### Comment

We consider that a hypermobility syndrome is a more plausible explanation for this patient's symptoms than a pauci-articular juvenile polyarthritis. We suggest that joint laxity deserves more recognition as a cause of chronic synovial thickening. The distinction from juvenile polyarthritis is important since hypermobile patients may be spared the uveitis of this condition and may be at risk of premature osteoarthrosis.

The nature of the effusion that may occur in hypermobile joints has not been adequately explained. Since joint laxity has now been linked with chondrocalcinosis,[1] it remains a possibility that it might be the first sign of crystal deposition disease in joints that will subsequently develop premature osteoarthrosis.


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# High-density lipoprotein cholesterol and antihypertensive drugs: the Oslo study

Thiazides and beta-blockers induce changes in serum lipid concentrations.[1 2] Thiazides increase triglyceride and urate concentrations, and propranolol seems to accentuate these effects.[3] Because of the increased risk of coronary heart disease associated with reduced serum concentrations of high-density lipoprotein cholesterol,[4] we studied the effects of various antihypertensive regimens on serum HDL cholesterol concentrations.

### Patients, methods, and results

The patients were selected from among men aged 40-49 with mild, symptom-free hypertension who were taking part in a controlled drug trial. The regimens and laboratory methods for determining total cholesterol, triglycerides, and urate have been described.[1 3]

From September to December 1977 HDL cholesterol was analysed in fresh sera at routine follow-up. The same analysis was performed on non-fasting pretreatment sera (from the same men) which had been stored at −20°C since 1973. HDL cholesterol was determined as follows: low density lipoproteins and very low density lipoproteins were precipitated with a heparin-manganese reagent[5] to final concentrations of 200 IU/ml heparin and 50 mmol/l $Mn^{++}$. After centrifugation at 4°C cholesterol was determined enzymatically in the supernatant (CHOD-PAP Boehringer Mannheim kits). Cholesterol determination was standardised and controlled with 1·29 mmol/l (50 mg/100 ml) cholesterol and 2·20 mmol/l (85 mg/100 ml) cholesterol standards (Preciset, Boehringer Mannheim and Seronorm, Nyco), and control sera (inter-series variation coefficient <2%) were included in all series. In frozen sera from the untreated controls HDL cholesterol concentrations were about 38% lower than in fresh sera, but there was a fair correlation between the individual values in frozen and fresh sera ($r=0·60$; $P<0·001$). In this study we used the HDL cholesterol values from frozen sera only for selecting groups. The patients on different drug regimens were selected so that they had the same means and distribution of pretreatment HDL cholesterol concentrations. Pretreatment triglyceride concentrations were also comparable in patients treated with hydrochlorothiazide and methyldopa, hydrochlorothiazide and propranolol, and hydrochlorothiazide alone and in the untreated controls. The lower pretreatment triglyceride value of the group given hydrochlorothiazide alone was not significant ($P>0·05$); differences between means were tested by a modified $t$ test accounting for unequal variances in groups.

During treatment mean HDL cholesterol concentrations were significantly lower in patients treated with thiazide-propranolol than in those treated with thiazide-methyldopa ($P<0·01$) or thiazide alone ($P<0·01$) or the untreated controls ($P<0·01$). Total serum cholesterol concentrations did not change significantly on the various regimens. The hydrochlorothiazide-propranolol combination also induced a significant increase in triglyceride concentrations ($P<0·01$), while values were increased only slightly on hydrochlorothiazide and methyldopa and fell slightly in the controls and patients treated with a thiazide alone (see table). After hydrochlorothiazide-propranolol treatment urate concentrations were significantly higher than pretreatment values or values after either of the other two treatment regimens ($P<0·05$). Urate concentrations fell over the four years in the controls ($P<0·01$).

### Comment

Our results have shown that treatment with a thiazide and propranolol in combination reduces serum HDL cholesterol concentrations and increases triglyceride and urate concentrations. The results are consistent with the reported inverse correlation between HDL cholesterol and triglycerides.[4] The effect of this drug combination on serum lipid concentrations may counteract the beneficial effect of blood pressure lowering. As the patient groups were small and not randomised, however, the results need to be confirmed in future studies.


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*Mean (±SE of mean) values before and after four years of treatment in patients on different drug regimens and in controls*

| | HDL cholesterol (mmol/l) | | Triglycerides (mmol/l) | | Urate (μmol/l) | | Total cholesterol (mmol/l) | | Relative body weight (weight (kg)/height² (m)) | | Diastolic blood pressure (mm Hg) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Before* | After | Before | After | Before | After | Before | After | Before | After | Before | After |
| Hydrochlorothiazide and propranolol (n = 33) | 0·85 ± 0·05 | 1·09 ± 0·05 | 1·87 ± 0·14 | 2·68 ± 0·26 | 324·2 ± 9·9 | 395·0 ± 13·9 | 6·76 ± 0·18 | 7·07 ± 0·18 | 24·6 ± 0·55 | 25·3 ± 0·55 | 97·0 ± 1·34 | 87·5 ± 0·72 |
| Hydrochlorothiazide and methyldopa (n = 33) | 0·87 ± 0·06 | 1·28 ± 0·05 | 1·72 ± 0·12 | 1·92 ± 0·21 | 324·2 ± 10·4 | 349·7 ± 15·0 | 7·04 ± 0·22 | 7·15 ± 0·24 | 25·4 ± 0·39 | 25·8 ± 0·39 | 98·0 ± 1·12 | 87·7 ± 0·81 |
| Hydrochlorothiazide alone (n = 26) | 0·85 ± 0·07 | 1·35 ± 0·07 | 1·61 ± 0·10 | 1·35 ± 0·06 | 306·9 ± 11·5 | 316·4 ± 16·1 | 6·97 ± 0·20 | 7·00 ± 0·18 | 24·4 ± 0·41 | 24·0 ± 0·39 | 92·4 ± 1·38 | 82·7 ± 0·97 |
| Controls (n = 33) | 0·85 ± 0·05 | 1·37 ± 0·06 | 1·91 ± 0·14 | 1·56 ± 0·11 | 334·9 ± 9·8 | 277·8 ± 8·5 | 7·12 ± 0·21 | 7·17 ± 0·24 | 24·8 ± 0·45 | 25·0 ± 0·45 | 95·8 ± 1·14 | 97·2 ± 1·55 |

*Samples kept frozen for four years (38% reduction—see text).

*Conversion: SI to traditional units*—Cholesterol: 1 mmol/l ≈ 39 mg/100 ml. Triglycerides as triolein: 1 mmol/l ≈ 89 mg/100 ml. Urate: 1 μmol/l ≈ 0·017 mg/100 ml.