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Fasting in the rat does not induce hyperfibrinogenaemia

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Abstract—The effects of fasting in the rat on the plasma fibrinogen concentration have been investigated. Fasting for 24–48 hr produced the expected sustained increase (4–5-fold) in the concentrations in the plasma of non-esterified fatty acids, but no accompanying increase in that of fibrinogen was detected.

Over the last decade, several large epidemiological studies have documented the association between elevated plasma fibrinogen concentrations and increasing risk of ischaemic heart disease and stroke [1–3]. Such evidence has attracted interest in the mechanisms regulating plasma fibrinogen concentrations and in the possibility that hyperfibrinogenaemia may promote vascular disease [4]. In this regard, non-esterified fatty acids (NEFAs) have been reported to promote the synthesis and release of fibrinogen from mouse liver slices [5]. Furthermore, infusion of exogenous NEFAs is reported to elicit a marked (plasma) hyperfibrinogenaemia in rabbits within 24 hr [6]. Accordingly, we have investigated whether fasting in the rat, which is associated with marked increases in the plasma NEFA concentration [for example, 7], would lead to hyperfibrinogenaemia.

Materials and Methods

Male AHA rats [300 ± 10 g; Glaxo Group Research (U.K.)], were used in this study, and allowed free access to water throughout. Blood samples (0.5 mL) were collected by tail venepuncture from animals allowed free access to food on days 1 and 2 of the study, after which food was withdrawn. Further blood samples were obtained on days 3 (24 hr fasted) and 4 (48 hr fasted) of the study. This procedure had no obvious effect on the well-being of the animals. Blood samples were divided between citrated [0.45 mL of blood added to 0.05 mL trisodium citrate (3.8% w/v)] and saline–EDTA [0.05 mL of blood being added to 0.1 mL 5% EDTA (w/v) made up in 0.9% (w/v) saline]. Plasma fibrinogen concentration (citrated blood) was then estimated by the method of Clauss [8], whilst plasma NEFA concentrations (EDTA blood) were determined using the NEFAC (Wako Chemicals GmbH, Osaka, Japan) assay.

Results and Discussion

Twenty-four hours of fasting was associated with an approximately 4-fold increase in the plasma NEFA concentration, which was further increased when the fasting period was extended to 48 hr. However, these profound changes in NEFA concentration were associated with a small (16%), but statistically significant ($P < 0.01$), fall in the plasma fibrinogen concentration (Table 1). These results, when compared with those of Carlson *et al.* [6] (where the infusion of various fatty acids in the rabbit tended to increase plasma fibrinogen concentration), suggest that fasting may blunt the ability of NEFAs to stimulate fibrinogen synthesis by the liver. Our observation is consistent with the report that fasting reduces rates of total plasma protein synthesis in the rat [9]. Alternatively, hypofibrinogenaemia may reflect a fasting-induced activation of a compensatory stimulation of fibrinolysis. Whatever the underlying mechanism, our results clearly show that fasting does not increase fibrinogen levels in the rat, and so does not constitute a simple *in vivo* procedure for inducing a NEFA-dependent plasma hyperfibrinogenaemia in this species.

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Table 1. Effect of fasting on plasma NEFA and fibrinogen concentrations in the conscious rat

	NEFA (mM)		Fibrinogen (g/L)	
	Concentration	Change	Concentration	Change
Day 1 (fed)	0.29 ± 0.03	—	2.25 ± 0.03	—
Day 2 (fed)	0.21 ± 0.02	−0.06 ± 0.02	2.31 ± 0.05	0.06 ± 0.05
Day 3 (24 hr fasted)	0.80 ± 0.04	0.51 ± 0.05*	2.18 ± 0.04	−0.07 ± 0.04
Day 4 (48 hr fasted)	1.01 ± 0.05	0.72 ± 0.05*	1.89 ± 0.07	−0.36 ± 0.07*

Data are shown as the means ± SEM for at least 15 animals.
* $P < 0.01$ (vs day 1 values) by Student's paired *t*-test.

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