

Primary Division Ratio of Umbilical Arteries and Vein of the Human Placenta in Abnormal States of Pregnancy and Development

Umbilical vessels on the chorial surface of the human placenta divide into primary divisions, the number of which ranges from 2–5¹. It has been shown that in placentae from cases with normal pregnancy and development, the umbilical vein has one division more than those of the arteries². In certain abnormal states, e.g. multiple pregnancy and abnormalities of development, this ratio is reversed, i.e. arteries have one division more than that of the vein³. This reversal of primary division ratio has been regarded as a 'Parameter of stress' of the anatomy of foetal blood vessels of the placenta, which slows down the circulation for facilitating exchanges

a significant association with incidence of multiple pregnancy and developmental defects, while the ratio is not altered significantly in prematurity, placenta previa and hydramnios.

The above findings suggest that reversal of primary division ratio represents a selective elongation of the arterial bed, representing an increased branching at the highest levels, without a concomitant elongation of the venous bed. Its association with increased tortuosities of arteries and an apparent widening of calibre support the above surmise. Consequently, it contributes towards a slowing of the blood stream in such conditions⁴.

Primary division ratio of arteries and veins

Entity	V > A vein more	V = A vein and artery equal	V < A vein less	Total	Individual X ² value	Signifi- cance
Normal	79 (47.30)	71 (42.52)	17 (10.18)	167 (100.00)	—	—
Prematurity	27 (50.94)	23 (43.40)	3 (5.66)	53 (100.00)	1.17 d.f.l.	—
Placenta previa	15 (55.56)	8 (29.62)	4 (14.82)	27 (100.00)	0.44 d.f.l.	—
Twins	59 (39.60)	57 (38.25)	33 (22.15)	149 (100.00)	7.70 d.f.l.	P < 0.01
Hydramnios	60 (51.72)	39 (33.62)	17 (14.66)	116 (100.00)	1.24 d.f.l.	—
Abnormal development	46 (38.98)	44 (37.29)	28 (23.73)	118 (100.00)	7.39 d.f.l.	P < 0.01
Hydramnios and abnormal development	18 (39.13)	16 (34.79)	12 (28.08)	46 (100.00)	8.71 d.f.l.	P < 0.01
Total	304	258	114	676		

across the placental barrier. The present communication is directed towards elaborating the manifestation of this parameter in various abnormal states of pregnancy and development.

509 placentae of cases with abnormal pregnancy or development (prematurity 53, placenta previa 27, multiple pregnancy 149, hydramnios 116, developmental defects 118 and coexisting hydramnios and developmental defects 46) have been subjected to injection corrosion preparations, using a continuous injection of 10–15% solution of cellulose acetate buterite in acetone, with pressures within physiological limits. The umbilical vein may have more, equal or lesser divisions than the umbilical artery. Cases, where vein has fewer primary divisions than the artery, have been regarded as abnormal. This abnormal manifestation in different clinical entities has been analyzed in comparison with similar observations on 167 normal placentae by means of Chi square test.

The relative incidence of the different primary division ratios in various clinical states is presented in the Table. It shows that the reversal of primary division ratio bears

Zusammenfassung. Es wird gezeigt, dass die Verzweigungen der Nabelschnurgefäße am Übergang auf die Membrana chorii bei Zwillingschwangerschaften, Fehlbildungen des Fetus sowie beim Hydramnion signifikante Abweichungen von der Norm zeigen.

INDRA BHARGAVA and P. T. K. RAJA⁵

Department of Anatomy,
Jawaharlal Institute of Postgraduate,
Medical Education and Research,
Pondicherry-6 (India), 27 February 1969.

¹ I. BHARGAVA, Thesis, D. Sc., Vikram University (1967).

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⁵ Department of Obstetrics & Gynaecology, Gandhi Medical College, Bhopal (India).

Cycloheximide-Induced Ultrastructural Changes in the Adrenal Cortex of the Rat

It is known that cycloheximide has a generally inhibitory effect on protein synthesis^{1,2}. Studying corticosteroid synthesis in rats treated with cycloheximide, a compound known to inhibit protein synthesis, a rapid decrease in the rate of steroid production has been observed with an increase in the free cholesterol content of the adrenal cortex^{3,4}. Adrenocorticotrophic hormone (ACTH), administered after cycloheximide, was found further to increase the free cholesterol. Having found that Δ^5 -pregnenolone intensified steroid synthesis, the authors concluded that the free cholesterol \rightarrow pregnenolone process was inhibited. A study of the cycloheximide

effect on pancreatic and hepatic ultrastructure has recently appeared⁵. The principal changes were the pre-

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³ L. D. GARREN, R. L. NEY and W. W. DAVIS, Proc. natn. Acad. Sci. USA 53, 1443 (1965).

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sence of nucleolus-like structures in the cytoplasm and collections of ribosomes in 'hook-like' configurations of the endoplasmic reticulum.

The purpose of our present study was to examine the ultrastructural changes of the adrenal cortex associated with the rapid sequence of biochemical events which followed the administration of cycloheximide.

Wistar rats weighing about 180 g were divided into 4 groups, each containing 6 male and 6 female animals, and injected i.p. with: 0.6 ml of isotonic saline followed 20 min later by 0.2 ml of isotonic saline (control group); 0.005 g of cycloheximide followed 20 min later by 0.2 ml of isotonic saline; 0.010 g of cycloheximide followed 20 min later by 0.2 ml of isotonic saline; 0.010 g of cycloheximide followed 20 min later by 2 IU of ACTH.

