Ultrafiltration Measurement of Paraprotein Particles in Four Cases of Macroglobulinemia

Blood proteins of patients suffering from macroglobulinemia WALDENSTRÖM[1] show, on electrophoretic examination, a homogeneous additional paraprotein fraction, containing macroglobulins. Up to the present time, very little is known about the form and dimensions of macroglobulin particles. In one case, GARD, HELLER, and MALMROS[2] found by direct observation in an electronic microscope that macroglobulins in a fixed preparation show practically spherical particles with diameters ranging approximately from 120 to 180 Å. In another case, WEBER and HÄSSIG[3] proved—by means of sedimentation, diffusion and viscosity measurements—the existence of barlike particles of macroglobulins.

We considered it necessary to state the dimensions of native, non-fixed paraprotein particles in macroglobulinemia. For this purpose we chose a new combination of methods: the ultrafiltration of macroglobulin sera through graded collodion membranes in connection with successive paper electrophoretic examination of filtrates. All methodical data were published elsewhere[4]. We emphasize here that from the theory of ultrafiltration[5] it is clear that by this method it is possible to find out just one diameter of the particles measured: this is the shortest diameter, regardless whether their shape be spherical, barlike etc. Therefore the shape of particles cannot be determined by the ultrafiltration alone.

For our study we had at our disposal suitable sera of four patients with macroglobulinemia WALDENSTRÖM, containing distinct, electrophoretically homogeneous paraproteinemic fractions. Detailed clinical and laboratory statements would exceed the range of this brief report. As agregates of macroglobulins originated by precipitation with distilled water cannot be fully returned into the state of isolated particles with physiological saline, which we proved ourselves[6], we carried out filtration of the whole native sera and not of the isolated macroglobulin fraction.

Average porosities of membranes used are mentioned in the Table; their thickness varied from 180 to 400 μ. Through membranes of individual porosities we filtered, on the average, 4·5 ml of the native undiluted serum; the usual filtration area was 8 cm^2. When applying a gradually increasing filtration pressure from 0·1 to 1·5 atm., the filtration lasted at least 15 h. Individual filtrates after being concentrated by dialysis were submitted to paper electrophoresis. Electrophoregrams of ultrafiltrates were evaluated visually as for the presence of the paraproteinemic fraction. All ultrafiltration experiments rendered clear results which are summarized in the table.

We used ELFORD's[5] formula to deduce the diameter of measured particles (p) from the value of the porosity of the limiting membrane (d):

$$p = F \cdot d$$

The values of the correcting factor (F) were interpolated according to the statements of the same author. In the last column of the table, the possible extents of the diameters of paraprotein particles in singular cases are given—taking into account the accuracy of ultrafiltration measurements. It is evident that the shortest diameters of native paraprotein particles in all four cases of macroglobulinemia are very similar or nearly the same, moving in the range of 140–220 Å. The relative shifting of the filtration end-point—and subsequently of the diameter of the particles—in case No. 2 was most probably due to the low density of the macroglobulin fraction in this case. It is possible to suppose that, if adsorption on the collodion membrane is taken into account, the contents of paraproteins in the filtrate of lower porosity (46 mμ) decreased under the level necessary to be provable electrophoretically.

It may be mentioned here that in five simultaneously investigated sera of plasmocellular myeloma the filtration end-point of analogous paraproteinemic particles lay between 11–20 mμ[6]. This corresponds to the diameter of particles of only 30–70 Å, i.e. to the range of the shorter diameters of the majority of normal serum fractions –38 Å.

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Zusammenfassung

Durch die Ultrafiltrationsmessung der im nativen Zustande im Serum sich befindlichen Paraproteine von vier Makroglobulinämiekranken konnte der kleinere Durchmesser der Teilchen bei 140–220 Å bestimmt werden. Der gleiche Diameter bei gleichzeitig untersuchten Myelom-Paraproteinen beträgt jedoch nur 30–70 Å.

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[4] D. WIEDERMANN and J. ŠMARDA, Schweiz. med. Wschr. *86*, 930 (1956).
[5] W. J. ELFORD, Trans. Faraday Soc. *33*, 1094 (1937).
[6] D. WIEDERMANN, J. ŠMARDA, and B. WIEDERMANN, Z. ges. exper. Med. (in press).

Table

Case No.	Average porosity in mμ												Filtration end-point (mμ)	ELFORD's factor F	Diameter of particles (mμ)
	60	54	51	49	47	46	40	39	35	34	22	17			
1			+			+	–	–			–	–	40	0·42	16–20
2	+		+	+		–	–			–			46	0·43	18–22
3					+			–		–			39	0·42	14–21
4		+				+	–		–	–			40	0·42	16–20

+ presence of paraprotein fraction in the filtrate
– absence of paraprotein fraction in the filtrate