ELIMINATION RATE OF HUMAN SERUM ALBUMIN IN PARAPLEGIC PATIENTS

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PREVIOUS studies (Lob *et al.*, (1971)) have shown that blood volumes of paraplegics, which are measured by the R-125-IHSA-method, may result in unreliable values because the elimination rate of homologous human serum albumin is often increased in these patients. It can be speculated on one hand that the increased elimination rate might be the result of an elevated catabolism of radio-iodinated human serum albumin; on the other hand immunological mechanisms could be the cause, *i.e.* a developing clinical incompatibility to homologous human serum albumin. With the following investigations it should be elucidated whether or not immune reactions are responsible for the high elimination of human serum albumin in paraplegic patients.

PATIENTS AND METHODS

The investigations were done in 24 male and six female paraplegic patients of ages between 18 and 60 years; the results were compared with those of ten normal healthy volunteers. The paraplegic lesions of the patients were at least two weeks old, with a maximum of 20 years. Six patients had lumbar spine lesions, 11 thoracic spine and 13 cervical spine lesions. Twenty-four patients were completely paralysed and six patients incompletely paralysed.

The elimination rate of human serum albumin (per cent/hour) was measured with 125-iodine labelled homologous human serum albumin (Fa. Buchler + Co, specific activity 10 $\mu\text{Ci./mg.}$). Before applying radio-active labelled human serum albumin the thyroid gland was blocked with Endojodin (R) (Fa. Bayer) in order to prevent a selective storage of radio-active iodine in this organ. After the intravenous application of 100 $\mu\text{Ci.}$ R-125-IHSA the radio-activity was measured in 1 ml. of heparinised blood samples at time intervals of 1, 5, 10, 20, 30 and 60 minutes.

Furthermore, the body weight, the hematocrit, the erythrocyte sedimentation rate (ESR), the osmolarity, the colloid osmotic pressure, the total serum protein and the serum electrophoresis were controlled.

In five patients the disappearance rate of homologous R-125-IHSA was compared with that of autologous 131-I human serum albumin according to the method of the immune elimination technique (Seifert *et al.*, 1971). For this purpose the radio-activity in 1 ml. heparinised blood was determined at daily intervals over a period of three weeks. The autologous albumins were produced by the same fractionation procedure as the normal homologous HSA and labelled with 131-iodine (Berson *et al.*, 1953; Glaubitt and Rippel, 1967). Autologous and homologous albumin fractions were compared prior to an administration by radiochromatography.

serum albumin in different concentrations as well as with Endojodin (R)—in order to exclude an iodine hypersensitivity. The skin tests were evaluated after 30 minutes and after 36 hours.

RESULTS

The albumin elimination rate was increased in all patients; this is shown in Figure 1; while controls eliminate homologous human serum albumin with a

FIG. 1

The elimination rates of homologous ^{125}J -Albumin in three groups of paraplegic patients compared to normal volunteers.

rate of 6.6 ± 0.5 per cent/hour, diplegic patients show an elimination rate of 17.8 ± 2.1 and tetraplegics even 35.2 ± 6.5 per cent/hour.

This corresponded to a slight difference in the serum albumin concentration (fig. 2). These patients showed a decrease of total serum albumin of eight per cent and ten per cent respectively. The total serum protein was decreased by four per cent and five per cent respectively. A possible sensitisation against albumin by prior human serum albumin infusions could be excluded by anamnestic evaluation.

FIG. 2

The serum protein and albumin concentrations in different groups of paraplegic patients.

FIG. 3

The erythrocyte sedimentation rate (ESR) in different groups of paraplegic patients.

The hematocrit of the paraplegics was with an average of 43 per cent essentially unchanged as well as the serum osmolarity with 290 mosm and the colloid osmotic pressure with 37 cm H₂O.

The erythrocyte sedimentation rate was increased in all groups of patients but did not show further correlation with the albumin elimination rates, neither with the albumin concentrations. Figure 3 shows that the highest values of ESR were found among diplegic patients with an average of 40/48 respectively in the group of patients without chronic pressure sore with an average of 39/49, while

FIG. 4

The elimination curves of radio-active labelled homologous and autologous human serum albumin in a paraplegic patient, compared to the curve of a patient with clinical albumin incompatibility.

tetraplegics with chronic pressure sores only showed values in the range of 14/25. Similarly, other pathological conditions as urinary bladder paralysis, pyelonephritis or chronic pressure sore alone could not be correlated to the increase of albumin elimination rate.

