sy in directions similar to that of androgen (table). Such findings implicate a gonadal-adrenal interaction. Unlike androgenization, however, prenatal stress did not alter vaginal opening (table). Gorski[12-14] describes anovulatory syndromes in androgenized females where full sterility is produced by large amounts of exogenously-administered androgens at critical periods, and partial sterility by ligher amounts at less critical times. Prenatal stress may operate similarly, producing different effects on different reproductive indices in either sex, depending upon maturation and patterns of hormone release.

1 Dahlof, L.G., Hard, E., and Larsson, K., Anim. Behav. *25* (1972) 958.
2 Dunlap, J.L., Zadina, J.E., and Gougis, G., Physiol. Behav. *21* (1978) 873.
3 Gotz, F., and Dorner, G., Endokrinologie *76* (1980) 115.
4 Meisel, R.L., Dohanich, G.P., and Ward, I.L., Physiol. Behav. *22* (1979) 527.
5 Rhees, R.W., and Fleming, D.E., Physiol. Behav. *27* (1981) 879.
6 Ward, I.L., Science *175* (1972) 82.
7 Ward, I.L., J. comp. physiol. Psychol. *91* (1977) 465.
8 Whitney, J.B., and Herrenkohl, L.R., Physiol. Behav. *19* (1977) 167.
9 Herrenkohl, L.R., Science *206* (1979) 1097.
10 Herrenkohl, L.R., in: Monographs in Neural Sciences, vol.9, p.176. Ed. M.M. Cohen. Karger, Basel 1983.
11 Herrenkohl, L.R., and Politch, J.A., Experientia *34* (1978) 1240.
12 Gorski, R.A., in: Neuroendocrinology, p.25. Eds D. Krieger and J. Hughes. Sinauer, Sunderland, MA. 1980.
13 Harlan, R.E., and Gorski, R.A., Endocrinology *101* (1977a) 741.
14 Harlan, R.E., and Gorski, R.A., Endocrinology *101* (1977b) 750.
15 Ward, I.L., and Weisz, J., Science *207* (1980) 328.
16 Ward, I.L., and Weisz, J., submitted.
17 Beckhardt, S., and Ward, I.L., Develop. Psychobiol., in press.
18 Chapman, R.H., and Stern, J.M., J. comp. physiol. Psychol. *92* (1978) 1024.
19 Clemens, L.G., Gladue, B.A., and Coniglio, L.P., Horm. Behav. *10* (1978) 40.
20 Meisel, R.L., and Ward, I.L., Science *213* (1981) 239.

0014-4754/84/010101-03$1.50 + 0.20/0

Free thyroxine in myocardial infarction

O.J. Kirkeby[1], C. Risöe and K. Kirkeby

Medical Department VII, and Institute for Medical Research, Ullevaal Hospital, Oslo (Norway), 23 March 1983

High values for the free thyroxine fraction were found in the serum of 24 patients during the early phase of myocardial infarction. A strong correlation between the free thyroxine fraction and free fatty acids suggests that they compete for protein binding sites. The increase in free thyroxine may have undesirable effects on myocardial oxygen demand during acute myocardial infarction.

Studies on lipid metabolism after a myocardial infarction (MI) reveal several characteristic patterns. Levels of cholesterol, phospholipids, and beta-lipoproteins in serum tend to fall a few days after the onset[2]. The fatty acid composition of the serum lipids also changes with an increase of arachidonate and palmitate percentages and a decrease of linoleate[3]. Thyroxine induces similar changes[4,5]. We have therefore measured the serum thyroxine (T_4) and free thyroxine (FT_4) fractions in the early course of MI.

Material and methods. T_4, FT_4 fraction, and free fatty acids (FFA) were assayed in 24 men, aged 43–68 years, with MI. They were accepted for the study if the onset of symptoms had occurred less than 6 h before the admission. The diagnosis was based on clear clinical and electrocardiographic evidence in addition to increased aspartate aminotransferase values. All patients were observed in the coronary care unit with continuous electrocardiographic monitoring. Venous blood samples were taken at the time of admission, then 4 times at fixed hours during the first 24 h, and at 08.00 h on the following 3 days. Patients were fasting at 08.00 h. The control group consisted of 37 men in the same age group without obvious disease. FT_4 fraction was determined by the tracer equilibrium dialysis of Vaerenberg et al.[6], and FFA by the method of Trout et al.[7]. A nonparametric test, the Median test, was used for the statistical evaluation together with Kendall's correlation coefficient.

