The relationship between VIII-A.H.F., VIII-A.G.N., and von Willebrand factor is still unresolved. The presence of decreased factor XII in von Willebrand's disease introduces yet another variable. Until further work clarifies these relationships, it is suggested that those patients who have been diagnosed as having von Willebrand's disease and reduced factor XII be referred to as patients with von Willebrand's disease San Diego.

We thank Charles G. Cochrane and Susan Revak, Department of Experimental Pathology, Scripps Clinic and Research Foundation, La Jolla, California, for the immunoassay measurement values.

This work was supported in part by the Bureau of Medicine and Surgery Clinical Investigation Program.

Requests for reprints should be addressed to A.D.C., Hematopathology Section, Department of Pathology, University of Southern Carolina School of Medicine, 2025 Zonal Avenue, Los Angeles, California 90033, U.S.A.

REFERENCES

1. Peake, I. R., Bloom, A. L., Giddings, J. C. *New Engl. J. Med.* 1974, **291**, 113.
2. Weiss, H. J. *New Engl. J. Med.* 1975, **293**, 580.
3. Bowie, E. J. W., Fass, D. N., Olson, J. D., Owen, C. A. *Mayo Clin. Proc.* 1976, **51**, 35.
4. Zimmerman, T. S., Ratnoff, O. D., and Powell, A. E. *J. clin. Invest.* 1971, **50**, 244.
5. Howard, M. A., Firkin, B. G. *Thromb. Diath. Hæmorrh.* 1971, **26**, 362.
6. Weiss, H. J. *in* Platelet aggregation (edited by W. J. Williams, E. Beutler, A. J. Ersley, and R. W. Rundler); p. 1415. New York, 1972.
7. Mielke, C. H., Kaneshiro, M. M., Weiner, J. M., Rappaport, S. I. *Blood*, 1969, **34**, 204.
8. Kaplan, A. P. *Microvaasc. Res.* 1974, **8**, 97.
9. Wilner, G. D., Norsl, H. L., LeRoy, E. C. *J. Clin. Invest.* 1968, **47**, 2608.
10. Cochrane, C. G., Revak, S. D., Aiken, B. S., Wuepper, K. D., in Inflammation: Mechanisms and Control (edited by H. Lepow and P. Ward). p. 119. New York, 1972.
11. Caen, J. P., Sultan, Y. *Lancet*, 1975, ii, 1129.

EVIDENCE FOR HYPERŒSTROGENÆMIA AS A RISK FACTOR FOR MYOCARDIAL INFARCTION IN MEN

GERALD B. PHILLIPS

Department of Medicine, Columbia University College of Physicians and Surgeons, Roosevelt Hospital, New York, New York 10019, U.S.A.

Summary Fifteen men who had had a myocardial infarction between the ages of 32 and 42 years were compared with fifteen age-matched healthy men. Seven of the patients had a strikingly slow rate of beard growth, three had evidence of gynæcomastia, and three had a loss of libido. The slow beard growth and decreased libido, and possibly the gynæcomastia, preceded the myocardial infarction. Mean serum œstradiol and œstrone concentrations were significantly increased in the patients, 43·5±8·8 (standard deviation) and 50·7±9·5, respectively, compared with 33·5±5·5 and 37·5±5·8 pg/ml in the controls ($P<0·001$). Mean serum testosterone and dihydrotestosterone concentrations were not significantly different in the two groups. Serum œstradiol and œstrone concentrations were directly proportional to each other as were those of testosterone and dihydrotestosterone. These results suggest that the hyperœstrogenæmia preceded the myocardial infarction and that hyperœstrogenæmia may be an important risk factor for myocardial infarction in men.

Introduction

MYOCARDIAL infarction commonly occurs in patients with none of the major known risk factors for the disorder. This suggests that important risk factors remain to be discovered. In a search for such risk factors, it was decided to study patients at the lower end of the age spectrum for myocardial infarction on the assumption that the evidence for a risk factor might be more exaggerated in this group and thus more easily identified. The first patient studied was a 38-year-old man who had had none of the risk factors except that he smoked. On examination there was evidence of feminisation—i.e., slight gynæcomastia and rounded hips—supported by a history of loss of libido for several years and a need to shave only two or three times a week. These findings were surprising since the pronounced male prevalence of myocardial infarction in this age-group had suggested masculinity as a factor.[1] Indeed, œstrogens have been administered in an attempt to prevent myocardial infarction.[2–4]

In order to evaluate the relation, if any, between sex hormones and the development of myocardial infarction, fifteen men who had had a myocardial infarction between the ages of 32 and 42 years were studied and compared with fifteen age-matched healthy men. The results suggest that hyperœstrogenæmia may be an important risk and possibly predisposing factor for myocardial infarction in men.

