The rate of loss of labeled plasma proteins from the circulation of tumor-bearing rats

It has been suggested that the liver hypertrophy in rats bearing transplanted tumors is a response to the tumor's demand for an increased supply of protein[1]. Since the tumor can efficiently utilize plasma protein for tumor protein synthesis[2], increased plasma protein synthesis by the livers of tumor-bearing rats might be anticipated. This possibility was investigated by measuring the rate of disappearance of labeled infused plasma proteins from the circulation.

DL-leucine-2-^{14}C and DL-tyrosine-2-^{14}C with specific activities of 0.60 and 0.42 mc per mmole respectively were obtained on allocation from the U.S. Atomic Energy Commission. Radioactive plasma was obtained from a 460 g rat which had been injected with 5 mg of leucine-^{14}C four hours previously. This was infused at a dose of 0.6 ml/100 g body weight into six 150 g rats of which three were normal and three bore seven day old Walker carcinoma 256 implants (about 15 g). The rats were sacrificed at intervals up to 20 hours, and the specific radioactivity of the plasma proteins was determined as previously described[3].

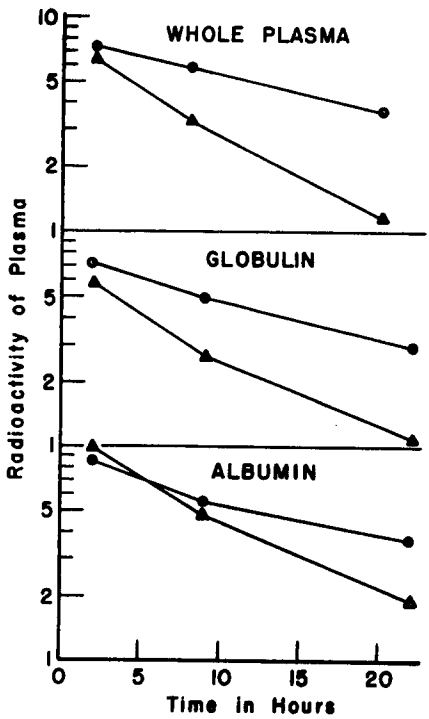

Fig. 1. The disappearance of infused ^{14}C-labeled plasma, globulins and albumin from the circulation of normal and tumor-bearing rats. The circles represent normal rats, and the triangles, tumorbearing rats. The radioactivity is expressed as the ratio of the radioactivity of the plasma to the radioactivity of the corresponding infusion $\times 10^{-3}$.

The top pair of curves in Fig. 1 show that the labeled plasma protein disappeared from the circulation of the tumor-bearing rats more than twice as fast as from the controls. Assuming that the total amount of plasma protein in circulation would not change materially during the experiment, and that the infused plasma protein behaved identically with the circulating protein, the experiment suggests that plasma protein was being synthesized in the cancerous rats twice as fast as in the normal rats. To determine whether this increased turnover of plasma proteins was due to one or both of the major plasma constituents, the experiment was repeated using radioactive albumin and globulins. Labeled plasma was obtained from two rats which had received an injection of 4 mg/100 g body weight of tyrosine-^{14}C ten hours previously. Globulins were precipitated by cold methanol[4]. After centrifugation the albumin was siphoned off, and the two protein fractions were dialyzed against distilled water, lyophilized and reconstituted with physiological saline. The curves illustrating the rates of disappearance of radioactive albumin and globulins from the circulation of normal and tumor-bearing rats are illustrated by the bottom and middle sets of curves in Fig. 1. It is apparent that both albumin and globulins disappeared from the plasma of the tumorous rats twice as fast as from the controls.

In all probability the observed relative rates of disappearance of the radioactivity correspond to relative turnover rates of the plasma protein. It would be difficult to explain the observed differences in terms of differences in mixing time, plasma volume or body water. However, differences in rate of equilibration between intravascular and extravascular extracellular compartments due to permeability differences cannot be overlooked.

I wish to thank Dr. THEODORE WINNICK for helpful discussions and the American Cancer Society for financial aid.

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1 A. L. BABSON, *Cancer Research*, 14 (1954) 89.
2 A. L. BABSON AND T. WINNICK, *Cancer Research*, 14 (1954) 606.
3 H. W. GERARDE, M. JONES AND T. WINNICK, *J. Biol. Chem.*, 196 (1952) 51.
4 L. PILLEMER AND M. C. HUTCHINSON, *J. Biol. Chem.*, 158 (1945) 299.

Received February 21st, 1956

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