The disappearance curves of the immune elimination technique did not show any difference between homologous and autologous fractions. With a value of 50 per cent on the tenth day, they corresponded well to a normal metabolism (Berson *et al.*, 1953; Cohen *et al.*, 1961). In the presence of a sensitisation against albumin the measured radio-activity would drop to values beyond ten per cent after one week (fig. 4) (Ring *et al.*, 1974). The results of the other immunological tests corresponded well to the immune elimination findings: the skin

tests were negative with homologous human serum albumin, as well as with autologous fractions as well as with Endojodin[®]. By the immunodiffusion technique (Ouchterlony, 1962) no precipitating antibodies could be detected in the sera of the patients.

DISCUSSION

The highest values of albumin elimination rates were found among the group of tetraplegic patients with a complete paralysis and chronic pressure sores. An explanation of this phenomenon might have been found by correlation of other pathological conditions with this group of patients. But none of the investigated values showed a satisfactory correlation. The ESR showed the highest values in the group of patients with thoracic spinal lesions without chronic pressure sore, while the albumin elimination rate in this group was one of the lowest. Even urinary bladder inflammation or chronic pressure sore per se cannot be regarded as causal factors.

If immunological mechanisms are responsible for the increased elimination of albumin, these reactions should develop together with a sensitisation against foreign protein or macroaggregates in the human albumin fractions. Sometimes these mechanism can lead to clinical incompatibility reactions (Ring *et al.*, 1974). In this case there should be a significant difference in the immune response of the organism against homologous and autologous human serum albumin. The most sensitive and most reliable method to detect an existing immune response against a foreign protein is the antigen elimination technique (Seifert *et al.*, 1971). By this method a sensitisation can be detected even if there are no precipitating or agglutinating antibodies in the serum nor positive skin tests. The presented results show clearly that the albumin elimination rate of paraplegic patients could not be explained by immunological mechanisms. Therefore, the cause of this phenomenon must probably be seen in a change of capillary permeability by central nervous mechanism. The clinical observation of the pastous, edematous condition of the skin would fit to this explanation as well as the fact that the elimination rates were the higher the more severe the lesions. A chronic pressure sore may accentuate the symptoms by an additional protein loss. Control studies on patients with chronic pressure sore without paralysis are, however, not yet done. It must be mentioned that all investigations were done on old lesions. It is still unknown what will happen immediately after the accident, which leads to the paraplegic lesion. However, in the therapy of paraplegics, whose lesions are older than some weeks, these high albumin elimination rates should be respected in infusion therapy.

SUMMARY

Investigations in 30 paraplegic patients and ten voluntary controls showed that in paraplegics the albumin elimination rate is significantly increased with the highest values of 35.2 ± 6.5 per cent/hour in tetraplegics compared to normal values of 7.6 ± 0.5 per cent/hour. This finding could not be explained by immunological mechanisms. There were no antibodies against human albumin in the sera of the patients nor positive skin tests. The disappearance curve of homologous and autologous 125-J-Albumin according to the antigen elimination technique corresponded without difference to a normal metabolic situation. Clinical criteria

(height of the lesion) indicate that permeability changes due to central nervous mechanisms may be regarded as an aetiological factor. A chronic pressure sore can accentuate the symptoms by its additional protein loss.

RÉSUMÉ

Les investigations chez 30 paraplégiques et 10 contrôles volontaires ont montré que chez les paraplégiques l'élimination de l'albumine est notablement augmentée avec des valeurs hautes, aux alentours de $35,2 \pm 6,5\%$ par heure chez les tétraplégiques comparées aux valeurs normales de $7,6 \pm 0,5\%$ per heure. Il n'a pas été possible de expliquer ces résultats par des mécanismes immunologiques. Le critère clinique, en ce qui concerne la hauteur de la lésion, pourrait indiquer que la perméabilité pourrait varier en rapport avec un mécanisme neurogène et être considéré comme un facteur étiologique.

ZUSAMMENFASSUNG

Untersuchungen an 30 Querschnittgelähmten und 10 freiwilligen Kontrollpersonen ergaben, daß die Albuminverschwinderaten bei Querschnittgelähmten mit Höchstwerten von $35,2 \pm 6,5\%$ pro Stunde bei Tetraplegikern signifikant über denen von Normalpersonen ($7,6 \pm 0,5$) liegen. Dieser Befund konnte nicht durch immunologische Reaktionen erklärt werden. Es wurden weder Antikörper gegen Albumin im Serum der Patienten gefunden noch positive Intrakutanteste. Die Verschwindkurven von homologem und autologem $^{125}\text{-J}$ -Albumin in der Antigeneliminationstechnik entsprachen ohne Unterschied denen einer normalen Stoffwechselsituation. Klinische Kriterien (Höhe der Verletzung) weisen vielmehr auf eine zentralnervös bedingte Permeabilitätsänderung als ursächlichen Faktor hin. Ein zusätzlicher Eiweißverlust durch vorhandene Druckgeschwüre scheint die Symptomatik weiter zu akzentuieren.

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