Effect of Nicotinic Acid on the Cholesterol Contents of Rat-Livers

Lowering of the blood cholesterol level by means of large doses of nicotinic acid has been described by Altschul[1], and this effect has been confirmed by others[2]. This effect is caused by nicotinic acid only and its mechanism has not yet been clarified. The use of the amide of the nicotinic acid is said to be without effect.

Table 1

Percentage nicotinic acid in diet	No. of rats	Liver content: Total cholesterol (mgm. per cent)	*P*	Total lipids (per cent fresh weight)
0	8	1,181·5		25·0
1	10	1,038·3	< 0·5	30·8
2	10	923·3	< 0·2	31·0
3	10	683·7	< 0·01	24·4
4	10	634·1	< 0·01	25·2
Normal diet (*C*)	10	220·0		5·0

50 Sprague–Dawley rats (male), ranging in weight from 110 to 120 gm., were fed for 21 days on a special hypolipotropic diet free from cholesterol. This caused an endogenous fatty liver of the cholesterol type (group *A*) (unpublished work). Another group received the same diet but with nicotinic acid in increasing amounts, namely, 1, 2, 3 and 4 per cent (group *B*). A third group (*C*) was fed a normal diet. All animals were killed at the end of this experiment under light ether anæsthesia; after exsanguination the livers were processed according to Sperry's method, and total lipid[3] and cholesterol contents were determined. The results are given in Table 1. Increased cholesterol contents were found in the livers of the animals fed the special diet, the content in group *A* (without nicotinic acid) being six times as great as that in group *C* (normal diet). Liver cholesterol decreased with increasing nicotinic acid in the special diet, but 4 per cent nicotinic acid did not reduce the cholesterol level to its normal value. Nicotinic acid, *per se*, tends to produce fatty degeneration of the liver[4] and intolerably large doses may be necessary to bring the liver cholesterol produced by the special diet to its normal level.

This antilipotropic effect of nicotinic acid can be interpreted as due to the demand of its detoxication products for methyl groups. Detoxication may occur via nicotinic acid, which needs coenzyme A for synthesis. It is suggested, therefore, that this effect is caused by infiltrative fattening of the liver and reduced synthesis of cholesterol (relative lack of coenzyme A).

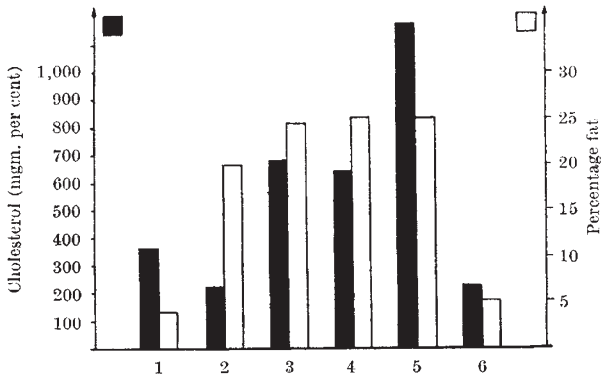

Fig. 1. Cholesterol and fat contents of rat livers after feeding the special diet with (1) 2 per cent α-phenylbutyric acid, (2) 2 per cent α-diphenylylbutyric acid, (3) 3 per cent nicotinic acid, (4) 4 per cent nicotinic acid, (5) control group *A*, (6) normal diet, group *C*

Altschul[1] explained the lowering of the level of cholesterol in the blood by nicotinic acid as due to increased oxidative catabolism of cholesterol. Merill[5], working with rabbits, has suggested possible detoxication products of nicotinic acid, but his work has not afforded clear proof of the inhibition of acetylation *in vivo*. Recent investigations *in vitro* have demonstrated inhibition of acetylation[6], but such experiments *in vitro* cannot establish the influence of nicotinic acid on synthesis of cholesterol.

Comparison investigations using α-phenylbutyric acid and α-diphenylylbutyric acid has led to the following suggestions (Fig. 1): (1) that synthesis of cholesterol is decreased by the influence of nicotinic acid, and (2) that a relative lack of coenzyme A is the causative mechanism.

Harald Schön

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Effect of Splenectomy on the Phagocytic Activity of the Reticulo-Endothelial System

The reticulo-endothelial system comprises groups of cells situated in various parts of the body having the ability to take up particulate and colloidal matter. The cells of this system, which have an intimate relationship with the circulation, are to be found mainly in the liver and spleen, from which organs about 95 per cent of intravenously injected particulate material may be recovered[1] and of this amount we have found in mice that the spleen contains less than 5 per cent.

It is generally recognized that the macrophages of the splenic sinusoids play an important part in various physiological and pathological processes. It has been shown by Nicol *et al.*[2] that prolonged œstrogenic stimulation appeared not only to produce a greater formation and activation of reticulo-endothelial cells in the spleen but also assisted their mobilization and liberation into the circulation. This might, therefore, suggest that the importance of the spleen in phagocytic activity is not adequately reflected by the small amount of injected particulate or colloidal matter which is to be found in that organ. The present investigations were planned to ascertain the effect of splenectomy on the rate of removal of particulate matter from the circulating blood.

The following experiments were carried out on 70 male white mice (*T.O.* Swiss strain) of 20–25 gm. body-weight. The phagocytic activity was measured by the rate of disappearance of a known amount of carbon from the circulating blood, as described in a