5	37
12	F 50	0	0	210 140	*	40
		250	26	210 130	5·3†	36
		250	30	180 100	5·1†	38
13	M 56	0	0	180 130	*	48
		40	34	150 100	4·8	56
14	M 39	0	0	195 115	*	31
		40	2	160 115	5·5	39
15	M 20	0	0	170 120	5·2	44
		30	2	150 105	5·4	41
		40	8	160 95	5·9	56
16	M 56	0	0	230/130	*	44
		60	26	190 120	5·9	46
17	M 51	0	0	220 165	*	50
		175	24	190 140	7·6	52
18	M 60	0	0	210 135	3·9	40
		20	4	220 130	4·9	40
19	M 51	0	0	225/140	*	40
		75	4	180 130	5·8†	39
		75	26	140 100	6·2†	34
20	M 61	0	0	250 160	4·3	52
		30	2	245 130	4·6	56
		50	8	190 100	5·3	54
21	M 58	0	0	230/145	6·6	26
		20	2	180/130	5·4	34
		30	12	170 120	5·3	37
		30	28	160 110	5·3	34
22	M 53	0	0	190 120	4·2	31
		30	8	210 115	5·0	41
		40	24	200 125	3·7	32

* Serum uric acid not determined. Patient on guanethidine before study commenced

† On chlorothiazide.

Of the 14 patients investigated before treatment, three (Cases 2, 3, and 4) had hyperuricaemia. (It may be added that a further six hypertensive patients not requiring hypotensive agents were investigated, of whom one female had hyperuricaemia.)

The length of time the subject had been receiving guanethidine did not influence the uric acid levels.

DISCUSSION AND CONCLUSIONS

The results show that guanethidine does not cause hyperuricaemia as Dollery *et al.* (1960) suggested for chlorothiazide, pempidine, and mecamylamine. Two of three patients in our series did in fact have hyperuricaemia while receiving chlorothiazide, which is in keeping with this action of chlorothiazide reported by Oren *et al.* (1958), Laragh (1958), Dinon *et al.* (1958), Aronoff (1960), and Warshaw (1960).

Of the three patients (two females and one male) found to have hyperuricaemia on guanethidine alone, two were known to have raised uric acid levels before treatment; the third subject unfortunately did not have his uric acid estimated before treatment. This finding is similar to those of Dollery *et al.* for hypertensive subjects having hyperuricaemia without drug treatment (7.3% males, 18.5% females). It is not known whether this is due to primary hyperuricaemia or to early renal failure secondary to the hypertension. As Dollery *et al.* noted, there is no obvious relationship between serum uric acid and serum urea concentrations. However, we hope to carry out clearance tests on hypertensive patients with and without drug therapy which may elucidate this point.

These results support the hypothesis that hyperuricaemia due to treatment of hypertension with chlorthiazide and ganglion-blocking agents is drug-induced and not related to alteration of glomerular filtration caused by a fall in blood-pressure. In our series 15 of the 22 patients achieved a satisfactory mean fall in blood-pressure without a significant rise in the serum uric acid. Although the control of hypertension is easier using thiazide diuretics with guanethidine (Hilden, 1960; Jaquerod and Spuehler, 1960; Blanchard and Essigman, 1961), the possible danger of prolonged hyperuricaemia causing further renal damage in hypertensives, as is found in patients with primary hyperuricaemia, has to be considered. It may be better to continue with guanethidine alone, and reserve the thiazide diuretics for patients proving resistant to guanethidine, for the latter at present appears to be free from the danger of causing hyperuricaemia. A prolonged study, comparing guanethidine alone and in combination with the thiazide diuretics, is required.

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Medical Memoranda

Peutz-Jeghers Syndrome in Childhood: Unusual Radiological Features

Familial intestinal polyposis, associated with a characteristic circumoral spotty pigmentation, was first recognized by Peutz (1921) in Holland. Jeghers *et al.* (1949) described a further 10 cases, and Dormandy (1957) made an extensive review of the literature, after describing 21 cases of the condition in five families. Recurrent intussusception is a common occurrence in the disease, and the following case history is of interest because of the unusual radiological demonstration of such an intussusception before operation.

CASE HISTORY

An 8-year-old boy was admitted to hospital on November 2, 1959, with abdominal pain, vomiting, and diarrhoea. For two years he had suffered from acute attacks of central abdominal pain and vomiting. He was eating poorly, had lost weight, and also complained of frequent headaches. He had had surgical treatment for a chronic antral sinusitis.

Family History.—He had two sisters, and one, aged 10 years, had circumoral pigmentation but was otherwise well. His mother, aged 34, said she had brown spots around her mouth until puberty, and had had a thyroidectomy for thyrotoxicosis. A maternal aunt was well but had complained of abdominal colic in the past. The maternal grandfather of the patient had died from "cancer of the bowel." The boy's father was healthy, but three of his sisters suffered from pulmonary tuberculosis.

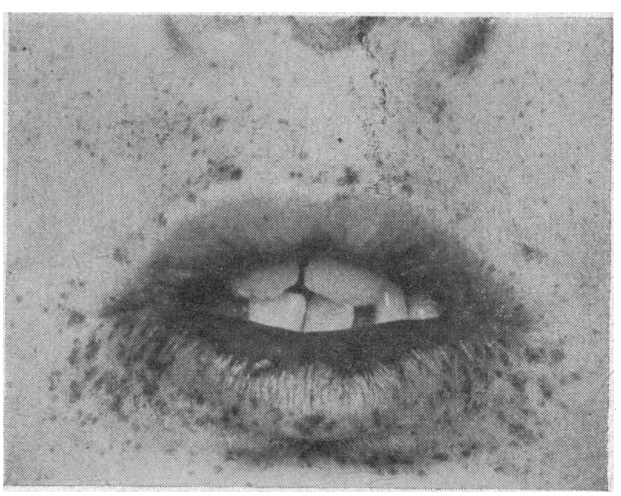

FIG. 1.—Linear streaks and brown spots of circumoral pigmentation on lips and skin.