Patients and Methods

All of the patients studied had been admitted to the Roosevelt Hospital at the age of 42 years or less with an acute myocardial infarction as evidenced by typical onset and pain pattern, increase in serum-enzyme (glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, lactic dehydrogenase, and creatine phosphokinase) concentrations, and characteristically evolving electrocardiographic changes. Patients were excluded from the study if they were left with any complication of the myocardial infarction or had any other serious disorder, had a history of alcoholism, or were regularly taking any drug. Patients with risk factors for myocardial infarction, such as hyperlipidæmia, diabetes, hypertension, or smoking were not excluded. Of the patients who qualified, fifteen volunteered and were studied. All were White and male. Six had had coronary angiography, which revealed complete occlusion of at least one major coronary vessel. As a control group, fifteen White men of similar age who were apparently healthy, had no history of alcoholism, and were not regularly taking any drug were studied in the same way. The age of the patients at the time of the myocardial infarction ranged from 32 to 42 years (mean±S.D. 37·6±3·5). Patients were 34–43 years old (39·5±3·1) when studied and the normal subjects were 33–43 years old (38·8±3·4). Three patients were studied 4 months after myocardial infarction, three patients at 6–8 months, seven patients at 15–26 months, one patient at 45 months, and one patient at 118 months. Patients and normal subjects were studied in the order in which they became available over a 2-year period.

Each patient and normal subject was instructed to ingest no alcohol or any drug for one week before testing and to consume at least 200 g of carbohydrate per day for 3 days before testing. Examination and blood sampling were performed on the same day. A detailed history and physical examination were carried out. The dietary history confirmed that all patients and normal subjects had followed instructions on carbohydrate ingestion. The diet of the two groups differed, however, in that eleven of the patients, but only two of the normal subjects, were limiting consumption of animal fat; in the patients limitation had begun at the time of the myocardial infarction. None of the other patients or normal subjects were consuming any special diet. Mean coffee intake was 3 cups per day in the patients and 2·7

cups per day in the normal subjects, 62% of the patients' coffee being decaffeinated. Tea intake averaged 0·6 cups per day in the patients and 0·5 cups per day in the normal subjects. Alcohol intake in both groups had been similar prior to a week before study. The mean±S.D. heights and weights of the patients were 173±9 cm and 78·1±14·0 kg, respectively, and those of the normal subjects 178±7 cm and 78·5±12·8 kg, respectively. None of the patients or normal subjects appeared obese.

Tests were carried out after a 12-hour overnight fast. After withdrawal of an initial venous blood-sample, a 3-hour oral glucose tolerance test was performed with 75 g glucose. All of the hormone and lipid determinations were carried out on the initial sample. The sera were separated and aliquots of the initial serum were removed for agarose-gel electrophoresis and lipid extraction. Aliquots of the initial serum sample for hormone and glucose measurements were stored at −20°C.

Radioimmunoassay (R.I.A.) of the serum sex hormones was carried out by a modification of the method of Coyotupa et al.[5] The antisera used for measurement of œstradiol-17β and œstrone (s-310 no. 5) and testosterone and 5α-dihydrotestosterone (s-741 no. 2) were supplied by Dr G. E. Abraham.[5] For œstradiol and œstrone determination, duplicate 2 ml aliquots of serum were each extracted twice with 6 ml of diethylether. For testosterone and dihydrotestosterone assay, two 0·2 ml volumes of serum were each similarly extracted twice with 2 ml of diethylether. Approximately 1000 c.p.m. of each tritiated hormone had been added to the respective serum for estimation of hormone recovery. The duplicate sample was always analysed in a separate run and samples from patients and controls were analysed simultaneously in each run. Separation of the hormones of the ether extract was carried out on 0·8 g 'Celite' (kieselguhr)/ethylene glycol (2/1) columns and isooctane/ethyl-acetate mixtures were used for elution. The dried eluate of each hormone fraction was dissolved in assay buffer, a volume removed for counting to determine recovery, and two different volumes taken for R.I.A. Included with each run were a sample of stock charcoal-adsorbed plasma,[6] which gave essentially the same value as the water blank, and a sample of serum pooled from three healthy men. The inter-assay means ± coefficient of variation for œstradiol and œstrone (13 runs) in pooled serum were 31·1±10·5% and 34·4±16·0%, respectively, and for testosterone and dihydrotestosterone (17 runs) 5·55±4·6% and 0·63±19·8%, respectively.

