Four interesting points may be deduced from the Table.

(1) Whereas with both samples of dextran given intraperitoneally or intravenously non-reactor rats failed to produce the anaphylactoid reaction, large *intravenous* doses of egg-white were effective.

(2) The component in egg-white responsible for the reaction shown by reactor rats was not destroyed by heat. In contrast, boiled egg-white in non-reactors gave a less intense reaction than did fresh egg-white.

(3) As egg-white was ineffective in non-reactor rats when given intraperitoneally but effective by the intravenous route, the active component when egg-white is given intraperitoneally may not reach the blood stream in concentrations sufficient to produce a response or it may be modified before absorption from the abdominal cavity.

(4) Whereas dextrin (Kerfoot) was ineffective by both routes in reactor and non-reactor rats, dextrin (Astra) when given intraperitoneally was equally effective in the two kinds of rat. However, the larger intravenous dose of dextrin (Astra) was less active in reactor rats than in non-reactors.

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Dexamphetamine and lipid mobilization in obesity

SIR,—We have studied the action of dexamphetamine on plasmatic free fatty acids (FFA) in rats. Albino Sprague-Dawley male rats were given amphetamine subcutaneously, 135 min before killing by decapitation. The drug induced a marked rise in levels of such a blood component (Table 1). The rise reached a maximum within 2–3 hr and lasted, at the highest dose levels, for more than 7 hr.

TABLE 1. CHANGES IN PLASMA FREE FATTY ACIDS (FFA) AFTER DEXAMPHETAMINE TREATMENT IN RATS

Dexamphetamine sulphate mg/kg	FFA % rise	P†
0·5	20 ± 9·9*	< 0·05
1·0	48 ± 2·3	< 0·01
2·0	101 ± 8·9	< 0·01
5·0	127 ± 4·7	< 0·01
10·0	69 ± 3·9	< 0·01

* Mean (6 animals) ± s.e.
† Statistical significance of difference from controls.
FFA were determined by the Dole (1956) method.

In our opinion, this increased mobilisation of lipids from adipose tissue may be important for the therapeutic use of amphetamine in obesity.

The value of sympathomimetic drugs such as amphetamine in the treatment of obesity in man, is generally ascribed to their anorexigenic effect, rather than to a peripheral increase of metabolic rate. The same effect of amphetamine in reducing bodyweight and desire for food, was demonstrated also in animals (Holm, Huus, Kopf, Möller Nielsen & Petersen, 1960).

The current view as to the mode of action of sympathomimetic drugs in producing anorexia, leans toward a central action. This central action would be not only a psychic or a generally exciting one, but a specific, direct influence on the mechanisms regulating food intake (Andersson & Larsson, 1961). In fact, a number of ring substituted α-methylamphetamines reduced food consumption in rats and lacked, at the same time, the motility-increasing effect of amphetamine. These results show that anorexigenic action is not necessarily linked to the same degree with stimulation of other central functions.

The weight loss of animals treated with such amphetamine-like compounds, was mainly due to reduction in body fat content. When instead, food intake was decreased by restriction, the weight loss was due to reduction in non-fatty dry matter. This suggested a mobilising effect of amphetamine-like compounds on depot fat (Holm, 1960).

Our results, showing that dexamphetamine has a striking specific action on fat metabolism, provide direct evidence for this hypothesis. The usefulness of amphetamine in the treatment of obesity appears then to be due not only to a central anorexigenic effect, but also to a metabolic action in peripheral tissues.

The question now arises whether the anorexigenic and the metabolic actions may somehow be connected.

Food intake is a centrally regulated mechanism. The existence of one or more "feeding centres" in the diencephalon, sensitive to a starvation state of the blood, was suggested as well. Thus far, the nature of the adequate feeding stimulus is not yet known. Heat production, dynamic action of food, glucostatic mechanisms, have been proposed as factors regulating food intake. It was also put forward that adjustment of feeding may be related to the amount of stored fat in the body: the central areas of the hypothalamus should thus be sensitive to the concentration of some metabolite in equilibrium with the stored fat (Andersson & Larsson, 1961).

According to the last hypothesis, the strong mobilising action of dexamphetamine on depot fat, or the consequent elevated concentration of plasmatic FFA, might possibly account for the anorexigenic effect of the drug.

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