of the red-cell stromata for properties A, B, Rh_o, Rh′, and Rh″ are approximately 8 to 32 times as high as the corresponding titers of the original red cells. When one considers that 250 cc of red cells yield about 10 cc of red-cell stromata, the results are in satisfactory agreement with the expectations. In the case of the M and N properties, on the other hand, the expected rise in titer was not obtained, though there was in general a slight increase. This suggests that the processing damages the M and N properties.‡

It might be mentioned that the inhibition and absorption titers obtained for the various Rh properties have been consistently lower than the titers obtained for A and B. While it is true that it is not possible to compare the reactions of two antisera of different specificities, still these findings suggest that the number of Rh haptens per red cell may be less than the number of A, B, or O haptens. If this is proved to be correct, it might furnish an explanation for some of the peculiarities of the Rh *in vitro* reactions.

Red-cell stromata prepared with sterile precautions have been injected intramuscularly into human volunteers, without systemic or local reactions of any kind; also the intravenous injection of large quantities of stromata into rabbits appears to be innocuous, provided these are prepared with sterile precautions and smooth emulsions containing no coarse particles are injected. It would appear, therefore, that the clinical trial of the material for attempting the desensitization of Rh-negative mothers of erythroblastotic fetuses may be justified.

Summary. From 250 cc of packed erythrocytes approximately 10 cc of red-cell stromata can be obtained. The titers of the group substances, A, B, and Rh, in the stromata are almost proportionately higher than the corresponding titers of the original erythrocytes. However, the calculated rise in titer was not obtained for properties M and N, suggesting that these may have been damaged by the processing of the cells. The possible use of red-cell stromata for treating sensitized Rh-negative individuals is discussed.

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‡ However, E. Witebsky and A. Heide (*Arch. Path.*, 1940, **30**, 1154) have reported the production of anti-N sera by injecting rabbits with boiled stromata of type N.

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Production and Implications of an Antiserum to Necrosin.*

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The writer has recently demonstrated that the pattern of injury in acute inflammation seems to be primarily referable to the liberation of a factor located in the euglobulin fraction of exudates.[1, 2] This factor has been termed necrosin. It is either a euglobulin or at least it seems to be associated with that fraction of exudates, *i.e.*, as obtained by precipitation with $(NH_4)_2SO_4$ at one third saturation. In addition, this fraction manifests pyrogenic and leukopenic properties.[2]

It occurred to the writer in connection with these studies that an antiserum to necrosin, if obtainable, may prove to be of theoretical interest and possibly also of clinical value. For this reason, in the fall of 1942, a series

* This is paper XXVIII of a series entitled "Studies on Inflammation."

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1 Menkin, V., *Science*, 1943, **97**, 165.

2 Menkin, V., *Arch. Path.*, 1943, **36**, 269.

of rabbits were immunized to varying doses of this fraction, in turn extracted usually from canine exudates by a technique previously described.[2] The immunizing procedure consisted of repeated subcutaneous injection of the material suspended either in physiological saline or in an aqueous medium. The injections were usually spaced at about 6 days apart. After about the fourth injection, a prominent edematous inflammation of the skin, with hemorrhagic necrosis, frequently developed. The reaction was far more intense than the effect of necrosin *per se*. The picture appeared to be typically that of an Arthus Phenomenon. From about a week to a month following the sixth injection of necrosin, blood was obtained either from the marginal vein of the ear or from the heart. The precipitin antibody titer was determined in the serum by utilizing necrosin as the antigen at various concentrations. Corresponding more or less with the elicited hypersensitive skin reaction (*i.e.*, Arthus Phenomenon), the antibody titer was found at high dilution of necrosin. A definite precipitin reading could be recorded at dilution of 1:100,000 of necrosin. On the other hand the interaction of normal rabbit serum with necrosin failed to induce any precipitin reaction.

These facts clearly indicate that necrosin or the euglobulin fraction of exudates is definitely antigenic, yielding as a result a serum containing a high antibody titer.‡ The implications of these findings are fairly obvious. For instance, it is conceivable that such a serum might be of value in hastening wound healing; in lessening the toxic or injurious manifestations of numerous inflammatory or infectious processes; and finally it may help in explaining the inability of the young animal to develop an adequate inflammatory reaction in contrast to the adult animal, as shown by Freund.[3] In other words, it is conceivable that the gradual development of resistance to infections occurring with age may in part be due to a subminimal immunization to necrosin, in turn liberated as a result of previous wounds or infections. These studies are being continued further by the writer.

Conclusions. Necrosin, the factor liberated in inflammatory exudates, and *per se* capable of explaining reasonably the basic mechanism of cellular injury in acute inflammation, is antigenic. As such, it is capable of inducing in the skin of sensitized rabbits a typical local anaphylaxis (Arthus Phenomenon), and in the serum of these same animals a high precipitin antibody titer. The implications of these observations are discussed.

‡ As indicated in the accompanying paper, No. 14660, entitled "Non-Antigenic Property of the Leukocytosis-Promoting Factor of Inflammatory Exudates," another protein fraction of canine exudate is *per se* essentially non-antigenic. Nevertheless, in an endeavor to determine the degree of specificity engendered by immunization with canine necrosin alone, similar observations are now in progress with the use of canine blood serum as the antigen.

[3] Freund, J., *J. Exp. Med.*, 1931, **54**, 171.