Glucose was measured by a glucose-oxidase method. Lipids and lipoproteins were determined as described elsewhere.[7,8] Solvents were distilled before use.

Statistical analyses for the significance of the difference between two means were performed by Student's *t* test.

Results

Clinical

Beard.—Separation of the shaving patterns into three categories facilitated comparison between the two groups. Pattern I was the need to shave each morning and again in the evening if a social event was anticipated—i.e., to remove a "5 o'clock shadow". Pattern II was the need to shave each morning but without developing a 5 o'clock shadow. Pattern III was the need to shave only every 2 to 3 days. Six patients and twelve controls had pattern-I beard growth, while seven patients and no normal subjects had pattern III. One patient with pattern III stated that he could not grow a beard over 1 cm long. Of the six patients with pattern-I beard growth, four had major risk factors such as hypercholesterolæmia, hypertension, glucose intolerance, or some combination of these. Of the seven patients with pattern-III beard growth, none had any of these risk factors. When the patient group was expanded to twenty-one by the addition of six patients who had had a myocardial infarction while they were aged less than 43 years but were not included in the rest of this study and the normal group expanded by the addition of six healthy subjects, a similar distribution was seen. Seven patients and fifteen controls had pattern-I growth, and nine patients and no normal subjects had pattern III. The shaving pattern appeared to have remained the same for any individual from the time shaving began and, thus, antedated the myocardial infarction.

Other hair.—There was no clear-cut difference between the two groups with regard to amount of hair or its distribution.

Gynæcomastia.—Three patients had gynæcomastia on the left associated with tenderness in two which preceded the myocardial infarction, in one for a year before the attack. One other patient had evidence of bilateral gynæcomastia. Gynæcomastia was not detected in any of the normal subjects.

Testes.—Mean testicular size was not significantly different in the patients and controls. One patient had an atrophic testis and three patients and one normal subject were thought to have small testes.

Skin.—The skin of four patients and one normal subject was unusually smooth.

Libido.—Three patients had gradually lost interest in sex over a period of several years. This decrease antedated the myocardial infarction. None of the controls reported this decrease in libido.

Fecundity.—Four patients had never been married (two of whom were homosexual), and two were divorced. One normal subject had never been married, one was divorced, and none were homosexual. Of those who had been married, six of the eleven patients and eleven of the fourteen normal subjects had children. One in each group had been involuntarily infertile for over 10 years.

