proved to be difficult because of the high anticomplementary effect of caseinogen but this phase of the problem is being studied.

Summary: Both native and phosphorized caseinogen proved to be precipitinogenic. The reactions occur in higher dilutions when the homologous proteins are employed. Antisera against the phosphorized caseinogen precipitate caseinogen and conversely antisera against caseinogen precipitate the phosphorized caseinogen. Phosphorylation of the caseinogen does not destroy its antigenic character.

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Intracutaneous Vaccination of Rabbits with Pneumococcus. I. Antibody Response.

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Suspensions of heat killed pneumococci were injected into the skin of rabbits at intervals of 7 days during a period of 10 to 14 weeks. The total amount of bacterial substance injected was equivalent to and often greater than that ordinarily employed in the routine immunization of rabbits by the intravenous method. Pneumococci of Types I and III and a degraded "R" strain derived from Type II were used. The sera of the treated rabbits were tested for the presence of agglutinins, precipitins, and protective antibodies. The serum obtained from 85% of the animals immunized intracutaneously with Type I pneumococcus failed to show the presence of any demonstrable type specific antibodies. Virulent cultures of Type I were not agglutinated, nor were solutions of the specific soluble substance from organisms of the homologous type precipitated by these sera even when used in high concentrations. Only rarely did the serum confer any passive protection upon mice infected with a virulent strain of Type I, and in these instances the protective titre was low. In only 15% of animals studied was there any serological evidence of type specific response to repeated intracutaneous inoculation of Type I organisms; in these instances the presence in the serum of specific agglutinins was demonstrable only in low dilutions varying from 1:1 to 1:20.

In terms of its capacity to stimulate the formation of type specific antibodies, Type III pneumococcus is at best a poor antigen. It was to be expected, therefore, that organisms of this type, when in-

jected intracutaneously into rabbits, would fail to elicit the type specific response. Such proved to be the case. None of the rabbits treated by the skin method developed demonstrable serum antibodies against Type III. The sera of these animals failed in every instance to react with the intact S cells or with the soluble specific substance of the homologous type; they failed also to protect mice against infection with minimal doses of a virulent strain of Type III pneumococcus.

Although repeated injection of type-specific pneumococci into the skin of rabbits failed in the majority of instances to stimulate the production of type-specific antibodies, the serum of all the rabbits so treated contained in high titre the species-specific, antiprotein antibodies which agglutinate the R cells derived from all types and precipitate solutions of nucleoprotein regardless of type derivation.

Immunization of animals with R forms of pneumococci evokes the formation of the antiprotein antibodies. The serum of animals containing only these antiprotein antibodies not only fails to agglutinate S cells of the homologous type but also fails to protect mice against infection with type specific strains. In the present experiments intracutaneous vaccination of rabbits with an R strain derived from Type II gave rise to the appearance in the serum of only the antiprotein antibodies. As far as the presence of these antibodies in the serum are concerned, the results of intracutaneous vaccination of rabbits with type specific pneumococci are similar to the results obtained by direct immunization with the R variants derived from type strains.

It is of interest to note that whereas the intravenous injection of Type I invariably evokes the production of type specific antibodies, the intracutaneous inoculation of the same organisms failed to stimulate the production of these antibodies in 85% of the rabbits studied. From these results it appears that after introduction into the animal body type specific pneumococci (S forms) under certain circumstances may lose more or less completely the property of eliciting the type specific antibodies, but still retain unimpaired the property of stimulating the antiprotein antibodies, and that under these conditions, they behave antigenically as do the degraded R cells and the protein extracts derived from them. These facts are significant in interpreting the phenomenon of dissociation of the complex antigen of pneumococcus in the animal body, and in determining the character of the immune response to bacterial antigens of this order.