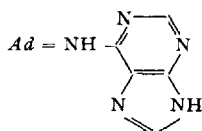
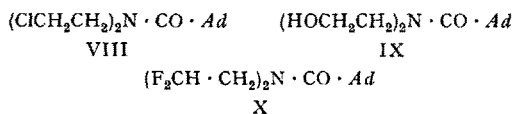
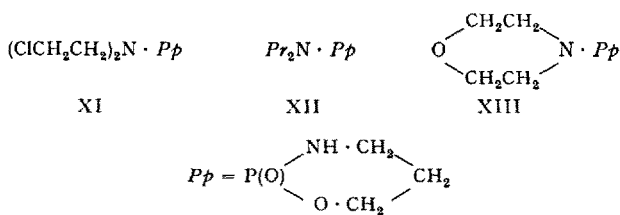


(2) Le traitement avec une urée substituée du type I doit être précédé par un traitement de «préparation» avec une urée analogiquement substituée, mais non moutarde azotée. Par exemple, le traitement avec le composé VIII² ne doit être appliqué qu'après l'administration d'un des composés IX, X, etc.; pendant toute la durée du traitement, le malade doit suivre un régime alimentaire très pauvre en adénine.



(3) Le traitement avec l'Endoxan (XI)^{5,6} doit être appliqué après une certaine période de «préparation» avec un des composés XII, XIII, etc., et pendant toute la durée du traitement le malade doit suivre un régime alimentaire très pauvre en composés phosphorés.



Summary. The cytostatic action of several urethanes and ureas-nitrogen mustards, as well as that of Endoxan, depends on the appropriate enzymatic activity of the cancerous cell. This enzymatic activity can be considerably stimulated by non-mustard analogues.

C.-S. DONGOROZI

Bucarest (Roumanie), Str. Sfinții Apostoli 61, le 6 octobre 1961.

⁵ H. ARNOLD und F. BOURSEAUX, *Angew. Chem.* 70, 539 (1958).

⁶ H. ARNOLD, F. BOURSEAUX und N. BROCK, *Arzneim.-Forsch.* 11, 143 (1961).

The Dynamics of Serum Lipoprotein Patterns in Vitamin C-Saturated and Vitamin C-Deficient Guinea-Pigs after Carbon Tetrachloride Poisoning

It follows from studies of a clinical nature¹ that vitamin C modifies, to a certain extent, the proportion of serum α - and β -lipoproteins in atherosclerotic patients. The purpose of the present study was to investigate on experimental material the problem of the influence of scurvy on the lipoprotein metabolism in an intact organism and in an organism affected with a hepatic lesion.

The work was conducted on mature guinea-pigs, mainly males, weighing 300–400 g and kept on a scorbutogenic diet². All animals were divided into two groups. The animals of the first group received 5 mg *l*-ascorbic acid daily by mouth, while the animals of the second group had no vitamin C. After 7 days the animals of both groups were divided into 4 subgroups, containing 7 animals each. The animals of the first subgroups, in both the vitamin C-saturated and scorbutic group, were sacrificed by decapitation. These animals served as controls without liver injury. The rest of the animals were administered 0.2 ml carbon tetrachloride diluted in olive oil by mouth and were sacrificed after 18, 48, and 168 h, always in two

parallel subgroups the first of which represented the animals saturated with vitamin C and the other subgroup the scorbutic animals. The blood serum of the animals was used for the determination of lipoprotein fractions by the method of paper electrophoresis according to SWAHN³. The regularly obtained 4 fractions were signed, in view of their mobility, α_1 -, α_2 -, β -, and 0 (fraction situated at the start).

The comparison of the results obtained in the animals saturated with vitamin C, and in the scorbutic animals in which no lesion was produced, showed that early phases of C avitaminosis caused significant changes in the lipoprotein patterns of the serum of the guinea-pigs. The situation is illustrated in the Table.

The administration of carbon tetrachloride caused in both normal and scorbutic guinea-pigs pronounced changes in all fractions of serum lipoproteins. These changes are illustrated in the Figures 1–4.

