

IMMUNE MILK IN THE TREATMENT OF HAY FEVER

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IT IS WELL KNOWN that the human infant receives, through the placenta, antibodies which confer protection against various infectious diseases for which the mother has acquired immunity. The young of a number of other species, including domestic cattle, are born with little or no gamma globulin and without passive immunity. Calves acquire immunity from the mother cow through the colostrum, a special type of milk, containing a high percentage of gamma globulin which is secreted during the first week after delivery.

Extensive studies of bovine colostrum by Peterson and Campbell¹ have shown that it is rich in various antibodies. Their studies indicate that the mammary gland of the cow contains many plasma cells and may act as an organ of antibody formation. Injection of various bacterial antigens, especially species of *Salmonella*, into the udders during the dry period shortly before the birth of a calf produced agglutinin titers in the colostrum as high as 1:100,000 or 100 times that of the serum of the same cow. When the secretion of colostrum gave way to that of ordinary milk, the titer fell to 1:1,000 but, considering the fact that several quarts were produced daily, the total output of antibodies was tremendous.

In an experiment designed to indicate whether human beings could absorb these antibodies, five adult volunteers whose sera showed no agglutinins for *Salmonella pullorum* drank one quart of milk with an agglutinin titer of 1:1,000 daily for a week. At the end of this period the sera of the volunteers showed titers as high as 1:10.¹

During 1955 at the University of Minnesota, cows were similarly injected with ragweed pollen and the colostrum was used by Blumenthal² to treat patients with hay fever. The results were considered encouraging and, in 1956, the Borden Company injected a series of cows with grass and ragweed pollens and collected colostrum for clinical trials. Some of their material was made available to the allergy clinics of the Roosevelt and Presbyterian Hospitals. Since the material was received at the onset of the ragweed pollen season, the clinical trials were necessarily carried out before any immunologic studies of the colostrum were made. This chance ensured that the therapeutic tests were not influenced by preconceived bias.

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PREPARATION OF COLOSTRUM

The cows were given 3 weekly injections into each udder during the dry period just before calving. Each injection contained low ragweed pollen, 9.5 mg.; giant ragweed pollen, 9.5 mg.; chenopod, cocklebur, and amaranth pollens, 2 mg. each; and grass pollens, which were not included in our study. The amounts chosen and the use of a mixture of pollen antigens were based on the results obtained by Peterson and Campbell with bacterial antigens. These had shown that the response to one antigen was not affected by others injected simultaneously.

During the first week after calving, colostrum was collected and processed into dried skimmed milk by the usual commercial methods which involve heating to 160°-180° F. (71°-82° C.) for a half hour. The resulting powder was similar in appearance and taste to commercial dried skimmed milk* from untreated cows which was used as a control for the dried colostrum. Both powders were packed in plain envelopes containing the equivalent of a quart of fluid milk and marked only with a lot number, the significance of which was not revealed to the clinic physicians until these tests were completed.

CLINICAL TRIALS

Patients with typical active ragweed hay fever were given one package of the powder a day, equivalent to a quart of milk. All patients included in the series took this amount for at least a week and the majority of them for two or more weeks during the season. Alternate patients were given the immunized and control milks. Each patient was asked to keep a daily written record of the severity of hay fever symptoms. Those who had previously received antihistamine drugs were allowed to use them as necessary but were asked to keep a daily record of the number of pills taken.

The group completing the test included thirty-three patients who had received preseasonal or perennial injections of pollen extract but who were having moderate or severe hay fever at the time they were added to the series, and thirteen patients who had not received previous specific treatment; a total of forty-six patients, twenty-six of whom received the immunized colostrum and twenty who received normal skimmed milk. Many patients were skin tested with ragweed at the start of the milk treatment and again when it was discontinued. Blood for serologic studies was taken from those who had not received pollen injections at the same time.

