# Effect of Growth Hormone on Plasma Triglycerides in Man[1] (37498)

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The rapid mobilization of free fatty acids following the administration of human growth hormone has been demonstrated repeatedly (1–4). More recently, studies have shown that the elevation in plasma free fatty acids can persist for at least 12 hr in normal subjects after a single 10 mg intramuscular dose of human growth hormone (5). Since circulating plasma free fatty acids are considered to be a major source of endogenous triglycerides (6–8), and an increase in fatty acids may be followed by increase in other lipids, plasma was examined for changes in triglyceride and cholesterol 12 hr after the administration of growth hormone. In view of the recognized lipid abnormalities in diabetics, it seemed possible that the effects might be enhanced in such subjects. The effect of a single dose of human growth hormone on plasma triglycerides and cholesterol was therefore studied in both diabetic and nondiabetic persons.

*Methods.* Control plasma cholesterol and triglycerides were measured after an overnight fast of at least 12 hr. Ten units of human growth hormone were administered intramuscularly at 8 PM and plasma cholesterol and triglycerides were measured in plasma obtained 12 hr later. Cholesterol was measured by the method of Abel *et al.* (9), and the triglyceride determination was done by the method of Kessler and Lederer (10).

The groups were composed of:

1. Three female and 3 male adult-onset diabetics who were not insulin dependent and 10 controls matched for age and sex without hyperglycemia, hypercholesterolemia or hypertriglyceridemia.

2. Six normal young men with no family history of diabetes mellitus and with normal plasma lipids.

3. Six normal young women who were taking contraceptive pills at the time of the test.

*Results.* Plasma triglycerides were elevated in all diabetics 12 hr after administration of growth hormone. The mean increase was 116 mg/100 ml and ranged from 24 to 295 mg. The percentage rise over the base line values ranged from 14 to 248% with a mean of 91%. In the control group, plasma triglycerides decreased in 2, with little change in 4, and moderate increase in another 4 subjects. The percentage change ranged from −13% to +35% with a mean of +10%. Although the base line values were not statistically different between diabetics and nondiabetic controls, the difference was significant ($p < 0.005$) after growth hormone administration. The percentage increase in plasma triglycerides was also significant. Changes in plasma cholesterol were not constant and there was no difference between the two groups (Table I). In the only two patients tested, plasma triglycerides continued to be elevated 36 hr following administration of growth hormone.

In normal young men, the responses were erratic but the increase for the group in plasma triglycerides 12 hr following growth hormone administration was significant (Table II). Plasma triglycerides increased substantially in 4 and remained unchanged in 2. The mean increment was 41 mg/100 ml with a

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TABLE I. Effect of 10 mg Human Growth Hormone on Plasma Lipids in Diabetics and Nondiabetic Controls.

| | | Plasma triglycerides (mg/100 ml) | | | | Plasma cholesterol (mg/100 ml) | |
|---|---|---|---|---|---|---|---|
| | Age/sex | Pre-GH | Post-GH | Absolute change (mg %) | Change (%) | Pre-GH | Post-GH |
| Diabetics | | | | | | | |
| 1 | 48-F | 119 | 414 | +295 | +248 | 163 | 200 |
| 2 | 59-F | 123 | 251 | +128 | +104 | 240 | 228 |
| 3 | 69-F | 270 | 308 | + 38 | + 14 | 307 | 286 |
| 4 | 60-M | 167 | 191 | + 24 | + 14 | 201 | 201 |
| 5 | 69-M | 80 | 151 | + 71 | + 89 | 228 | 252 |
| 6 | 70-M | 184 | 323 | +139 | + 75 | 276 | 287 |
| Mean | | 157 | 273 | +116 | + 91 | 235 | 242 |
| SD | | 67 | 96 | 99 | 86 | 52 | 39 |
| Paired $t$ test | | $p < 0.05$ | | | | NS | |
| Nondiabetic controls | | | | | | | |
| 7 | 47-F | 84 | 75 | — 9 | — 11 | 240 | 232 |
| 8 | 52-F | 134 | 154 | + 20 | + 15 | 237 | 235 |
| 9 | 52-F | 106 | 114 | + 8 | + 7 | 308 | 308 |
| 10 | 54-F | 135 | 118 | — 17 | — 13 | 264 | 282 |
| 11 | 60-F | 61 | 79 | + 18 | + 30 | 214 | 200 |
| 12 | 60-M | 66 | 66 | 0 | 0 | 167 | 144 |
| 13 | 60-M | 113 | 111 | — 2 | — 2 | 285 | 256 |
| 14 | 62-M | 164 | 221 | + 57 | + 35 | 220 | 177 |
| 15 | 63-M | 75 | 76 | + 1 | + 1 | 150 | 170 |
| 16 | 69-M | 136 | 160 | + 24 | + 18 | 192 | 204 |
| Mean | | 107 | 117 | + 10 | + 10 | 228 | 221 |
| SD | | 35 | 49 | 21 | 21 | 50 | 52 |
| Paired $t$ test | | NS | | | | NS | |

range of 2 to 89 mg. The percentage change ranged from 2 to 124% with a mean of 56%. Triglycerides also increased in the normal young women on contraceptive pills. The increase was not significant at the $p = 0.05$ level by the paired $t$ test, but was significant by the sign test (Table III). The percentage increase for the group was the same as for the young men (56%), but the base line value before growth hormone was higher, 102 versus 71 mg/100 ml. Plasma cholesterol was not changed in any group.