Sex Hormones

Serum concentrations of œstradiol, œstrone,

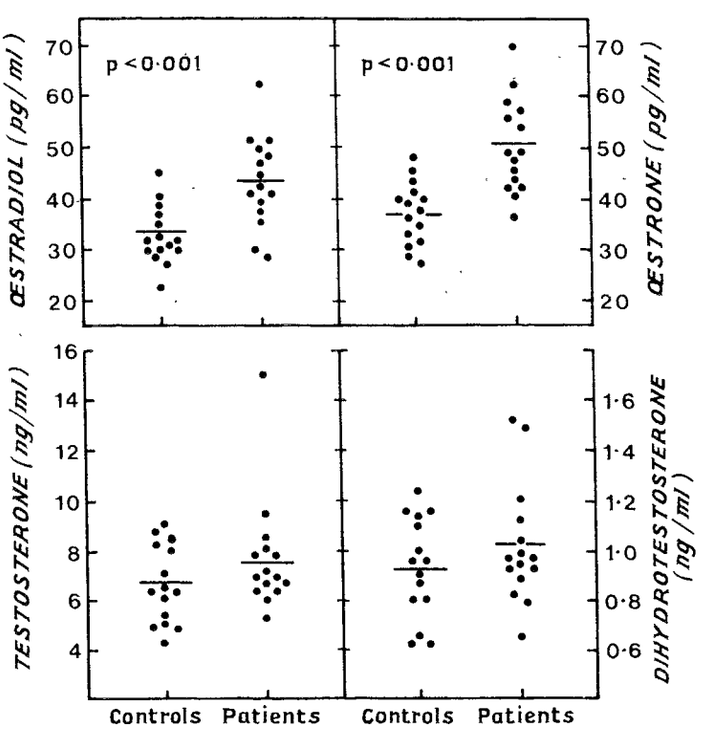

Fig. 1—Comparison of serum concentrations of œstradiol, œstrone, testosterone, and dihydrotestosterone in patients and controls.

testosterone, and dihydrotestosterone were compared in patients and controls (fig. 1). For œstradiol, the mean values±S.D. of the patients and controls were 43·5±8·8 and 33·3±5·5 pg/ml, respectively; for œstrone, 50·7±9·5 and 37·5±5·8 pg/ml; for testosterone, 7·68±2·27 and 6·78±1·57 ng/ml; and for dihydrotestosterone, 1·02±0·24 and 0·93±0·20 ng/ml. Both the mean serum œstradiol and œstrone concentrations in the patients were significantly increased ($P<0·001$), whereas mean serum testosterone and dihydrotestosterone concentrations were not significantly different from those in the controls. When the testosterone concentration of 15·0 ng/ml found in one patient, a value that was confirmed by quadruplicate analysis, was excluded, the mean testosterone concentration in the patients was 7·16±1·09 ng/ml. Only two patients had serum-œstradiol concentrations less than the mean value in the healthy men. One of these patients had hypertension, glucose intolerance, and hypertriglyceridæmia, while the other had glucose intolerance, hypertriglyceridæmia, and a history of smoking 50 pack-years. Both had pattern-I shaving.

Serum-œstradiol concentration was directly proportional to serum-œstrone concentration ($P<0·001$) in the combined samples of patients and normal subjects (fig. 2). The patient samples by themselves also showed this correlation ($P< 0·02$). The increase in both serum œstradiol and œstrone concentrations and the correlation between the two supports the validity of the presence of hyperœstrogenæmia in these patients. Serum concentrations of testosterone and dihydrotestosterone were also directly proportional to each other ($P<0·001$) (fig. 3).

Comparison of the patients and normal subjects with regard to major known risk factors[9 10] for myocardial infarction showed the following results.

Serum-lipids

Mean ±S.D. serum cholesterol, triglyceride, and phospholipid concentrations in the patients were 222±57, 114±50, and 214±44 mg/dl, respectively, as compared with 203±48, 71±30, and 200±35 mg/dl in the normal subjects. Of these lipids, only the triglyceride was significantly increased ($P<0·01$) in the patients. In two

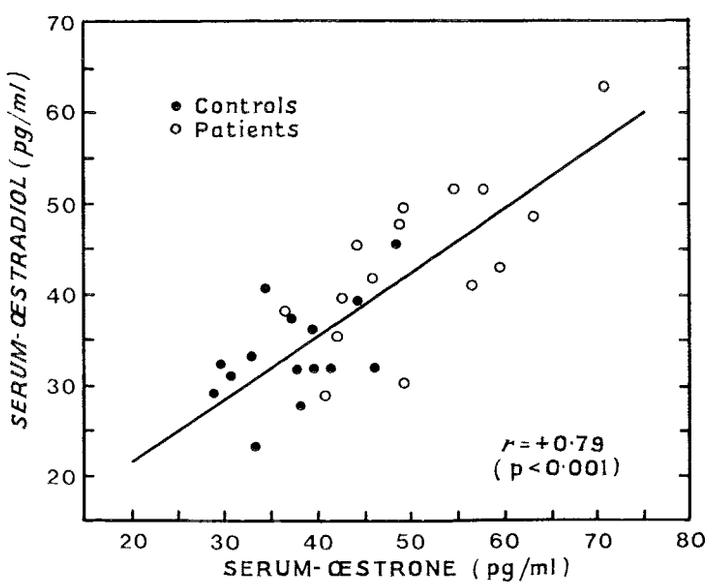

Fig. 2—Relation of serum œstradiol and œstrone concentrations in patients and controls.

