Résumé. Nous avons étudié les concentrations de dopamine et de noradrénaline du prosencéphale après lésion unilatérale des neurones monoaminergiques correspondants. Les deux méthodes employées soit biochimique et histochimique ont mis en évidence sensiblement le même phénomène, à savoir: une augmentation importante et rapide du taux de dopamine entre 15 min et 24 h suivie d'une chute due selon toutes probabilités à la dégénerescence axonale. Quand à la noradrénaline, seule la deuxième phase, la chute, a pu être observée.

N.-E. ANDÉN, P. BÉDARD, K. FUXE and U. UNGERSTEDT

Department of Pharmacology, University of Göteborg, S-400 33 Göteborg 33, and Department of Histology, Karolinska Institutet, S-104 01 Stockholm 60 (Sweden), 17 August 1971.

Inhibition of Acute Inflammation by Hyperlipemia

Dextran-induced anaphylactoid inflammation is inhibited by diabetes[1]. It has been suggested that this is due to the elevation of the blood sugar level[2]. Hyperlipemia is also very characteristic of diabetes. Therefore, experiments were carried out to determine the influence of the artificially induced hyperlipemia on the inflammatory response evoked by dextran.

Methods. Female rats of R Amsterdam strain weighing 100–200 g were used. Inflammatory response was produced by subplantar injections of dextran (300 µg Intradex in 0.1 ml) and carrageenin (500 µg in 0.1 ml). The volumes of the hind paws were measured by a mercury displacement method before and 60 min after dextran and 4 h after carrageenin injection. The degree of inhibition was expressed as percent of the control value.

Hyperlipemia was induced by oral administration of sunflower seed oil (oleum helianthi) and oleic acid by a stomach tube and by i.v. injection of Lipofundin® (B. Braun, Melsungen, 10% soybean oil emulsion (and oleic acid)/3% emulsion prepared by Tween 20 in isotonic saline). Inflammation was induced 2 h after oral and 30 min following i.v. administration. Serum samples were withdrawn at the time when inflammation was provoked. Lipids were extracted[3] and evaporation was done under N_2 atmosphere[4]. Triglyceride and free fatty acids (FFA) were determined by thin layer chromatography[5]. Blood sugar was measured by orthotoluidine reagent[6].

Results and discussion. The experiments showed that oleum helianthi (5.0 g/kg by mouth) and Lipofundin® (0.5–1.0 g/kg i.v.) considerably inhibited the anaphylactoid inflammation (Table I). The effect depended upon the dose applied and the body weight of the animals. The inhibition was only moderate in rats weighing 100 or 150 g, whereas animals weighing 200 g responded more intensively to the pretreatment. This fact emphasizes the significance of age in the inhibitory response induced by fat load.

Oleic acid in a dose of 150 mg/kg i.v. was ineffective in blocking dextran edema. Oleic acid and glycerol (5.0 g/kg) given by mouth had no significant effect on the inflammatory process evoked by dextran (Table I).

Lipid determinations indicated that 1.0 g/kg of oleum helianthi which had no effect on the inflammation did not

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Table I. Effect of oleum helianthi, Lipofundin®, oleic acid and glycerol on the acute inflammation induced by dextran

Pretreatment	Dose (g/kg)	Route of administration	Body weight[a] (g)	Inhibition (%)	*P*
Oleum helianthi	1.0	per os	200 (6)	11	N.S.
	5.0		150 (6)	33	0.01
	5.0		200 (10)	51	0.001
Lipofundin®	0.25	i.v.	200 (6)	28	0.01
	0.5		200 (10)	55	0.001
	1.0		100 (6)	36	0.01
	1.0		150 (6)	36	0.01
	1.0		200 (10)	61	0.001
Protamine sulphate	0.005	i.v.	200 (10)	0	N.S.
Protamine sulphate	0.005	i.v.			
plus Lipofundin®	0.5		200 (10)	75	0.01[b]
Oleic acid	0.15	i.v.	200 (10)	0	N.S.
	5.0	per os	200 (10)	12	N.S.
Glycerol	5.0	per os	200 (6)	0	N.S.