Our results point to the fact that carbon tetrachloride poisoning, producing an extensive liver damage, represents also a great interference with the lipoprotein metabolism which involves all their serum fractions. The changes observed take place very soon after the administration of the hepatotoxin. A comparison of the course of the serum lipoprotein changes in the scorbutic animals and in those saturated with vitamin C suggests that, disregarding the different initial values, the course of the changes in the majority of the fractions is analogous in both groups studied and may be characterised as follows: in the first phases there are marked departures from the initial values, on the seventh day after carbontetrachloride administration, one may, however, observe in saturated as well as in vitamin deficient animals, a pronounced tendency of all fractions to return to normal levels. This finding is further

Serum lipoprotein levels (expressed in %) in the guinea-pigs saturated with vitamin C and in vitamin C deficient animals

Fraction	Mean $\pm$ standard deviation of mean Saturated group	Vitamin deficient group	Statistical significance
α_1	13.0 $\pm$ 0.9	18.0 $\pm$ 0.6	$P < 0.001$
α_2	46.5 $\pm$ 1.1	35.2 $\pm$ 2.4	$P < 0.01$
β	23.5 $\pm$ 1.5	28.4 $\pm$ 1.9	—
0	17.0 $\pm$ 1.0	18.4 $\pm$ 0.6	—

¹ N. M. LOBANOVA, *Ateroskleroz i infarkt miokarda* (Medgiz, Moskva 1959), p. 124.

² H. HANKE, *Vitamine und Chirurgie* (Leipzig 1943).

³ B. SWAHN, *Scand. J. clin. lab. Invest.* 5, Suppl. 9, 1 (1953).

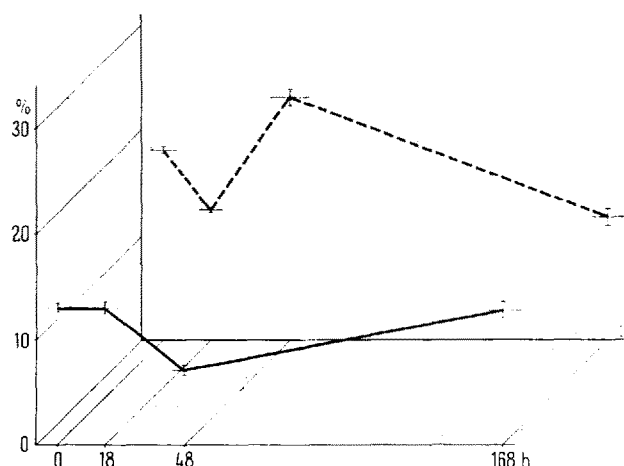


Fig. 1. The course of the level of the α_1 -fraction of serum lipoproteins in vitamin-C-saturated (full line) and vitamin C deficient animals (dashed line) following carbon tetrachloride poisoning. The length of the perpendicular line in each case signifies the magnitude of the standard deviation from the mean.

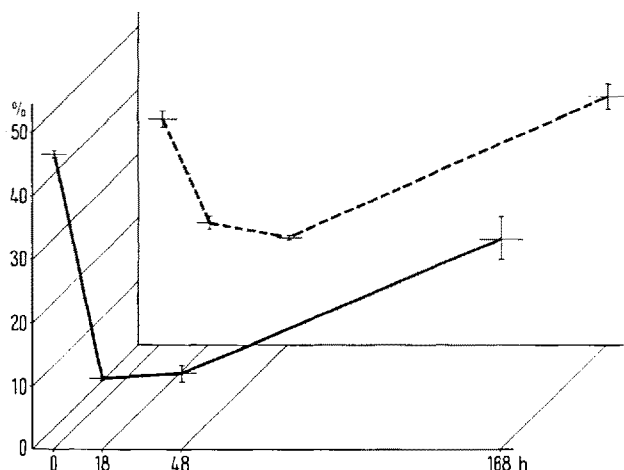


Fig. 2. The course of the α_2 -fraction of serum lipoprotein levels in the vitamin C-saturated and vitamin C-deficient guinea-pigs after carbon tetrachloride poisoning. (Marking same as for Table.)

confirmed by the results obtained by studying the regeneration processes in the liver poisoned with carbon tetrachloride in normal and vitamin C-deficient guinea-pigs, which show that the regeneration processes in the liver are not markedly affected by the early phases of C-avitaminosis⁴.

