PATHOLOGY

Function of Collagen: Blood Pressure in Lathyritic Rats

COLLAGEN constitutes approximately one-third of the body protein in mammals. While its significance in maintaining form is obvious, little is known of its possible role in physiological processes. Discovering functions of collagen would be of particular importance in regard to ageing. Physical properties of collagen change markedly with age, presumably because of increased cross-linkages, but these changes have not been related to the decrease in efficiency of physiological processes characteristic of ageing. The changes in collagen with age and their possible significance have recently been reviewed[1].

Because of its distribution in and around blood vessels, collagen would be expected to influence haemodynamics. The production of lathyrism in laboratory animals by the administration of certain nitriles provides a system in which the role of collagen in blood vessel reactivity can be studied. In lathyrism, maturation of collagen by cross-linking is defective, and affected animals have less than the normal amount of mature collagen[2]. The present work was based on the supposition that if mature collagen influences the reactivity of blood vessels, differences in blood pressure between control and lathyritic animals should be detected when animals are treated with norepinephrine.

Male Holtzman rats weighing approximately 110 g were used. Three animals were kept as controls and four were given β-amino-propionitrile fumarate intraperitoneally, one mg per g body wt. per day, as a 20 per cent solution in 0·15 M NaCl. After 8 days treatment the animals were anaesthetized with 0·2 ml. 'Nembutal' per 100 g body wt. and heparinized polyethylene catheters (gauge No. 50) were secured in femoral arteries and veins. Each arterial catheter was attached to a mercury manometer and mean blood pressures were read directly. After baselines were established, each animal was given, in the venous catheter, 0·1 ml. 5 per cent dextrose containing 0·1 μg norepinephrine. All the control rats showed a greater rise in blood pressure than the lathyritics (Fig. 1). The mean maximum blood pressure rise for the controls was 49·3 mm Hg; that for the lathyritics, 33·0.

A possible explanation for this observation is that mature collagen fibres are oriented in such a way that, when arterioles constrict, they stabilize the vessels in their new configuration and maintain pressure. Without collagen support, the smooth muscle cells cannot remain adequately contracted in opposition to the force exerted by the blood. Similar conclusions concerning the role of collagen fibres in the aorta were arrived at on morphological grounds by Wolinsky and Glagov[3]. If future work indicates that lathyrism causes significant changes in smooth muscle cells, other explanations may be more reasonable.

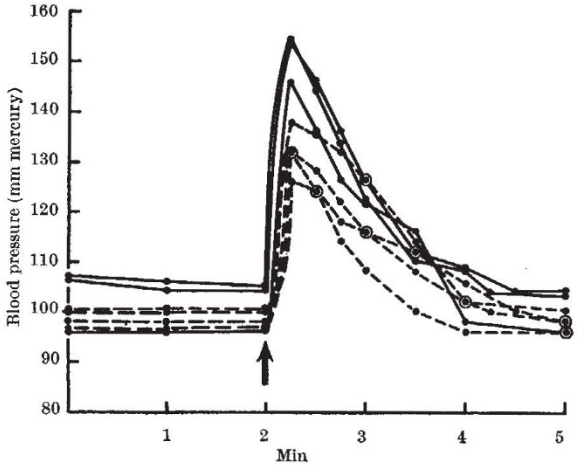

Fig. 1. Mean blood pressures of control and lathyritic rats as a function of time. Arrow indicates time of intravenous injection of norepinephrine. ———, Controls; — — — —, lathyritic rats

This work was supported by U.S. Public Health Service grant *HD*-00669 and a grant from the Muscular Dystrophy Association of America.

ROBERT R. KOHN
JOSÉ M. RIVERA-VELEZ

Institute of Pathology,
Western Reserve University,
Cleveland,
Ohio.

[1] Kohn, R. R., *J. Chron. Dis.*, **16**, 5 (1963).
[2] Martin, G. R., Gross, J., Piez, K. A., and Lewis, M. S., *Biochim. Biophys. Acta*, **53**, 599 (1961).
[3] Wolinsky, H., and Glagov, S., *Circ. Res.*, **14**, 400 (1964).

Growth-promoting Effect of Chondroitin Sulphate on Solid Ehrlich Ascites Tumour

IN the course of studying the interaction between connective tissue and cancer cells, I found that chondroitin sulphate promoted the growth of solid Ehrlich ascites tumour. Tumour cells used in this study were of Ehrlich hypotetraploid stock (Kaziwara[1] 4N) which was maintained intraperitoneally in *SM* male mice.

The first series of experiments was made with the chorioallantoic membrane (CAM) of the White Leghorn chick embryo. A disk, 8 mm in diameter and 3 mg in weight, made of 'Spongel' (Yamanouchi Seiyaku Co. Ltd., Tokyo), was soaked with solutions of various concentrations of chondroitin sulphate *C* (av. mol. wt., 50,000; Kaken Yakukako Co. Ltd., Tokyo). For controls, 0·85 per cent saline was used. 0·01 ml. of Ehrlich tumour ascitic fluid containing 5×10^5 cells was dropped on to the disk placed in a Petri dish. Then the disk, which contained both tumour cells and the solution, was implanted on the CAM of the chick, on the 6–7th day of its incubation. The embryos were killed on the 8th day after tumour implantation, and the solid tumour developed in and around the 'Spongel' disk on CAM was excised and weighed.

The effect of chondroitin sulphate on tumour growth on CAM is shown in Table 1. A statistically significant increase in weight of tumour tissue was noted in all the chondroitin sulphate-treated groups. The chondroitin sulphate absorbed in the 'Spongel' disk was demonstrated in the excised tumour mass as a metachromatic spot on the filter paper.

The second series of experiments were made with *SM* male mice about 100 days old, fed with standard pellet diet and water *ad libitum*. One ml. of 2 per cent chondroitin sulphate *C* solution was subcutaneously injected into the right flanks of the mice, immediately followed by inoculation of 0·1 ml. of the Ehrlich tumour ascitic fluid

Table 1. EFFECT OF CHONDROITIN SULPHATE ON GROWTH OF SOLID EHRLICH ASCITES TUMOUR ON CAM OF CHICK EMBRYO

Exp. No.	1	2	3	4	5	6	7	Totals
No. tumour Control	10	7	8	10	6	10	6	57
No. tumour 2% Chondr. S.	9	7	8			6	4	34
Tumour weight Control % 100	112	127	130			123	123	133
No. tumour 0·3% Chondr. S.			6	8	2	8	6	30
Tumour weight Control % 100			177	144	225	128	110	129
No. tumour 0·03% Chondr. S.			4	8	4	9	6	31
Tumour weight Control % 100			111	153	146	154	138	127

Average tumour weight ± *S.E.* based on: (*n*)

Control	70·5 ± 3·3 mg	(57)	
2% Chondroitin sulphate	91·9 ± 4·1 mg	(34)	$P<0·001$
0·3% Chondroitin sulphate	91·1 ± 4.0 mg	(30)	$P<0·001$
0·03% Chondroitin sulphate	90·0 ± 3·7 mg	(31)	$0·001<P<0·005$