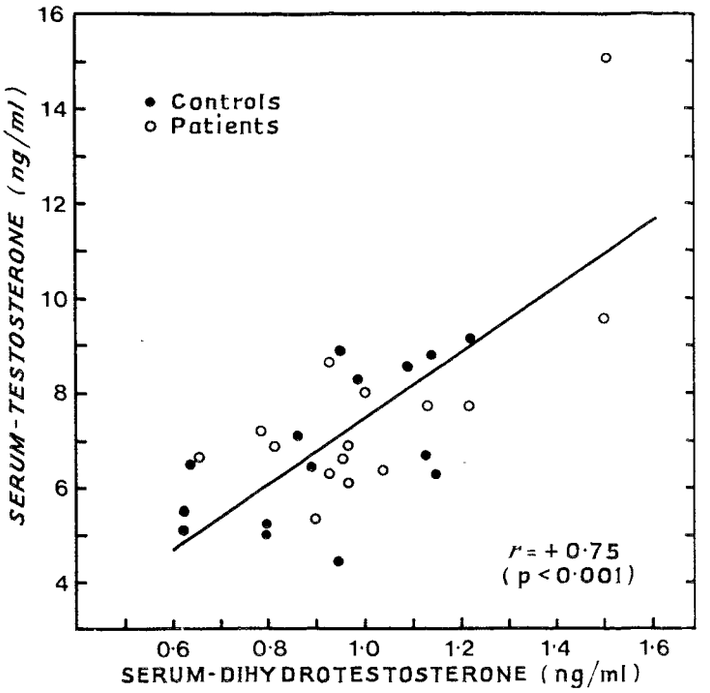

Fig. 3—Relation of serum testosterone and dihydrotestosterone concentrations in patients and controls.

patients, but no normal subjects, serum-cholesterol concentration was less than 140 mg/dl. The relative amounts of serum β, pre-β, and α lipoprotein in the patients were 50±6 (S.D.), 23±7, and 28±10%, respectively, as compared with 46±7, 15±7, and 39±8% in the normal subjects, a significant increase ($P<0·01$) in pre-β and decrease ($P<0·01$) in α lipoprotein in the patients. Mean serum concentration of pre-β lipoprotein was also increased ($P<0·02$) and α lipoprotein reduced ($P<0·01$) in the patients. At the time of admission to hospital for myocardial infarction, the mean ±S.D. serum cholesterol and triglyceride concentrations of the patients were 235±54 and 130±32 mg/dl, respectively. Only the triglyceride concentration was significantly different ($P<0·001$) from the value in the controls.

Blood-pressure

Two patients and three normal subjects showed evidence of mild hypertension. In one patient, blood-pressure was 155/107 mm Hg and in the other 135/98 mm Hg, while in the three normal subjects, blood-pressures were 145/98, 140/100, and 135/105 mm Hg.

Glucose Tolerance

Compared with controls, two patients had significantly increased ($P<0·01$) serum-glucose concentration in the 2-hour sample of the glucose tolerance test and another patient had a significant increase in the 30-minute and 1-hour samples ($P<0·05$). The glucose tolerance curves differed in the two groups in that the peak serum-glucose concentration was at 1-hour in twelve patients and three normal subjects and at 30-minutes in three patients and twelve normal subjects.

Smoking

Of the normal subjects, five had never smoked cigarettes and five had stopped smoking at least 4 years before study. Three had smoked for one pack-year (packs of cigarettes per day x years of smoking), four for 4 to 8 pack-years, and three for 12 to 31 pack-years. Of the

patients, three had never smoked cigarettes, although one had smoked three to four cigars per day for 14 years. Six had smoked for 12 to 31 pack-years, and six for 32 to 60 pack-years. Three had stopped smoking 3 to 4 years before the myocardial infarction, and all had stopped immediately after the myocardial infarction.

Family History

Of the normal subjects, five had first or second degree relatives with hypertension, five with diabetes, and three with myocardial infarction. Six had no relatives with any of these disorders. Of the patients, seven had first or second degree relatives with hypertension, four with diabetes, six with myocardial infarction, and two with hypercholesterolæmia. Only one had no relatives with any of these disorders.