Cycloheximide was dissolved in isotonic saline (100 mg/6 ml) and ACTH (Cortrophin; Organon) in its own solvent (50 IU/5 ml). From each group, 3 male and 3 female rats were decapitated 50 min, and the other 6 animals 110 min, after the first injection. The left adrenal

gland was rapidly removed and placed in 4.5% glutaraldehyde buffered with 0.12M sodium cacodylate, in which it remained for 2 h. After prefixation, the tissue was washed, postfixed for 1½ h in 1% OsO₄, dehydrated in a graded series of ethanols, and then embedded in Durcupan ACM. Sections, cut on a Reichert OmU₂ ultramicrotome, stained with 20% uranyl acetate in methanol for 5 min, counterstained with lead citrate for 25 min, and examined in a JEM-6AS electron microscope or a Siemens Elmiscop I.

Conspicuous changes in the ultrastructure of the zona fasciculata cells have been observed even after the lowest (5 mg) dose of cycloheximide and at the 50-minute decapitation time. At lowpower magnification, compact masses of irregular shape, medium density, and blurred outlines were seen to have accumulated between organelles, appearing as if it had pushed them apart (Figure 1). In experiments involving both cycloheximide and ACTH treatment the changes are similar, although the cells appear swollen. This swelling involves the mitochondria and the compact masses, which at higher magnifications can be seen to be made up of small vesicles. The vesicles in places are regularly aligned (Figure 2). Around mitochondria and lipid droplets, compact, concentric membrane structures were numerous (Figures 1 and 3). Most lamellar systems were surrounded by a more or less electronlucent halo. Apart from a few occasional myelin-like figures, none of the ultrastructural changes described could be observed in the control animals.

Observations similar to those just described were also made in some cells of the zona reticularis, but not of the zona glomerulosa.

The earlier pathological and biochemical findings suggest a correlation between the substance seen to accumulate among organelles (compact masses) and the increased cholesterol content of the adrenal cortex. SCHWARZ and SUCHOWSKY⁶ found that both Metopiron and Amphenone B changed the ultrastructure of the zona fasciculata cells in a way that made it possible to localize some enzymes involved in the synthesis of steroids. On this ground, they presumed that C₁₁ hydroxylase was bound to the mitochondria, and C₁₇ and C₂₁ hydroxylase, as well as 3β-dehydrogenase, were bound to the endoplasmic reticulum. Similar considerations have led to the conclusion that free cholesterol was converted to pregnenolone by the enzyme system of the endoplasmic reticulum. As it may be seen, the ultrastructural changes are the consequence of an impairment of the enzyme system⁷.

Zusammenfassung. Cycloheximid als allgemeiner Inhibitor der Proteinsynthese verursacht submikroskopische Veränderungen in der Nebennierenrinde der Ratte. Kompaktes Material und konzentrische Membranstrukturen im Zytoplasma von Zellen der Zona fasciculata finden sich um Mitochondrien und Lipidtröpfchen.

Cs. DZSINICH, D. SZABÓ and I. ÖKRÖS

*Institute of Experimental Medicine,
Hungarian Academy of Sciences,
Budapest 8 (Hungary), 1 April 1969.*

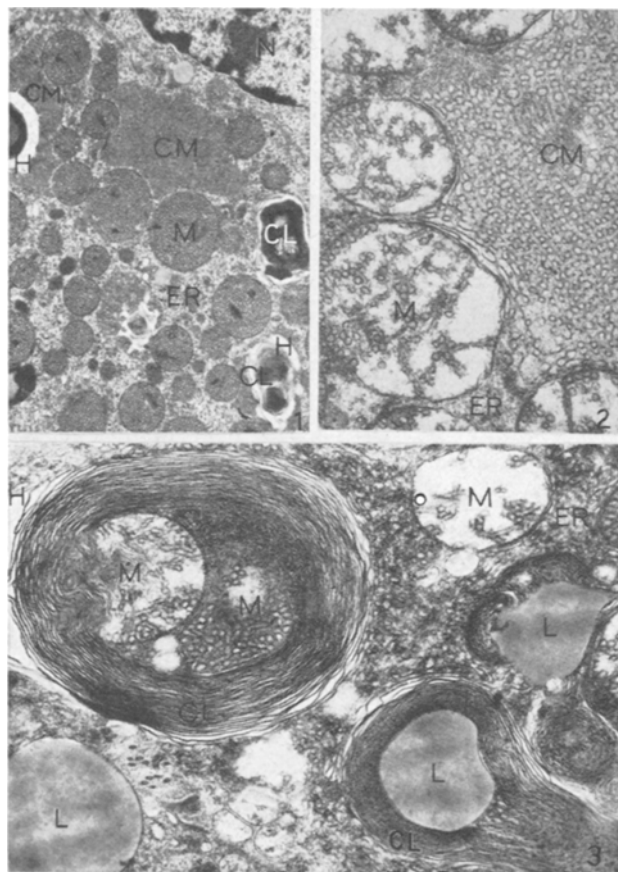


Fig. 1. Zona fasciculata of rat 110 min after treatment with 5 mg cycloheximide. $\times 14,000$. CL, concentric lamellar system; CM, compact masses; H, electron lucent halo; L, lipid droplets; M, mitochondria; N, nucleus; ER, endoplasmic reticulum.

Fig. 2. Zona fasciculata of rat 110 min after treatment with 10 mg of cycloheximide + 2 IU ACTH. $\times 23,000$. Note the regular alignment of vesicles.

Fig. 3. Zona fasciculata of rat 110 min after treatment with 10 mg of cycloheximide. $\times 34,000$. Concentric membranes surround some of the mitochondria and lipid droplets.

⁶ W. SCHWARZ and G. K. SUCHOWSKY, *Virchows Arch. path. Anat. Physiol.* 337, 270 (1963).

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