Results. T_4 concentrations in the samples drawn less than 6 h after the onset of symptoms are significantly higher than in the control group (table). In the period from 6 to 19 h the mean value is still slightly higher than in the control group, but the difference is not statistically significant. Later values do not differ from those of the controls. The FT_4 fraction shows high values on admission, with a mean of 0.095% against 0.047% in the control group ($p < 0.001$). Later values are lower, but remain significantly elevated during the entire period studied.

Admission values of FFA were often very high with a mean value more than 3 times the mean value of controls. A strong correlation was found between FFA and FT_4 frac-

Thyroxine (T_4), free thyroxine (FT_4) fraction, and free fatty acids (FFA) in patients with myocardial infarction and in controls. (Mean values with range in parentheses)

Hours after onset of symptoms	T_4 (nmol/l)	FT_4 (%)	FFA (μmol/l)
< 6	184** (84–322)	0.095* (0.051–0.195)	1655* (563–4120)
6–19	154 (77–368)	0.077** (0.052–0.138)	873** (419–1635)
20–39	145 (89–243)	0.075** (0.045–0.310)	723 (187–1283)
40–59	117 (45–254)	0.078** (0.050–0.145)	608 (230–1250)
60–79	138 (59–248)	0.076** (0.043–0.131)	561 (168–1250)
Controls	131 (53–202)	0.047 (0.032–0.109)	513 (184–1478)

* $p < 0.001$; ** $p < 0.01$.

tions in values obtained at admission (correlation coefficient 0.807, $p < 0.001$). There was no significant correlation between the infarct size, as measured by the peak level of aspartate aminotransferase, and the peak values of T_4, FT_4 fraction or FFA.

Discussion. The increased FT_4 fraction in our study reflects a weaker protein binding of the hormone. A number of factors have been suggested that may affect this protein binding, and some of them may be active in MI; e.g. decreased thyroxine binding prealbumin levels caused by the 'acute phase reaction'[8,9], increased secretion of catecholamines and cortisol[10,11], metabolic acidosis[12], elevated body temperature[13], and increased serum FFA. It has been suggested by Hollander et al.[14] that FFA act as competitive inhibitors of T_4 binding. Our results, with significant correlation between FFA and FT_4 fractions on admission, support this hypothesis. However, increased FFA cannot fully explain the increased FT_4 fraction, since the former normalizes so quickly. Other factors mentioned above may therefore contribute.

Does an increase in free T_4 in serum imply a correspondingly increased hormone effect in tissues? T_3 is deiodinated to 3,3′,5-triiodothyronine (T_3) or 3,3′,5′-triiodothyronine (reverse T_3). Reverse T_3 is metabolically inactive. Other investigators have shown that in MI there is a reduced peripheral conversion of T_4 into T_3 with a concurrent increase in reverse T_3 production[8,14]. The mechanism of this shift in T_4 metabolism is unknown, but it certainly leads to lower concentrations of T_3 together with the increased FT_4 fraction. Thus, the level of hormone activity is not easily discerned by looking directly at concentrations. Assumptions can, however, be made indirectly by looking for T_4 effects in MI. Theoretically, high thyroid activity could be expected to shorten the S-T segments in patients with MI, as action potentials in hyperthyroid animals are shortened[16]. We could not confirm this on the electrocardiograms in our patients. The increase in thyroid hormones may be too moderate to induce electrocardiographic changes.