Possible Risk Factor[11]

Of the normal subjects, three drank coffee for less than 6 cup-years (cups of coffee per day × years consumed), eleven for 6 to 75 cup-years, and one for 128 cup-years. Of the patients, three drank coffee for less than 6 cup-years, four for 6 to 75 cup-years, and eight for 75 to 180 cup-years. After the myocardial infarction, one patient stopped drinking coffee, four cut consumption to about half, and six switched to decaffeinated coffee.

Discussion

Although the fifteen patients in this study had experienced a myocardial infarction before the age of 43 years, eleven had none of the major known risk factors[9 10] except for smoking in nine, and three of these had not smoked for 3–4 years before the infarction. Hypercholesterolæmia, hypertension, glucose intolerance, or some combination of these was observed in four patients and three control subjects. These findings suggest that other important risk factors remain to be identified. The present study provides evidence that signs of feminisation, especially with regard to rate of beard growth, correlate with myocardial infarction in men in the age-group studied. Seven patients but no control subjects had to shave only every 2–3 days. None of these seven had any of the major known risk factors except for smoking. Of the six patients who had rapid beard growth, four had major known risk factors in addition to smoking. Three patients had gynæcomastia and three had experienced a loss of libido.

These clinical signs of feminisation in the patients were supported by the finding of a significant increase in mean serum-œstradiol. Only two patients had serum-œstradiol concentrations less than the mean value in the controls and both had more than one major known risk factor. The validity of this increase in serum-œstradiol concentration is enhanced by the finding of a significant increase in the mean serum-œstrone concentration and a direct correlation between the œstradiol and œstrone concentrations. There was no significant difference in mean serum-testosterone and dihydrotestosterone concentrations between patients and controls. The data in the present study do not allow any conclusions to be reached about the mechanism of the hyperœstrogenæmia.

The hyperœstrogenæmia could have been secondary to the myocardial infarction or the result of an exogenous factor. Since nine patients were studied at least 15 months after myocardial infarction and none before 4 months, it seems unlikely that the myocardial infarction itself influenced the œstrogen concentrations. The finding that slow beard growth, breast tenderness, and loss of libido preceded the infarction supports this conclusion. With regard to an exogenous factor, the patients had had a higher rate of smoking and intake of coffee, but immediately after the infarction, all of the patients stopped smoking and five decreased their coffee intake so that cigarette and coffee consumption was similar in the patient and control groups at the time of study. Nevertheless, the previously increased cigarette or coffee consumption, or both, in the patients might have had a lasting effect on serum-œstrogen concentrations through unknown mechanisms. Another difference between the two groups was the lower intake of fat of animal origin in the patients. The relation, if any, between fat intake and serum œstrogen has not been studied. The two groups appeared to be otherwise similar, and no other factor could be identified to account for the hyperœstrogenæmia.

The observation that signs of feminisation preceded the infarction suggests that the hyperœstrogenæmia also preceded the infarction and that hyperœstrogenæmia may be an important risk factor in myocardial infarction in men. That the hyperœstrogenæmia observed may also be an important predisposing factor for myocardial infarction in men is supported by the Coronary Drug Project, which showed that men receiving œstrogens daily over an 18-month period had an increased incidence of myocardial infarction.[3] How the œstrogens produced this increase is not known, although the higher incidence of thrombophlebitis and pulmonary embolism in the œstrogen-treated group suggests that an effect on the clotting mechanism may have been involved. An increase in serum-triglyceride without an increase in serum-cholesterol was also observed in the œstrogen-treated group.[4] Concentrations of serum triglyceride and pre-β-lipoprotein, the main lipid component of which is triglyceride, were significantly increased in our patients as compared to the controls, a finding previously observed in this laboratory and reported by Hatch et al.[12] in patients under 50 years of age with myocardial infarction. Thus, an effect on serum lipids or lipoproteins may provide a link between hyperœstrogenæmia and myocardial infarction. The abnormal glucose tolerance observed in these patients may be another such link. Another possibility is that hyperœstrogenæmia in men may lead to emotional changes,[2] which may in turn increase susceptibility to myocardial infarction, perhaps through increased cigarette and coffee consumption. On the other hand, even if hyperœstrogenæmia did induce in certain patients these factors and others, such as hypertension, associated with myocardial infarction, it might still act through some entirely different mechanism.

