vivors seemed to recover and to resume their usual habits more promptly than control survivors.

We have been unable to replicate to our satisfaction a PTU sparing effect on imipramine-injected mice. There is no evidence for such an effect in the case of DMI. More refined studies are in progress to determine whether PTU interferes with *in vivo* demethylation of imipramine. Both DMI and imipramine show enhanced lethal effects in HR mice. DMI is more potent, acts more quickly, and yields steeper dose-mortality curves than its methylated parent compound.

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Salicylate, a Powerful Inhibitor of Free Fatty Acid Release

THE level of utilizable glucose represents a control of the release of free fatty acids (FFA) and, therefore, of the level of serum FFA[1]. Drugs acting on glucose utilization are therefore likely to be effective in changing the level of FFA. The observation that salicylate increases oxidative reactions[2,3] led us to the finding that this drug is a powerful inhibitor of FFA release. Previous investigations carried out in man were contradictory. While Carlson[4,5] found a decrease of plasma FFA in normal and diabetic subjects, Gilgore *et al.*[6] did not confirm these results. However, it is likely that in the latter data there was an interference of salicylate in the determinations of FFA carried out according to Dole's method.

Male Sprague–Dawley rats of the average weight of 150 g were used for all experiments. Sodium salicylate was given intraperitoneally in resting animals as well as in animals submitted to treatments designed to increase the level of FFA.

FFA were determined according to the method of Trout[8] to avoid interference of salicylic acid with the titration. The inhibitory effect of salicylate is very clear in suckling, adult or adrenalectomized animals and in rats with an increased level of FFA induced by fasting, cold, noradrenaline, ACTH or chlorpromazine. The blockade of thyroid activity did not affect the inhibition exerted by salicylate.

Table 1

Treatment or experimental condition	FFA μequiv./1,000 ml. plasma	
	Controls	Salicylate 300 mg/kg i.p.
Saline	215 ± 21	137 ± 6
Fasting 18 h*	671 ± 64	341 ± 11
Cold, 2° C 4 h*	765 ± 60	111 ± 3
Norepinephrine s.c. 1 mg/kg †	723 ± 54	252 ± 36
ACTH 20 units* ¶	957 ± 37	201 ± 22
Chlorpromazine, i.v. 1,5 mg/kg‡	505 ± 22	138 ± 29
Adrenalectomy*	380 ± 60	143 ± 22
Suckling rats*	540 ± 77	308 ± 40
Suckling rats on propylthiouracil diet§	648 ± 36	326 ± 20

* Salicylate given 30 min before rat killed.
† Norepinephrine given in oil suspension; both drugs administered at the same time. Time between treatment and killing 60 min.
‡ Salicylate given 10 min before chlorpromazine injection. Rats killed 30 min after chlorpromazine injection.
§ Propylthiouracil 0·4 per cent in the diet given to the mothers (ref. 7) during 17 days before salicylate administration.
¶ ACTH was given 120 min before rat killed.

By using the test of the increased level of FFA after cold it was observed that quite small amounts (25 mg/kg) of salicylate exerted an effect, and the effect of a large dose (300 mg/kg) lasted about 2 h. Orally administered salicylate was also effective in a dose of 50 or 100 mg/kg. Acetylsalicylic acid and benzoic acid shared the effect of salicylate, while *p*-aminosalicylic acid and salicylamide were ineffective up to a dose of 300 mg/kg.

Preliminary experiments show that salicylate may act directly on the adipose tissue because it slightly inhibits the release of FFA by the epididymal fat pad *in vitro*. Large doses are necessary, however, so it cannot yet be said that there is a causal relationship between the inhibition of FFA release *in vitro* and the decrease of plasma FFA *in vivo*.

The effect of salicylate on the FFA is obtained without significant changes of blood glucose, but this should not be considered to contradict the hypothesis previously mentioned because a small increase in glucose oxidation would not necessarily be reflected in the level of blood glucose.

These results are relevant to the interpretation of the reported hypoglycæmic and hypocholesteræmic effects of salicylate[8].

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Effect of Drugs on the Amount of Substance P in Rabbit Brain

THE content of 'Substance P' (SP) in the central nervous system under the influence of drugs has been studied repeatedly. Paasonen and Vogt[1] did not find an influence of D,L-amphetamine, ephedrine, insulin, caffeine, β-tetrahydronaphthylamine, and reserpine on the SP content of the hypothalamus and nucleus caudatus of anæsthetized dogs. Zetler and Ohnesorge[2] estimated the SP content of mouse brain after treatment with various centrally-acting substances, and found that substances which are centrally exciting in mice (benzedrine and morphine) increased the total content of SP in the brain, whereas chloroform, urethane and phenobarbital lowered it. Stern and Kocič-Mitrovič[3] found an increase in SP content in rabbit brain after treatment with reserpine, but Laszlo[4] did not find any striking change of SP content in rabbit brain after reserpine and numerous other drugs.

The present experiments were made in order to obtain further data, using the purification technique of Pernow[5] for SP. Whole rabbit brain except cerebellum was used. The brain was ground, and boiled in acidified distilled water. After precipitation with ammonium sulphate SP was adsorbed on aluminium oxide and eluted with distilled water as described in detail by Pernow[5], Euler[6] and Radmanovič[7].

Bioassay was performed on the isolated guinea-pig ileum with addition of atropine, promethazine and