The fatty acid composition of serum is, however, susceptible to the T_4 concentration, and the composition in MI is characteristic for high thyroid activity[3,4]. We therefore believe that hormone effects are increased in MI, probably because of the increase in FT_4 shown in this study. In heart muscle this increase could lead to greater oxygen consumption, and the myocardium might suffer further damage. T_4 also sensitizes the myocardium to catecholamines and might induce arrythmias. A high FFA level has been shown to be arrythmogenic[17]. Patients with the combination of increased FFA and increased FT_4 fraction could thus be prone to develop arrythmias. However, our sample is too small to assess the relation between FFA, the FT_4 fraction, and the clinical course of MI.

1 Address for correspondence and reprints: O.J. Kirkeby, Nordfjord Hospital, 6771 Nordfjordeid, Norway.
2 Fredricson, D.S., Circulation *39* (1963) suppl. 4, 99.
3 Kirkeby, K., Acta med. scand. *192* (1972) 523.
4 Kirkeby, K., Acta endocr. *71* (1972) 62.
5 Kirkeby, K., Acta endocr. *71* (1972) 73.
6 Vaerenberg, M., Bekaert, J., and Vaerenberg, P.M., Gesellschaft für Nuclearmedizin. 7. Jahrestagung, Zürich 1971.
7 Trout, D.L., Estes, E.H., and Friedberg, S.R., J. Lipid Res. *1* (1960) 199.
8 Johanssom, B.G., Kindmark, C.O., and Trell, E.Y., Scand. J. clin. Lab. Invest. *29* (1972) suppl. 124, 17.
9 Westgren, V., Burger, A., and Levin, K., Acta med. scand. *201* (1977) 269.
10 Hays, M.T., Solomon, S.M., and Religa, A., J. clin. Invest. *48* (1969) 1114.
11 Blomstedt, B., and Einhorn, J., Metabolism *16* (1967) 319.
12 Rosin, A.J., and Exton-Smith, A.N., Br. med. J. *1* (1964) 16.
13 Harvey, R.F., Lancet *1* (1971) 208.
14 Hollander, C.S., Scott, R.L., and Burgess, J.A., J. clin. Endocr. *27* (1967) 1219.
15 Wiersinga, W.M., Lie, K.I., and Touber, J.L., Clin. Endocr. *14* (1981) 367.
16 Freedberg, A.S., Papp, J.Gy., and Vaughhan Williams, E.M., J. Physiol. *207* (1970) 357.
17 Borbola, J., Papp, J.Gy., and Szekeres, L., Experientia *30* (1974) 262.

0014-4754/84/010103-02$1.50 + 0.20/0

Testosterone in royal jelly[1]

J. Vittek and B.L. Slomiany

Department of Medicine, Sections of Endocrinology and Gastroenterology, New York Medical College, Valhalla (New York 10595, USA), 8 September 1982

Summary. A compound with immunoreactivity, and TLC and GLC mobility of testosterone was isolated from royal jelly of honeybee *(Apis mellifera)*. This is the first demonstration of vertebrate steroid hormone in this species.

The hormone-like effects of royal jelly (larval food of honeybee *Apis mellifera*) in insects[2,3], experimental animals[4,5], and humans[6,7] have evoked considerable interest among scientists. The results of immunological and biological assays suggest that this material exhibits insulin- and gonadotropin-like activities[8-11]. The corticoid activity of royal jelly has been demonstrated in its acetone extracts, while its chloroform extracts contain estrogenic- and androgenic-like activities[13,14]. However, to date except for cholesterol[15,16], no other vertebrate steroid was isolated from this material. In this report, we present further evidence for the presence of testosterone in royal jelly.

Material and methods. Content of testosterone was determined in:

1. Native royal jelly (RJ) samples from Sigma Chemical Co. (Sigma 1981) and from OAC-Apiary (Guelph, Canada), collected in 1956 (OAC-1956) and in 1980 (QC-1980).
2. Lyophilized RJ samples from OAC-Apiary, collected in 1945 by G.F. Townsend (GFT-1945) and in 1981 by R.W. Shuel (RWS-1981), and in Prairie Vien Honey Co. (Michigan, USA) collected in 1981 and lyophilized in Dr Shuel's laboratory. All samples (except Prairie-1981 and Sigma-1981) were stored at −15 °C until processed. The samples from Prairie Honey Co. and Sigma Chemical Co.,