*Discussion.* Previous studies on the relationship between growth hormone and fat metabolism in man have been concerned largely with the interaction between growth hormone and acute changes in plasma free fatty acid (1–5). The studies reported here have examined the early response of plasma triglycerides and cholesterol to human growth hormone.

It seems clear from the results that a single dose of growth hormone can raise plasma triglycerides, and that this effect is most marked in diabetic subjects. Since circulating free fatty acids are considered to be a major source of endogenous triglycerides (6–8), the mobilization of fatty acids by growth hormone might be a contributing factor in the elevation of plasma triglycerides frequently seen in diabetics (11). Considering that plasma triglycerides continue to remain elevated for 12 to 36 hr after a single injection of growth hormone, it seems reasonable to speculate on the significance of growth hormone in diabetics. In view of recent findings which demonstrate higher growth hormone levels in diabetics (12) than in normals, one wonders whether the failure of normal control of secretion of growth hormone contrib-

TABLE II. Effect of 10 mg Human Growth Hormone on Plasma Lipids in Normal Young Men.

| Subject | Age | Plasma triglycerides (mg/100 ml) Pre-GH | Post-GH | Absolute change (mg %) | Change (%) | Plasma cholesterol (mg/100 ml) Pre-GH | Post-GH |
|---|---|---|---|---|---|---|---|
| 17 | 22 | 34 | 52 | +18 | + 52 | 198 | 212 |
| 18 | 23 | 72 | 120 | +48 | + 67 | 207 | 198 |
| 19 | 27 | 65 | 69 | + 4 | + 6 | 183 | 183 |
| 20 | 27 | 87 | 89 | + 2 | + 2 | 229 | 213 |
| 21 | 28 | 101 | 190 | +89 | + 88 | 182 | 185 |
| 22 | 29 | 67 | 150 | +83 | +124 | 195 | 188 |
| Mean | | 71 | 112 | +41 | + 56 | 199 | 196 |
| SD | | 23 | 52 | 39 | 47 | 17 | 13 |
| Paired $t$ test | | $p < 0.05$ | | | | NS | |

utes to the elevated plasma triglycerides.

The marked difference in the response of triglycerides between diabetics and normals raises the question of using the response to growth hormone as a means of identifying potential diabetics while they are still asymptomatic. Before such a prospective study could be undertaken, additional tests would have to be performed on large numbers of normals, prediabetic and overtly diabetic subjects. Juvenile-type diabetics were not included in this study, mainly because of their insulin dependency which makes the interpretation of data difficult, and because of their tendency to ketoacidosis following administration of growth hormone.

The importance of growth hormone in cholesterol metabolism and in prevention of hypercholesterolemia in athyroid rats has been stressed in recent reports (13, 14). The suggestion has been made that the effect of growth hormone is mediated via stimulation of pancreatic alpha cells with the subsequent discharge of glucagon (15). Recently, the same workers found that, after 1 wk of treatment with human growth hormone at a dose of 5 mg every 12 hr intramuscularly, the serum cholesterol was lowered and the triglycerides were raised in "coronary-prone (type A)" hypercholesterolemic subjects (16). In the present study, there was no consistent change in plasma cholesterol 12 hr following a single administration of growth hormone in man.

TABLE III. Effect of 10 mg Human Growth Hormone on Plasma Lipids in Young Women on Oral Contraceptive Pills.

| Subject | Age | Plasma triglycerides (mg/100 ml) Pre-GH | Post-GH | Absolute change (mg %) | Change (%) | Plasma cholesterol (mg/100 ml) Pre-GH | Post-GH |
|---|---|---|---|---|---|---|---|
| 23 | 25 | 121 | 149 | + 28 | + 23 | 191 | 192 |
| 24 | 24 | 66 | 122 | + 56 | + 85 | 168 | 143 |
| 25 | 22 | 89 | 106 | + 17 | + 19 | 145 | 161 |
| 26 | 27 | 204 | 429 | +225 | +110 | 266 | 264 |
| 27 | 23 | 48 | 77 | + 29 | + 60 | 203 | 197 |
| 28 | 31 | 86 | 122 | + 36 | + 42 | 214 | 217 |
| Mean | | 102 | 167 | + 65 | + 56 | 198 | 196 |
| SD | | 55 | 130 | 79 | 36 | 42 | 43 |
| Paired $t$ test | | NS | | | | NS | |
| Sign test | | .031 | | | | NS | |

The higher base line values of triglyceride in the young women on contraceptive pills compared with the young men is consistent with the observations that a rise in plasma triglycerides frequently occurs with the use of oral contraceptives (17–20). An increase in endogenous growth hormone may contribute to the rise in triglyceride since it has been observed that women on contraceptive pills secrete about 3 times as much growth hormone as other normal premenopausal women (2.59 vs 0.85 mg/24 hr) and almost 4 times as much as adult males (0.68 mg/24 hr) (21).

*Summary.* Twelve hours after the intramuscular administration of a single 10 mg dose of human growth hormone (HGH), fasting blood samples were obtained and analyzed for levels of triglycerides and cholesterol. Growth hormone was found to raise fasting plasma triglycerides significantly in a group of 6 middle-aged and elderly diabetic subjects but not in 10 nondiabetic midde-aged and elderly controls. Smaller and less consistent increases were also observed in a group of 6 normal young men and in 6 young women who were taking contraceptive pills at the time. In no group was there any significant change in plasma cholesterol level 12 hr following growth hormone administration.

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