obtained. It is conceivable that the presence or liberation of necrosin will explain, in part at least, the leukopenia frequently accompanying inflammatory processes. Finally, necrosin hastens markedly the rate of coagulation of blood *in vitro*. Whether this fact is due to thrombokinase associated with necrosin in the latter's present state of purification remains to be seen. Repeated injections of necrosin subcutaneously into rabbits induce the formation of precipitin antibodies to this substance. The implication of this finding remains to be determined.

In conclusion, the demonstration of an injury factor in the exudates of dogs and man, as brought down in the euglobulin fraction, and termed *necrosin* suggests further studies both in regard to the biological properties and the chemical purification of this substance. These investigations will form the subject of future communications.

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COLD AGGLUTININS (AUTOHEMAGGLUTININS) IN PRIMARY ATYPICAL PNEUMONIAS[1]

THREE cases have been encountered recently in which acute hemolytic anemia occurred in patients with the prevalent type of primary atypical pneumonia of unknown etiology. In two of these patients, difficulties in determining the blood group led to the discovery of a reversible autohemagglutinin (cold agglutinin). In certain other cases phlebothromboses and pulmonary emboli occurred during the latter part of the illness or during convalescence. Further study revealed that the great majority of the patients with primary atypical pneumonia tested this season showed cold agglutinins in dilutions of serum or plasma ranging from 1:10 to over 1:10,000 at 0° C.

This preliminary report is made because of the possibility that the development of cold agglutinins may serve as a criterion for segregating some of the prevalent cases of primary atypical pneumonia until definite etiological agents are established. The mechanism producing the autohemagglutinins is not known.

The maximum titer of cold agglutinins (in most cases 1:160 or 1:320 at 0° C.) was usually obtained at or near the end of the febrile period, and a rapid decline in titer occurred during convalescence. High titers were usually but not always obtained in the clinically severest cases. Essentially the same titers were obtained in serum from clotted blood and in plasma from oxalated samples. No hemagglutination was noted when the same samples were examined at 37° C. and the titer of cold agglutinins (tested at 0° C.) was unaffected by adsorption at 37° C. with erythrocytes of each of the four major blood groups.

A few of the patients in whom cold agglutinins were demonstrated also developed complement fixing antibodies for psittacosis and for the meningopneumonitis virus,[2] but these tests were negative in most instances.

A slight increase in the osmotic fragility of the erythrocytes was noted in some instances, but this was of a significant degree only in one of the patients who had acute hemolytic anemia. Tests were negative for autohemolysins, cold hemolysins (Donath-Landsteiner test), and the hemolysis test with acidified serum (Ham[3]).

Although the three patients with hemolytic anemia all had received sulfathiazole or sulfadiazine and many of the others in whom cold agglutinins were demonstrated were also treated with these drugs, a large percentage of those showing increased concentrations of autoagglutinins did not receive sulfonamide therapy throughout the course of their illness.

A number of samples of serum obtained from cases of primary atypical pneumonia of unknown etiology during the 1941–42 season failed to show cold agglutinins after six or more months of storage at 5° C. It is not known, however, whether or not this property was originally present in these samples or, as yet, whether the present sera will retain the property after 6 months under these conditions. Control sera obtained from cases of pneumococcus pneumonia and a variety of other febrile illnesses, most of them under treatment with sulfathiazole or sulfadiazine, were also examined for cold agglutinins with almost uniform absence of the agglutinins above a dilution of 1:4.

A brief review of the literature indicates that true reversible cold hemagglutinins have been demonstrated in significant titer only very rarely in cases of pneumonia. They have been noted in a few cases of various liver diseases or blood dyscrasias and, in a few instances, have been associated with peripheral vascular manifestations.[4,5] The only other infectious disease in which cold agglutinins have been found regularly is trypanosomiasis.[6]

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[2] These tests were carried out for us by Drs. Karl F. Meyer and Thomas Francis, Jr.

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