[a] In parentheses number of experiments. [b] Compared to the group treated with only Lipofundin®. [c] Inflammation was evoked 1 h after the administration of oleic acid. N.S.: not significant.

Table II. Serum triglyceride and FFA levels after administration of oleum helianthi, Lipofundin® and oleic acid[a]

Pretreatment[b]	Dose (g/kg)	Route of administration	Triglyceride levels ± S.D. (mg/100 ml)	FFA
Control (10)	–	–	102 ± 26	53 ± 15
Oleum helianthi (6)	1.0	per os	116 ± 19	308 ± 41
(6)	5.0		445 ± 57	673 ± 28
Lipofundin® (6)	0.5	i.v.	546 ± 47	647 ± 54
Protamine sulphate plus Lipofundin® (6)	0.005 0.5	i.v.	680 ± 48	501 ± 66
Oleic acid (6)	0.15	i.v.	87 ± 16	347 ± 32
(6)	5.0	per os	227 ± 22	624 ± 68

[a] The experiments were carried out on rats of 200 g body weight. [b] In parentheses number of experiments.

Table III. Effect of oleum helianthi and Lipofundin® on the acute inflammation induced by carrageenin

Pretreatment	Dose (g/kg)	Route of administration	Body weight[a] (g)	Inhibition (%)	*P*
Oleum helianthi	5.0	per os	200 (6)	45	0.001
Lipofundin®	0.5	i.v.	200 (10)	51	0.001
	1.0		200 (10)	69	0.001
	1.0		150 (10)	65	0.001

[a] In parentheses number of experiments.

influence the serum triglyceride level, while FFA concentration was increased. 5.0 g/kg of oil and 0.5 g/kg of Lipofundin®, both causing the same degree of inhibition in the inflammatory response, produced a 4 to 5 times elevation of the serum triglyceride and an 11 times rise of the FFA levels. Injection of protamine sulphate (5 mg/kg i.v.) 20 min prior to Lipofundin® potentiated its blocking effect on the inflammation and resulted in a further increase in triglyceride and a decrease in FFA concentration. 1 h after 5.0 g/kg of oleic acid given by mouth, the serum FFA level rose to the value measured following either oil or Lipofundin® administration, however, only an insignificant decrease of the inflammatory response was induced (Tables I and II). These findings indicate that the inhibition of the anaphylactoid inflammation runs parallel with the elevation of the serum triglyceride level rather than with that of the FFA concentration. It should be noted that after oil administration there was no difference between the serum lipids of the animals weighing 100 or 200 g. No alteration in the blood sugar level due to the fat load was found.

The mechanism of the experimental results obtained is not clear. The observations do not favour the assumption that the enormous activation of lipoprotein lipase by triglyceride intake plays a role in the inhibition of dextran edema. In 1958 JAQUES[7] reported that some mineral oils but not fatty acids inhibited systemic and local cutaneous anaphylaxis. This finding, together with our present results, strongly suggests that lipid metabolism is involved in the inhibition of allergic events in the organism.

Our experiments also showed that both oleum helianthi and Lipofundin inhibited carrageenin-induced inflammation. In this case, however, the inhibition did not depend upon the age of the animals (Table III). In conclusion, the inhibition of the early vascular phase of the acute inflammation induced by hyperlipemia seems to be a more general phenomenon than a selective blockade of the dextran-induced anaphylactoid reaction.

Zusammenfassung. Experimentell wurde an R-Amsterdam-Ratten gezeigt, dass Triglyceride (Oleum helianthi und Lipofundin®) die von Dextran und Carrageenin hervorgerufene akute Entzündung hemmen können, dass dies von der Triglycerid-Dosis abhängt und mit dem Serum-Triglycerid-Spiegel parallel läuft.

M. KOLTAI, E. MINKER and ANNA OTTLECZ

Departments of Pharmacology and Pathophysiology, University Medical School Szeged, Szeged (Hungary), 30 July 1971.

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