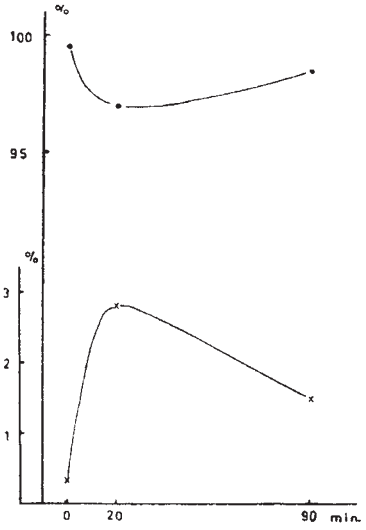

Fig. 1. Percentage composition of glycerides from fat depot before and after injection of adrenaline. ●——●, Triglycerides; ×——× di- and mono-glycerides

Some experiments have been carried out in this laboratory in order to ascertain if the neutral fat is hydrolysed in the depots after injection of adrenaline. The results of one of these experiments are given in Fig. 1. A male rabbit (3,500 gm.) was given 0·01 mgm. adrenaline intravenously. Subcutaneous fat from the pubic region was taken before and 20 min. and 90 min. after the injection. Tri-, di- and mono-glycerides were determined by the method of Borgström[6].

The percentage composition of the depot glycerides is given in Fig. 1. The increase of the lower glycerides found in this experiment indicates that injection of adrenaline activates a lipolysis of the depot neutral fat. Essentially similar results have been obtained in other experiments.

Lars B. Wadström

King Gustaf V Research Institute and
Department of Surgery,
Karolinska Sjukhuset,
Stockholm 60.

Nov. 9.

[1] Laurell, S., *Scand. J. Clin. and Lab. Invest.*, **8**, 81 (1956).
[2] Dole, V. P., *J. Clin. Invest.*, **35**, 150 (1956).
[3] Gordon, R. S., and Cherkes, A., *J. Clin. Invest.*, **35**, 206 (1956).
[4] Shapiro, B., and Wertheimer, E. *Metabolism Clin. and Exp.*, **5**, 79 (1956).
[5] Borgström, B., *Biochim. Biophys. Acta*, **13**, 491 (1954).
[6] Borgström, B., *Acta Physiol. Scand.*, **30**, 231 (1954).

Inhibition of Fibrinolysis *in vivo* by feeding Cholesterol

We have produced[1], by the technique of Grossi, Cliffton and Cannamela[2], a clot in the marginal vein of the ear of rabbits and found that these clots lysed in 8–39 hr., the mean being 20 hr. with a standard deviation of 8 hr. A biopsy specimen of the vein was taken 48 hr. after production of the thrombosis, and on histological examination in every case the vein appeared normal. Extending these observations, we have found (unpublished) that the lysis was due to the production of fibrinolysin locally in the vein, and that it still occurred even when the thrombosed segment of vein was ligatured above and below the thrombus and all visible veins draining into it occluded by cautery. We have shown that the lysis of such clots can be prevented by the administration of corticotropin[1].

Greig[3] has reported the inhibition in humans of spontaneous fibrinolytic activity of the plasma by a fatty meal. As pointed out by Fearnley[4], this spontaneous fibrinolytic activity is of a very low order. We would emphasize, too, that there is no evidence that the spontaneous fibrinolytic activity *in vitro* of the plasma of a specimen of venous blood represents the fibrinolytic activity which may arise *in vivo*. For example, in the rabbit, while clotted whole blood is being rapidly lysed in the marginal vein of the ear, no spontaneous fibrinolytic activity can be demonstrated by the low-temperature technique[5] in the plasma of blood removed from another vein. An investigation of the effect of feeding cholesterol on the lysis of clots experimentally produced *in vivo* would be free from both these criticisms.

Twenty-one adult white rabbits were fed cholesterol in doses of 1 gm. per kgm. of body-weight daily. On the tenth day a clot was produced in the marginal vein of one ear by the technique of Grossi, Cliffton and Cannamela[2]. The thrombosed segment of the vein was observed at intervals by transillumination, and the time taken for a free flow of blood to be established through the segment was recorded. A biopsy of the segment of vein was taken ten days after production of the thrombosis. In 30 per cent of the animals a free flow was established within the range encountered in control animals. On histological examination the veins were normal. In the remaining 70 per cent, free flow was established in 72–122 hr., the mean being 86 ± 7 hr. On histological examination the veins were abnormal. The thrombus in each case had become organized and this had resulted in variable and irregular thickening of the intima. In the interstices of the granulation tissue 'foam' cells were present in varying numbers.

These observations establish that the feeding of cholesterol to rabbits inhibits the fibrinolytic activity normally induced by the production of a clot in the marginal vein of the ear.

There are two major and apparently conflicting hypotheses concerning the etiology of atherosclerosis. Among others, Keys[6] emphasizes the importance of dietary fats, whereas Duguid[7], whose observations have been confirmed by others[8], holds that the initial phase of development of atherosclerosis is the occurrence of mural thrombi. Greig[3] suggested that a common ground between these two hypotheses might be found in the influence of lipæmia on fibrinolytic activity. Our observations support this suggestion.

H. C. Kwaan
A. J. S. McFadzean

University Department of Medicine,
Queen Mary Hospital,
Hong Kong.

Oct. 31.

[1] Kwaan, H. C., and McFadzean, A. J. S., *Lancet*, i, 136 (1956).
[2] Grossi, C. E., Cliffton, E. E., and Cannamela, D. A., *Blood*, **9**, 310 (1954).
[3] Greig, H. B. W., *Lancet*, ii, 16 (1956).
[4] Fearnley, G. R., *Lancet*, ii, 149 (1956).
[5] Fearnley, G. R., Revill, R., and Tweed, J. M., *Clin. Sci.*, **11**, 309 (1952).
[6] Keys, A., *Circulation*, **5**, 115 (1952).
[7] Duguld, J. B., *J. Path. Bact.*, **58**, 207 (1946).
[8] Harrison, C. V., *J. Path. Bact.*, **60**, 289 (1948). Geiringer, E., *ibid.*, **63**, 201 (1951). Crawford, T., and Levene, C. I., *ibid.*, **64**, 523 (1952).