Half-Lives of Homologous Serum Albumins in Several Species.* (20336)

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It has been shown that the half-lives of homologous gamma globulins vary from species to species (1). As a corollary, the half-lives of homologous serum albumins have been determined using the I^{131} protein label, a convenient tool for the measurement of protein catabolism.

Materials and methods. Albumin was separated from human, bovine, and rabbit serum in the laboratories of Armour and Co. according to the alcohol fractionation procedure of Albumin from dog and mouse Cohn(2). serum was obtained by electrophoretic separation in a Tiselius apparatus in the laboratory of Dr. D. H. Moore of Columbia University. To the albumins in a pH seven 0.2 M phosphate buffer was added a slightly acid solution of I^{131} as free iodine and then the pH of the mixture was raised to 9 by the addition of 0.1 N NaOH. Non-protein-bound iodine was eliminated by dialysis against refrigerated tap water for 72 hours. The entire procedure was carried out at 0°-5° C. Final preparations contained less than one iodine atom per molecule of protein and at least 99% of the radioactivity was protein bound, as determined by trichloracetic acid precipitation. (1) The following subjects were used: Eleven men ages 23 to 75 who were institutionalized in a county home. These men had the following diagnoses: 5 - multiple sclerosis, 2 - hemiplegia old, one - healed osteomyelitis, one - chronic arthritis, one - post operative bladder cancer, and one - asthma. (2) Three nonlactating full grown Swiss and Jersey cows. (3) Nine full grown mongrel dogs. (4) Nine young albino male rabbits weighing between 2 and 2.2 kg for rabbit albumin half-life determination. (5) Eight young albino male rabbits weighing between 2 and 2.2 kg for the determination of the effect of metabolic rate on albumin half-life. (6) Thirty young adult CFW strain female mice weighing from 20 - 21 g. All subjects were given oral potassium iodide supplements to saturate iodine utilizing tissues and minimize retention of I¹³¹ liberated by catabolism of labelled albumin. I¹³¹ labelled homologous albumin, in amounts less than 10 mg per kilo body weight, was injected intravenously into all species except the mouse in which injections were made subcutaneously. Two or more days were allowed after injection for the labelled protein to equilibrate completely between the intravascular and extravascular components of the plasma protein pool before the half-life determinations were started. After equilibration the humans, cows, dogs and rabbits were bled at six or seven day intervals and the concentration of protein bound I¹³¹ in the plasma was determined (3,4). All 30 mice received identical injections of labelled albumin and ten were exsanguinated 3, 5, and 7 days later. The blood from the mice in each group was pooled and labelled protein concentration of the pooled plasma was determined.

As was suggested by our earlier study of gamma globulin half-life(1) the metabolic rate of the host appeared to influence the protein half-life. To further test this hypothesis we determined the albumin half-life in rabbits made hypermetabolic by daily injections of 0.1 to 0.2 mg of thyroxin per kilo body weight throughout the period of observation.

Results and discussion. The half-lives of I^{131} labelled homologous albumins were: cows, 20.7 days; humans, 15.0 days; dogs, 8.2 days; rabbits, 5.7 days; and mice, 1.2 days (Table I). These values are calculated for the entire period of observation indicated on Table I. In spite of obvious differences in structure, size, origin, and function of albumin and gamma globulin, the albumin half-lives correspond closely to the gamma globulin half-lives reported earlier: cow, 21.2 days; human, 13.1 days; dog, 8.0 days; rabbit, 4.6-5.7 days; and mouse, 1.9 days(1). It would appear that

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 Species	No. of subjects	Method of fractionation	Interval after inj. for which half-life is cal- culated in days	Half-life with stand. dev. in days	
 Cow	3	Alcohol	2-30	20.7 ± 1.1	
Human	11	**	7-28	15.0 ± 1.9	
Dogs	9	Electrophoresis	7-28	8.2 ± 1.2	
\mathbf{R} abbit	9	Alcohol	4-22	$5.7 \pm .3$	
Mouse	30	Electrophoresis	3- 7	1.2	

TABLE I. Albumin Half-Lives.

the dominant role in the catabolism of these proteins is played by the metabolic characteristics of the host and not by the characteristics of the protein molecules themselves.

The same inverse relationship between protein half-life and metabolic rate of the host noted previously for gamma globulin also held for albumin. This relationship was further supported by the finding of a 4.4 ± 0.3 day albumin half-life in the 8 rabbits given thyroxin. The metabolic rates of these animals were increased an average of 120% as indicated by measurement of oxygen consumption with a Benedict Roth metabolor attached to an airtight cage.

The homologous albumin half-lives reported here agree fairly well with those reported by others. Using the same technique Sterling found an albumin half-life of 10.5 ± 1.5 days in medical students(5). The difference between this figure and the 15 day value we found for institutionalized males may be largely the result of the difference in activities and, therefore, metabolic rates of the two groups of subjects. Tracing albumin labelled with N¹⁵, London found a half-life of approximately 20 days in humans(6). This value would be expected to be somewhat greater than the true half-life since some of the N¹⁵ label is used in resynthesis of protein after catabolism of the originally labelled protein. Calculations based on the 2 to 6 day post injection determinations of Fink, et al., give an 8.4 day half-life for total plasma protein in dogs(7) which agrees well with our

8.3 day albumin half-life and 8.0 day gamma globulin half-life.

Summary. The half-lives of homologous serum albumins in humans, cows, dogs, rabbits and mice have been presented. The albumin half-lives are similar to the gamma globulin half-lives for the same species and apparently are dependent upon the metabolic characteristics of the host.

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