Dr. Albert B. Sabin,
The Children's Hospital
Research Foundation,
Elland Ave. and Bethesda,
Cincinnati, Ohio.

Dear Albert:

I will be very glad to send you reprints on the ethylene oxide work as soon as they arrive.

I have not yet published, and do not yet have ready for publication, anything on the anti-streptococcal substance in milk, but hope to before the summer is over. Dr. Herman Rosenblum and I have been working on the problem for well over a year. It has been a good problem: full of interest and full of difficulties.

We first encountered the anti-streptococcal substance in milk in the course of a projected study of the growth of streptococci in naturally occurring biological fluids. Milk was used in the initial step of the study because of its cheapness and availability. The antibacterial activity of milk has been described and studied fitfully since the early days of bacteriology, perhaps the best work being that of Jones and Sims which they published in a series of articles in the J.E.M. about 1930. They showed that streptococci from bovine mastitis of the usual sort grew well in fresh, unboiled milk, whereas streptococci from bovine mastitis from a cow whose milk had caused an epidemic of scarlet fever were inhibited by fresh milk but grew well in milk which had been boiled. They called the antistreptococcal substance "lactenin" and studied it as well as could be done at the time.

After development of the ethylene-oxide sterilization technic it was possible to make a large scale study of the action of lactenin on many streptococcal strains.

We first investigated lactenin from the point of view of the susceptibility of streptococci of various serological groups to it. All Group A streptococci we have encountered have been sensitive. With rare
exceptions organisms belonging to Groups B, C, D and E have been resistant to it. Strains of Groups F, G, H, K and L vary; some being resistant and others, resembling in this respect Group A strains, being susceptible.

We have undertaken studies of the nature and mode of action of lactenin. This work is incomplete, but some insight has been gained into both phases of the problem. Although we have been unable to isolate lactenin in anything approaching pure form, we have achieved considerable concentration by enzymatic digestion and by precipitation of whey. Our preparations do not allow any definition of the substance in chemical terms, except, as was already known, that it is a large, non-dialyzable molecule. We have studied the effect of various agents on lactenin, and have shown that it is inactivated by reduction and by certain enzyme inhibitors. Oxidizing agents do not inactivate it, and indeed, in critical concentrations, oxidizing agents themselves have a lactenin-like effect on streptococci of the various groups. We believe that lactenin is concerned in some way with the oxidative metabolism of the streptococcal cell, either serving as an inhibitor (or competitor) of some process essential for those strains which are lactenin-sensitive; or that it acts as a hydrogen-acceptor, allowing to proceed an oxidative reaction which is harmful to the cell and which does not take place in the absence of a suitable hydrogen-acceptor. At the moment this is mostly speculation.

Lactenin in human milk is similar to lactenin in cow's milk in its inhibition of streptococci of the various streptococcal groups. We have not tested other species.

We have been unable to demonstrate in vivo protection by means of lactenin, using mice inoculated intraperitoneally with highly virulent, lactenin-sensitive Group A streptococci, and giving milk intraperitoneally or per os.

Studies are in progress of the antigenicity of lactenin.

I think the most important of our findings concerns the inactivation of lactenin by reducing agents. This explains why lactenin fails to prevent mastitis due to lactenin-sensitive Group A streptococci, since milk in the cow's udder is in the reduced state; it thus allows a more complete explanation of the events which occur in milk-borne streptococcal epidemics than it has hitherto been possible to offer.
I am naturally much interested in your finding of anti-viral activity in milk, and wonder whether it may be due to lactenin or to an entirely different substance. If there is any aspect of the work we have in progress which particularly interests you, I would be pleased to elaborate on it.

Incidentally, you will probably want to investigate the relationship of your anti-viral principle to xanthine oxidase (shown to be antistreptococcal by Green and Pauli, but, as we have shown, distinct from lactenin) and to lysozyme as well as to nicin, which might possibly be in milk, although probably not as you collect and treat it.

With best wishes,

Sincerely yours,

Armine T. Wilson, M.D.