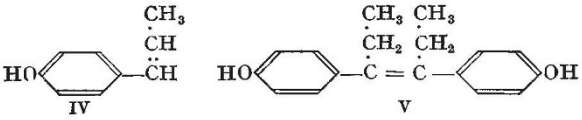
The steps leading to the finding of trypanocidal activity in compounds of type (III) would provide an interesting parallel to the course of events in quite a different field, that of synthetic sex hormones. The sequence leading to the discovery of œstrogenic activity in symmetrical compounds of the type of stilbœstrol (V) consisted in exploring simplifications of the naturally occurring *cyclo*pentenophenanthrene type of compound, followed by the demonstration of activity in crude preparations of anol (IV); purified preparations of (IV) were, however, found to be inactive, and the activity of the earlier crude preparations was then shown to be due to their contamination by (V)[2,3,4].




This work was supported by grants from the Medical Research Council and Messrs. May and Baker, Ltd.

J. R. Kenefford J. C. E. Simpson
E. M. Lourie J. Williamson
J. S. Morley P. H. Wright

Warrington Yorke Department of Chemotherapy,
Liverpool School of Tropical Medicine.
Dec. 30.

[1] First described by Browning, Morgan, Robb and Walls, *J. Path. Bact.*, **46**, 203 (1938); later work reviewed by Walls, *J. Soc. Chem. Ind.*, **66**, 182 (1947).
[2] Dodds and Lawson, *Nature*, **139**, 627 (1937).
[3] Dodds and Lawson, *Nature*, **139**, 1068 (1937).
[4] Dodds, Golberg, Lawson and Robinson, *Proc. Roy. Soc.*, B, **127**, 140 (1939).

## Effect of Under-nutrition in Man on Hepatic Structure and Function

During August 1946 investigations were carried out on twenty-one civilian citizens of Wuppertal, an industrial German city south of Essen. For at least three months the official rations had not provided more than 35 gm. of protein, 15 gm. of fat and 176 gm. of carbohydrate a day, a total of 1,050 calories. Most of the subjects had been on short commons for twelve months. They were all under-nourished and had lost 6–46 per cent of their body weights. All stated that they had had nutritional œdema, and in sixteen this was clinically detectable. There was nothing in their clinical histories or examinations to suggest hepatic dysfunction. Their livers were not enlarged and no examples of gynecomastia, spider nævi or palmer hyperæmia were encountered.

Liver tissue was obtained from each subject by aspiration biopsy[1]. Histologically this tissue was generally normal, and there were no signs of necrosis, cirrhosis or fatty change. The liver cells sometimes contained considerable amounts of iron and chromolipoid pigment. Diminished blood volumes and low concentrations of hæmoglobin were found in these under-nourished subjects. There was, therefore, a withdrawal of hæmoglobin from the circulation with the liberation of much iron. Moreover, muscle myoglobin, released as muscles waste, may have provided further free iron. Iron in excess of immediate requirements cannot be excreted to any extent[2], and is stored in the liver. The hepatic siderosis observed in these subjects was never of the same extent or distribution as that reported in malnutrition in South Africa[3]. 'Ceroid' pigment was not present in the liver.

The urinary urobilinogen was often increased, and the fæcal urobilinogen diminished. The serum total bilirubin was within normal limits, and the bromsulphthalein excretion test gave normal results. Hepatic glycogen estimated quantitatively, fasting blood sugar concentration, oral glucose tolerance, adrenalin tolerance, and insulin sensitivity tests were all normal. Alkaline phosphatase in the liver was normal both in amount and in histological distribution. Serum alkaline phosphatase was also within normal limits.

In fourteen of the subjects the serum taken in the recumbent position contained a concentration of less than 6·0 gm. of protein/100 ml. The serum colloidal gold reaction was usually negative. The concentration of total serum cholesterol was often low. The percentage of the total cholesterol in ester form was also low. The intravenous hippuric acid synthesis test gave normal results.

The subjects had been living for about a year on a diet the protein content of which was low and mainly of vegetable origin. The intake of lipotropic compounds (which are mainly in and associated with animal protein) must have been diminished. We have failed, however, to demonstrate the hepatic necrosis, cirrhosis or fatty change produced in experimental animals by low dietary protein or a deficiency of lipotropic compounds. Correlation of our results with recent reports of malnutrition in the Far East and elsewhere, and in experimental animals, is extremely difficult. The present report refers only to the effects of under-nutrition on one group of Europeans in one town in Germany, at one particular time, namely, August 1946.

The detailed results of this work will be given in a Medical Research Council Special Report now in preparation.

Sheila Sherlock
(Beit Memorial Research Fellow)
Veryan Walshe

Medical Research Council Unit,
Wuppertal, B.A.O.R., and
Department of Medicine,
Postgraduate Medical School of London.
Jan. 6.

[1] Sherlock, S., *Lancet*, ii, 397 (1945).
[2] McCance, R. A., and Widdowson, E. M., *Nature*, **152**, 326 (1943).
[3] Gillman, J., and Gillman, T., *Arch. Path.*, **40**, 239 (1945).

## Isolation of Stilbœstrol Monoglucuronide from Human Urine

In a recent letter[1] in *Nature*, Dr. A. E. Wilder Smith reports that he finds, by indirect methods, that about 50 per cent of stilbœstrol administered to human beings is excreted as a monoglucuronide. He was, however, unable to isolate this conjugate from the urine of patients treated with the drug. Although stilbœstrol monoglucuronide has been isolated[2,3] from the urine of rabbits receiving relatively large doses of stilbœstrol, it has never been isolated from human urine owing to the small doses normally used. We have now succeeded in isolating a glucuronide of stilbœstrol from human urine and proved it to be identical with that obtained from rabbit urine.