Interesting is the observation that even early phases of C-avitaminosis markedly affected the lipoprotein metabolism as manifested by statistically highly significant changes in α_1 - and α_2 -serum lipoprotein fractions in the animals with intact liver. This finding is probably in connection with our earlier observation of changes in the levels of serum globulins in guinea-pigs during the early phases of C-avitaminosis⁵. *l*-Ascorbic acid deficiency seems to interfere, by a certain hitherto unknown mechanism, with the metabolism of lipoproteins.

Zusammenfassung. Aus einer Experimentalarbeit, bei welcher die Konzentration der papierelektrophoretisch gewonnenen Lipoproteinfraktionen des Serums Vitamin-

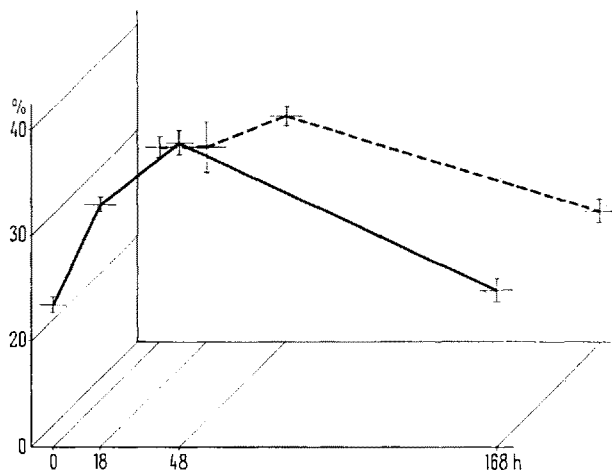


Fig. 3. The course of the β -fraction of serum lipoproteins in vitamin C-saturated and vitamin C-deficient guinea-pigs after carbon tetrachloride poisoning. (Marking same as for Table.)

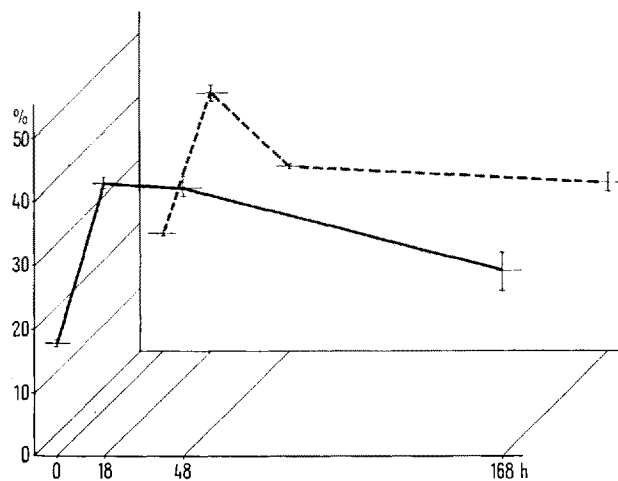


Fig. 4. The course of the level of the 0-fraction of serum lipoproteins in vitamin C-saturated and vitamin C-deficient guinea-pigs after carbon tetrachloride poisoning. (Marking same as for Table.)

C-gesättigter und avitaminöser Meerschweinchen verglichen wurde, geht hervor, dass die Frühstadien der C-Avitaminose den Spiegel der α_1 -Lipoproteine bedeutend erhöhen und den der α_2 -Lipoproteine herabsetzen. Dies und die Ergebnisse der durch Tetrachlorkohlenstoff hervorgerufenen Leberschädigung weisen auf die Tatsache hin, dass die Frühstadien der C-Avitaminose den Mechanismus, der den normalen Spiegel der Serumlipoproteine reguliert, beeinflussen, obwohl gleichzeitig die Regenerierungsprozesse der durch Tetrachlorkohlenstoff geschädigten Leber der Beeinflussung entzogen bleiben.

P. BOBEK and E. GINTER

Institute of Nutrition Research, Bratislava (Czechoslovakia), October 23, 1961.

⁴ E. GINTER, V. ŠIMKO, and J. BABALA, *Epatologia*, in press.

⁵ E. GINTER, *Physiologia Bohemoslov.* 7, 234 (1958).