There are few studies relating sex hormones and myocardial infarction. In an extensive analysis of patients who had had a myocardial infarction while under the age of 40 years, Gertler and White concluded that these patients were morphologically more masculine than the controls, but psychologically more feminine.[1] Although they studied the distribution and amount of hair growth, they apparently did not estimate rate of beard growth. No significant difference in the excretion of urinary 17-ketosteroids was observed. Others have reported a decrease in urinary androsterone within 10 days of infarction,[13] or a decrease in urinary andros-

terone with an increase in other urinary 17-ketosteroid components, but no change in urinary œstrogens, when patients were studied at least 3 months after the infarction.[14]

Although patients in the present study were less than 44 years of age, the reported increase in plasma-œstradiol concentration with ageing in men[15] suggests that hyperœstrogenæmia might persist or even develop as a risk factor in older men.

I thank Monique Lores for technical assistance. This work was supported in part by grants HL-10950 and RR-05663 from the National Institutes of Health, U. S. Public Health Service.

REFERENCES

1. Gertler, M. M., White, P. D. Coronary Heart Disease in Young Adults. A Multidisciplinary Study. Cambridge, Massachusetts, 1954.
2. Russ, E. M., Eder, H. A., Barr, D. P. *AM. J. Med.* 1955, **19**, 4.
3. The Coronary Drug Project. *J. Am. med. Ass.* 1970, **214**, 1303.
4. The Coronary Drug Project. *ibid.* 1973, **226**, 652.
5. Coyotupa, J., Parlow, A. F., Abraham, G. E. *Analyt. Letters.* 1972, **5**, 329.
6. Heyns, W., van Baelen, H., de Moor, P. *Clinica chim. Acta.* 1967, **18**, 361.
7. Phillips, G. B., Dodge, J. T. *J. Lipid Res.* 1967, **8**, 676.
8. Wille, L. E., Phillips, G. B. *Clinica chim. Acta.* 1971, **34**, 457.
9. Truett, J., Cornfield, J., Kannel, W. *J. chron. Dis.* 1967, **20**, 511.
10. Garcia, M. J., McNamara, P. M., Gordon, T., Kannell, W. B. *Diabetes*, 1974, **23**, 105.
11. Boston Collaborative Drug Surveillance Program. *Lancet.* 1972, ii, 1278.
12. Hatch, F. T., Reissell, P. K., Poon-King, T. M. W., Canellos, G. P., Lees, R. S., Hagopian, L. M. *Circulation.* 1966, **33**, 679.
13. Rao, L. G. S. *Lancet.* 1970, ii, 390.
14. Marmorston, J., Geller, P. J., Weiner, J. M., Allain, C. C., Pare, J. H., Bush, I. E., Roberts, J. B. *Physiol. Chem. Phys.* 1970, **2**, 337.
15. Pirke, K. M., Doerr, P. *Acta Endocr.* 1973, **74**, 792.

GLUCAGON RESISTANCE AS A CAUSE OF HYPERTRIGLYCERIDÆMIA

R. S. ELKELES J. HAMBLEY

Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex HA1 3UJ

Summary The hypothesis that glucagon resistance is a cause of hypertriglyceridæmia has been tested by studying the effects of exogenous glucagon in patients with hypertriglyceridæmia and controls. Glucagon had a greater triglyceride-lowering-effect in hypertriglyceridæmic patients than in controls. The other metabolic responses to glucagon were similar in both groups. No evidence of glucagon resistance was found.

Introduction

ENDOGENOUS hypertriglyceridæmia may be caused by various factors. It has been suggested that one of these factors could be resistance to the action of glucagon.[1 2] We have attempted to test this hypothesis by studying the effects of exogenous glucagon in patients with hypertriglyceridæmia and controls.

Patients and Methods

6 patients (5 male and 1 female) with endogenous hypertriglyceridæmia whose mean age was 51 years (range 39–64) were studied. 4 were diagnosed as a result of screening procedures and 2 had intermittent claudication. 4 had both raised serum triglyceride and cholesterol concentrations and 2 had hypertriglyceridæmia only. Lipoprotein electrophoresis[3] was carried out on all the patients and all were classified as having Frederickson type-IV hyperlipoproteinæmia. All had a normal oral glucose tolerance test and normal thyroid function. Other secondary causes of hyperlipidæmia were excluded. Their mean percentage desirable body-weight[4] was 111% (range 100–132). The controls consisted of 6 healthy laboratory personnel (4 male and 2 female) mean age 32·5 years (range 23–47), whose mean percentage desirable body-weight was 95·6% (range 78–104).