The results produced by the two batches of material were so similar that, at the end of the test, none of the physicians were able to distinguish which lot was the immunized and which the control milk. On the basis of the records kept, the degree of benefit to each patient was classified on a basis of 0 for no benefit, 1 for slight improvement, and 2 for moderate relief. None reported marked or complete relief. When the scores were totalled, the results

*Starlac, manufactured by the Borden Company, New York, N. Y.

were essentially the same in the groups receiving the immunized milk and the control milk. Actually the average relief for the control group (0.77) was slightly higher than that for the group receiving the treated milk (0.69), indicating that ordinary Starlac was just as effective as the immunized colostrum.

Like many other new medications, this preparation produced a significant number of side effects. Although patients with known allergy or strong aversion to milk were excluded from the series, four patients, or 15 per cent, of the twenty-six taking the immunized colostrum had untoward effects such as diarrhea, abdominal pain, indigestion, and hives. The incidence of side effects in the control group was also 15 per cent or three in twenty patients.

The skin tests with ragweed pollen extract before and after the treatment showed no significant changes.

IMMUNOLOGIC STUDIES

Sera taken before and after at least two weeks of the milk treatment from four patients who had never received pollen injections were tested for blocking antibodies by the passive transfer neutralization method of Loveless.² None showed any evidence of blocking activity. Sera from four patients in the control group were similarly tested, also with entirely negative results.

In order to test the colostrum itself for antibodies, the whey fraction was separated from it. This showed no evidence of precipitins for low ragweed pollen extract (80,000 P.N. units per milliliter) in ring tests or the Oudin method.

The whey fraction from the colostrum of the injected cows and that from skimmed milk of normal cows were compared in passive transfer neutralization tests for blocking antibody using the same methods² employed for measuring blocking antibody in serum. No blocking antibody was demonstrable in the undiluted whey.

It was thought that the failure to demonstrate antibodies in the colostrum of the treated cows might be due to (1) the use of so many pollens for immunization that the doses of ragweed, the only pollen considered in our study, were inadequate, or (2) that the degree of heat involved in drying the colostrum might have destroyed antibody. During the following spring an attempt was made to avoid these difficulties. Three groups of three cows each were injected during the dry period before calving with low ragweed pollen in amounts comparable to the total of all pollens used in the 1956 series. The udders of three cows were injected with whole ragweed pollen grains, those of three with saline ragweed extract, and those of three others with a glycerinated ragweed extract (52,000 P.N. units per milliliter). The technique and timing of the injections was as described previously. Colostrum from each of these nine cows and from an untreated control cow was collected on the first and fifth days after freshening, quick-frozen in one quart containers, and kept frozen until testing.*

*Courtesy of Protective Foods Corporation, Minneapolis, Minn., and the Borden Company.

Each of these 20 samples of colostrum was tested for blocking antibody by the passive transfer neutralization method previously described. None showed evidence of activity, and no clinical studies were undertaken with these preparations.

DISCUSSION

While both the clinical and laboratory results were clearly negative, and those of the 1956 studies were reported at the meeting of the American Academy of Allergy in February, 1957, publication was delayed at the time in hopes that more effective methods of immunizing the cows might be developed. Since 1957 the authors have had no opportunity for further study of the problem and no immunologic evidence of an improved product has been offered by others. Meanwhile, without the publication of any controlled clinical studies, the use of "protective milk" for the treatment of hay fever has been widely exploited commercially and publicized in popular magazines. Since this promotion has attracted the attention and raised the hopes of many people suffering from allergic diseases, publication of these negative results of controlled studies now seems timely.

SUMMARY

Colostrum collected from cows after injections of ragweed pollen into the udders showed no evidence of precipitating or blocking antibodies for ragweed pollen antigens. A series of twenty-six ragweed hay fever patients treated with the equivalent of a quart of such colostrum daily showed no greater benefits than twenty controls taking an equal amount of commercial skimmed milk.

REFERENCES

1. Peterson, W. E., and Campbell, B.: Use of Protective Principles in Milk and Colostrum in Prevention of Disease in Man and Animals, *J. Lancet* 75: 494, 1955.
2. Loveless, M. H.: Immunological Studies in Pollinosis. I. The Presence of Two Antibodies Related to the Same Pollen-Antigen in the Serum of Treated Hay Fever Patients, *J. Immunol.* 38: 25, 1940.
3. Blumenthal, J. S.: Unpublished results.