LITERATURE CITED

1. N. L. Garmasheva, N. N. Konstantinova, N. A. Tripol'skaya, et al., in: Structural and Functional Principles of Systems Genesis [in Russian], Moscow (1976), pp. 10-12.
2. Z. N. Zhakhova, N. A. Tripol'skaya, and N. N. Konstantinova, Akush. Ginekol., No. 10, 65 (1977).
3. N. N. Konstantinova, N. A. Tripol'skaya, and Z. N. Zhakhova, Akush. Ginekol., No. 6, 61 (1977).
4. T. H. Ji, Anal. Biochem., 52, 517 (1973).
5. K. Kloos, Geburtsh. Frauenheilk., 34, 233 (1974).
6. E. M. Widdowson, in: Nutricia Symposium. Metabolic Processes in the Foetus and Newborn Infant, Leiden (1971), p. 165.

PORPHYROBILINOGEN BIOSYNTHESIS FROM δ-AMINOLEVULINIC ACID BY THE VISCERA OF ALBINO RATS

P. N. Lyubchenko, B. N. Gladyshev, and V. F. Mostun

UDC 612.015.36:[547.979.733:547.484.451

Ability to synthesize porphyrobilinogen (PBG) from δ-aminolevulinic acid (ALA) was determined in homogenates of tissues of the lungs, heart, liver, kidneys, spleen, pancreas, and small intestine of 77 albino rats. All these organs were found to be able to synthesize PBG. Highest ALA dehydratase activity was found in the liver tissue, followed in descending order by the kidneys, lungs, pancreas, small intestine, heart, and spleen. On the addition of a lead solution to the synthesizing system a significant decrease in enzyme activity was observed in the liver tissue, but in kidney tissue its activity was unchanged. On the addition of lead and D-penicillamine simultaneously no changes were found in the toxic effect of lead.

KEY WORDS: porphyrins – synthesis, localization in organs and tissues of rats; lead poisoning.

The biological role of heme and heme-containing compounds is exceptionally great. Functions such as participation in oxygen and electron transport require the presence of heme-containing compounds in every cell of the body. Whether porphyrins and heme also are formed in every cell or whether they are transported to the cells from the organs which synthesize porphyrins has not yet been finally settled.

Barta [1] considers that porphyrin is synthesized in the erythrocytes and liver. Idel'son [2] considers that porphyrin biosynthesis takes place in all cells of the living organism. There are few reports in the literature on the comparative study of the ability of different tissues to synthesize porphyrins. In particular, the synthesis of porphyrobilinogen (PBG) from δ-aminolevulinic acid (ALA) by homogenates of various rabbit organs and also by the liver, kidneys, and Harder's gland of rats [5] has been studied. The results have shown that the liver, kidneys, and bone marrow have the highest activity as regards PBG formation from ALA in both species of animals. According to the same workers, ALA dehydratase, an enzyme converting ALA into PBG, is widely distributed in nature and is evidently present in all cells with aerobic metabolism.

ALA dehydratase is known to be inactivated by lead; moreover, this action in vivo is abolished by various complexones, including D-penicillamine (D-PAM) [6-10]. The mechanism of the therapeutic action of D-PAM in lead poisoning is linked with the "exposure" of SH groups necessary for restoring the activity of the enzymes, and the chelating reaction of the compound with lead and its subsequent elimination. The study of the more precise mechanism of action of D-PAM could be assisted by an investigation of whether D-PAM can interact with lead in vitro, but this problem has received virtually no attention in the literature.

M. F. Vladimirskii Moscow Regional Clinical Research Institute.

(Presented by Academician of the Academy of Medical Sciences of the USSR S. S. Debov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 86, No. 12, pp. 687-689, December, 1978. Original article submitted October 24, 1977.

TABLE 1. Quantity of PBG Synthesized from ALA by Tissue Homogenates of Viscera of Albino Rats (M ± m)

Organ	PBG, in μg/mg protein · 2 h of incubation
Lungs	3,62±0,35
Heart	2,7±0,49
Liver	15,5±0,84
Kidneys	4,31±0,25
Spleen	2,47±0,2
Pancreas	2,89±0,48
Small intestine	2,88±0,35

The object of the present investigation was to study the localization of porphyrin biosynthesis in the animal organism with specific reference to the formation of PBG from ALA by homogenates of the viscera of rats, and also to examine the effect of lead, added to the synthesizing system either alone or simultaneously with D-PAM on this process.

EXPERIMENTAL METHOD

Experiments were carried out on 77 noninbred male albino rats weighing 250-300 g. ALA dehydratase activity in the tissue homogenates was determined by the method described in [2, 4]. Before weighing, the lumen of the small intestine was thoroughly washed with water. Lead was added to the synthesizing system in 20 experiments as a 1 mM solution of lead acetate in a volume of 0.1 ml; D-PAM was added in a volume of 0.1 ml of the freshly prepared solution containing 1.5 mg of the compound in 1 ml. Activity of ALA dehydratase was expressed in micrograms synthesized per milligram protein during 2 h of incubation. Protein in the homogenates was determined by Lowry's method.

