## Permeability Tracers and Serum Proteins

The knowledge of normal and abnormal vascular permeability and transport across the vessel wall is an essential prerequisite of the study of the pathomechanism of various vascular lesions 1-5. The follow-up of such processes is partly by demonstration of the intramural deposition of a tracer substance or by light- or electron microscopic detection of the tracer's passage across the vessel wall<sup>6-13</sup>. But no unequivocal conclusions can be drawn until it is clarified whether or not the tracer present in the vessel wall is bound by serum proteins. If there is a durable linkage between the tracer and a given serum protein fraction, the former serves as an indicator of the fraction's mural transport, but if there is no such linkage, the presence of the tracer in the vessel wall signifies only the increase of vascular permeability.

The nature and duration of linkage between tracer substances and serum proteins have been examined in the present study.

Materials and methods. 18 male Wistar rats, weighing 110-150 g, were given the substances indicated i.v. 30 min prior to sacrifice.

Serum samples were examined by immunoelectrophoresis. Commercial antirhodent rabbit serum (Human) was used as immune serum. For the identification of iron, ferritin and peroxidase molecules in the precipitation lines, the Prussian blue and the peroxidase 10 reactions were used.

Group Tracer Dose 1 Suspension of colloidal iron 1.5 ml/100 g (Ferrlecit; Natterman Co., Köln) body weight Containing approximately 12.5 mg of iron/ml 2 Suspension of colloidal iron 0.5 ml/100 g (Jectofer; Astra Co., Sweden) containing approximately 50 mg of iron/ml Ferritin, 2X cryst. B grade 20 mg/100 g (Calbiochem Inc., USA) dissolved in physiologic saline Suspension of colloidal carbon 0.2 ml/100 g (Pelican; Gunther Wagner Co., Hannover) containing approximately 100 mg of carbon/ml Evans blue (Gurr Ltd., England) 20 mg/100 g dissolved in physiologic saline Horseradish peroxidase, B grade 15 mg/100 g (Calbiochem Inc., USA) dissolved in physiologic saline

Peroxidase was demonstrated in the  $\beta$ -globulin and IgG fractions; Evans blue was present in the albumin and α-globulin fractions; while the rest of the tracer substances examined were apparently not bound by any serum protein fraction. In vitro binding of Evans blue by albumin was demonstrated previously 14, 15. By electrophoresis on cellulose acetate, colloidal iron was shown to form a precipitate of varying charge and motility, migrating together with certain plasma components 12 but this does not mean the presence of a linkage.

It appears, therefore, that unless the binding between serum protein and tracer is not reversed during the former's passage across the vessel wall, peroxidase signifies the mural transport of  $\beta$ -globulin and IgG, and Evans blue that of albumin and a-globulin. The other tracer substances, being apparently not bound by serum proteins, serve only as indicators of increased vascular permeability.

Zusammenfassung. Es wird gezeigt, dass die Permeabilität der Gefässwand durch an Serumeiweissfraktionen gebundene Markierungssubstanzen geprüft werden kann.

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- <sup>1</sup> P. Schürmann and H. E. McMahon, Virchows Arch. path. Anat. Physiol. 291, 47 (1933).
- <sup>2</sup> I. H. PAGE, Circulation 10, 1 (1954).
- <sup>8</sup> J. Giese, Acta path. microbiol. scand. 53, 167 (1961).
- <sup>4</sup> A. C. Lendrum, Canad. med. Ass. J. 88, 442 (1963).
- <sup>5</sup> C. W. Adams, O. B. Bayliss and I. C. Aton, J. Atheroscler. Res. 7, 473 (1967).
- <sup>6</sup> M. FRIEDMAN and S. O. Byers, Arch. Path. 76, 99 (1963).
- J. STAUBESAND, Z. Zellforsch. 58, 915 (1963).
  I. R. CASLEY-SMITH, Ann. N.Y. Acad. Sci. 116, 803 (1964).
- 9 R. S. COTRAN, E. R. SUTER and G. MAJNO, Vasc. Dis. 4, 107 (1967).
- M. J. Karnovsky, J. Cell. Biol. 35, 213 (1967).
  G. Majno and M. Leventhal, Lancet 2, 99 (1967).
- 12 H. Jellinek, Z. Nagy, I. Hüttner, A. Bálint, A. Kóczé and T. KERÉNYI, Br. J. exp. Path. 50, 13 (1969).
- 18 F. GIACOMELLI, J. WIENER and D. SPIRO, Am. J. Path. 59, 133 (1970).
- <sup>14</sup> G. Narkus and I. P. Baumberger, J. biol. Chem. 206, 59 (1954).
- 15 P. HANSEN and N. C. NIELSEN, Scand. J. clin. Lab. Invest. 16, 491 (1964).

## Direct Autonomic Nerve Fibers to the Renal Medulla in Man<sup>1</sup>

Blood flow to the renal medulla is regulated in part by the antagonistic action of the sympathetic and parasympathetic nerves on the medullary blood vessels2. Earlier studies<sup>3-6</sup> with the specific catecholamine fluorescence test showed that the arterioles supplying the renal pyramid - the juxtamedullary efferent arterioles and the proximal parts of the arterial vasa recta - receive sympathetic innervation from the periarterial plexuses of the afferent arterioles. These fibers traverse the vascular pole of the juxtamedullary glomeruli to reach the corresponding efferent arterioles.

In the thin sections  $(4 \mu m)$  used for the fluorescence technique it is not possible to resolve the question whether some of the fibers innervating the medullary vessels originate directly from the plexuses around the arcuate arteries without passing across the juxtamedullary glomerular poles. If such direct nerve pathways exist, neural vasoregulation in the medulla may be achieved independently of any effects on the glomerular blood flow.

Materials and methods. Traditional silver impregnation (Bielschowsky, Gros and Schultze) was used to study