After an overnight fast, an indwelling cannula was inserted into a large antecubital vein, and the subjects were allowed to rest for 20 min. After the basal sample had been taken, glucagon (Eli Lilly) 10 μg/kg was rapidly injected through the cannula. Blood-samples were taken at 5, 10, 15, 30, 45, and 60 min for estimation of blood-glucose, plasma cyclic-adenosine-monophosphate (CA.M.P.), serum-insulin, serum-triglyceride, and plasma-fatty-acids (F.F.A.). Blood-glucose was measured by an automated glucose-oxidase method, serum-triglyceride by an enzymic method (Boehringer Corporation), and serum-insulin by a modified double-antibody method.[5] Plasma-CA.M.P. was measured by a competitive protein-binding assay[6] (Radiochemical Centre, Amersham), and plasma-F.F.A. by Dole's method.[7] Changes in serum-triglyceride and plasma-F.F.A. from the basal value were compared with those after glucagon by Student's paired *t*-test.

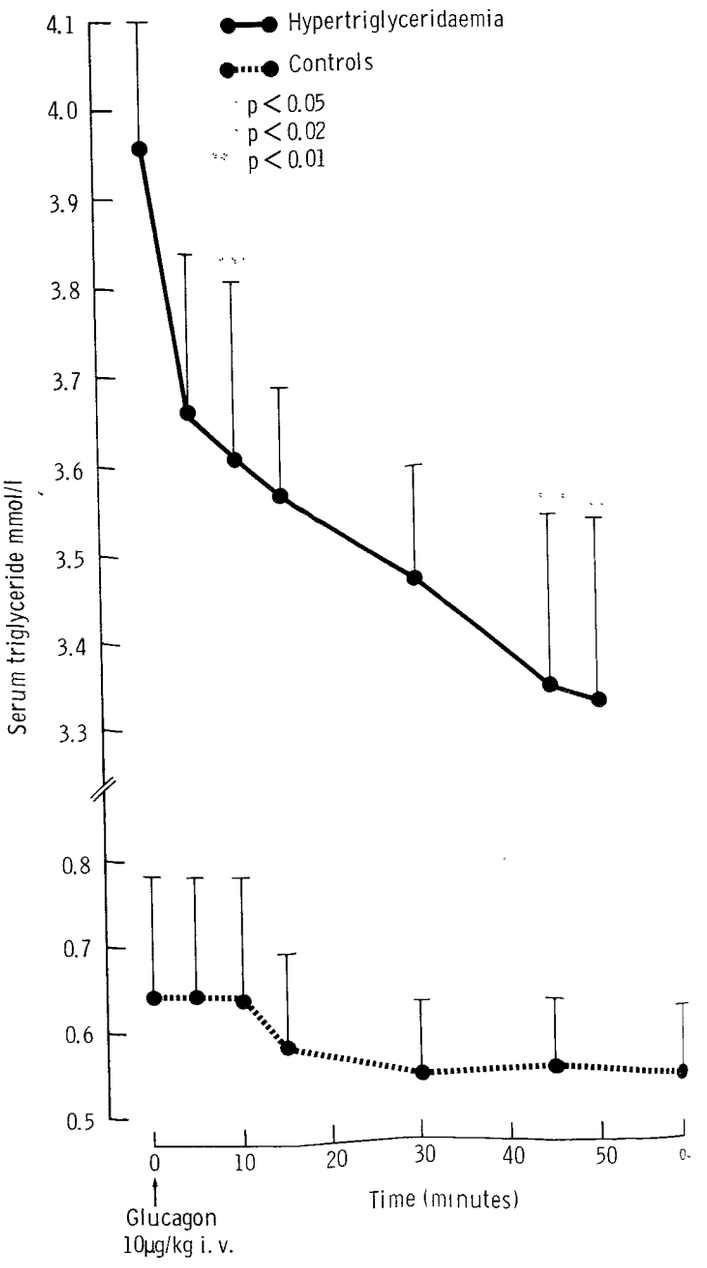

Fig. 1—Serum-triglyceride response to i.v. glucagon (mean+S.E.M.).