EXPERIMENTAL RESULTS

PBG was found after incubation of homogenates of all the organs mentioned above with ALA.

As Table 1 shows, highest ALA dehydratase activity was found in homogenates of liver tissue, followed by the kidneys and lungs (approximately one-quarter of the activity in the liver), and it was present in about equal amounts in the other tissues.

The results obtained after the addition of lead and D-PAM to the synthesizing system containing homogenates of the most active organs (the liver and kidneys) are given in Table 2.

As Table 2 shows, the addition of lead was followed by a significant decrease in ALA dehydratase activity in liver tissue homogenate but had no effect on its activity in the kidney tissue homogenate. Addition of lead together with D-PAM to the synthesizing system did not change the experimental results.

The absence of any reaction to the addition of lead to the kidney homogenate can be explained by the different responses of the organs to the specific action of lead. This suggestion is confirmed by the observations of Gibson et al. [5], who studied PBG biosynthesis by homogenates of organs of animals with experimental anemia and porphyria: In anemia ALA dehydratase activity was increased threefold in the blood and spleen but unchanged in the liver; in porphyria the activity of this enzyme in the liver and kidneys was doubled but in the blood and spleen it was unchanged.

TABLE 2. PBG Biosynthesis in Liver and Kidney Homogenates after Addition of Lead Acetate and D-PAM (M ± m)

Organ	PBG content, μg/mg protein · 2 h of incubation	Quantity of PBG after addition of lead	Quantity of PBG after addition of lead and D-PAM
Liver	15,5±0,84	12,35±1,33*	12,65±1,67
Kidneys	4,31±0,25	4,4±0,51	4,51±0,58

* $P<0,05$.

The results of the present experiments thus show that porphyrin synthesis takes place in all the organs studied in the albino rats, despite differences in their functions. In relation to ALA dehydratase activity the viscera of albino rats can be arranged in the following descending order: liver > kidneys > lungs > pancreas > small intestine > heart > spleen.

LITERATURE CITED

1. I. Barta, in: The Spleen. Anatomy, Physiology, Pathology, and Clinical Features [in Russian], Moscow (1976), pp. 152-154.
2. L. I. Idel'son, Clinical Disturbances of Porphyrin Metabolism [in Russian], Leningrad (1968).
3. L. I. Idel'son, Gig. Truda, No. 2, 55 (1968).
4. G. K. Popov and L. I. Krupitskaya, Pat. Fiziol., No. 4, 77 (1974).
5. K. D. Gibson, A. Neuberger, and J. J. Scott, Biochem. J., 61, 618 (1955).
6. S. L. Gibson and A. Goldberg, Clin. Sci., 38, 63 (1970).
7. R. Hampp, C. Kriebitzsch, and H. Ziegler, Naturwissenschaften, 61, 504 (1974).
8. S. Hernberg and J. Nikkannen, Pracov. Lek., 24, 77 (1972).
9. G. Niemann, Arbeitsmed. Sozialmed. Arbeitshyg., 3, 224 (1968).
10. S. Selander, Brit. J. Indust. Med., 24, 272 (1967).

CHOLESTEROL BIOSYNTHESIS IN THE BLOOD OF RABBITS WITH EXPERIMENTAL ATHEROSCLEROSIS

V. N. Mironova and P. P. Chayalo

UDC 616.13-004.6-092.9-07:616.153.922-07

Blood of normal rabbits and of rabbits on an atherogenic high-cholesterol diet was incubated with sodium acetate-2-[^{14}C]. After incubation, cholesterol and its precursors (squalene and lanosterol) were found and identified in the unsaponified fractions of leukocytes and platelets. Both in normal rabbits and in rabbits with atherosclerosis the highest specific activity in the leukocytes was found in cholesterol, followed by lanosterol and squalene; in the platelets the label accumulated mainly in lanosterol.

KEY WORDS: experimental atherosclerosis; blood; leukocytes; platelets; cholesterol biosynthesis.

The biological role of cholesterol is largely determined by the fact that it is a key compound in the biosynthesis of the most important steroids. Since cholesterol is a component of the lipid part of the cell membrane, ideas exist on its functional role as transmembrane carrier of various biological substances [8]. Finally, the role of cholesterol in pathology is generally familiar, especially in atherosclerosis and ischemic heart disease [1, 2]. Elevation of the cholesterol level under these circumstances is one of the main risk factors.

It is generally agreed that the principal site of cholesterol biosynthesis in the body is the liver and small intestine, although nearly all organs and tissues are capable of forming this steroid compound [4]. It is difficult at present to decide whether the blood is a site for the biosynthesis of cholesterol or its specific precursors. Yet the solution to this problem is of considerable importance not only from the theoretical, but also from the practical point of view, in connection with the development of new biochemical tests for the diagnosis of atherosclerosis and the production and testing of hypocholesteremic drugs.

A. V. Palladin Institute of Biochemistry, Academy of Sciences of the Ukrainian SSR. Institute of Gerontology, Academy of Medical Sciences of the USSR, Kiev.

(Presented by Academician of the Academy of Medical Sciences of the USSR N. N. Gorev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 86, No. 12, pp. 689-691, December, 1978. Original article submitted February 27, 1978.