

Serum Cholesterol Studies in Infants

A Comparison of Infants Fed Breast Milk, Evaporated Milk and Prepared Milk Formulas

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THE relationship of lipid metabolism and serum cholesterol levels in atherosclerosis is still not resolved. However, it has been shown in adults that unsaturated fats added to the diet in sufficient proportions will lower serum cholesterol levels.

Man is presumably an atherogenic animal. Dr. Holman has shown that atherogenesis may occur very early in childhood. If the serum cholesterol level is a true barometer of the degree of susceptibility to atherosclerotic changes, then the area of infancy and childhood deserves intensive study. Present day efforts are concerned with reversing the atherosclerotic changes which occur in adults and with averting sequelae. Preventive medicine, however, would be better served if alterations in etiologic factors were attempted during the formative years.

It is quite possible that many nutritional aspects of infancy and childhood play prominent roles in the pathophysiology of adulthood, not only by virtue of habits learned but also through metabolic alterations which are maintained.

Since 1957, Drs. L. B. Slobody, Alta Goalwin and I, as well as other members of our department, have conducted intensive research on the

relationship of serum lipid levels to infant feeding procedures. At birth the mean serum cholesterol level is 75 mg. per 100 ml. and rises rapidly during the first four months of life when it approximates adult levels. Infants fed a specially prepared corn oil replacement formula manifest a slower rise and a lesser peak of serum cholesterol.^{1,2} The clinical significance of these findings is unclear. It would be unwise to infer a relationship between these laboratory findings and the pathogenesis of aortic and coronary atheromatosis.

Our present study is an extension of previous experimental procedures and includes a comparison of serum cholesterol levels in breast-fed infants, infants fed a typical evaporated milk formula and infants fed an isocalorie formula prepared from milk and containing corn oil as a replacement for butter fat. Four groups of normal infants were evaluated over a sixteen-week period. Group I was comprised of forty-eight infants fed an evaporated milk formula with fruits as the only supplement until the twelfth week of life, after which no dietary restrictions were imposed. In group II, twenty-eight infants received a prepared milk high in unsaturated fats and fruit supplement until the twelfth week after which a free diet was permitted. Six infants in group III were fed similarly but the original diet was maintained for sixteen weeks. Group IV consisted of six breast-fed infants observed for twelve weeks.

Infants in group I manifested the usual rapid rise in serum cholesterol level, with a mean value 187 mg. per 100 ml. at twelve weeks of age. No further increase in serum cholesterol level was produced by supplementation with cereals, vegetables, meat and other dairy

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products at twelve weeks. Infants in group II had a significantly lower mean serum cholesterol level of 127 mg. per 100 ml. Shortly after cereal, meat and vegetable supplementation after twelve weeks, the serum cholesterol level rose to 172 mg. per 100 ml.

This precipitous rise in serum cholesterol level did not occur after the twelfth week in infants in group III who did not receive the supplementary food offered to those in group II. Infants in group IV who were breast fed showed a serum cholesterol pattern remarkably similar to those in group I. There was a rapid rise in serum cholesterol.

REFERENCES

1. POMERANZE, J., GOALWIN, A., and SLOBODY, L. B. Effect of a corn oil-evaporated milk mixture on serum cholesterol levels in infancy. *Am. J. Dis. Child.*, 95: 622, 1958.
2. POMERANZE, J., GOALWIN, A., and SLOBODY, L. B., Influence of diets high in essential fat. (Abstract.) *Am. J. Dis. Child.*, 98: 498, 1959.

DISCUSSION

DR. ALASTAIR C. FRAZER (*Birmingham, England*): I was extremely interested in Dr. Holman's observation on children with pancreatic fibrosis. While I am sure he is right, that the metabolic activity of the arterial wall is a very important matter, it is, of course, interesting that the main change, so far as blood lipid composition is concerned in children with fibrocystic disease, is the almost complete absence of particulate fat. The ordinary alimentary hyperlipemia is commonly absent in children who have no pancreatic enzymes. All patients with fibrocystic disease, however, do not necessarily have complete absence of pancreatic enzymes.

It might be interesting to know whether those who show some changes in the lipid content of the blood vessel wall are those who, in fact, do not have a complete absence of pancreatic enzymes and are, perhaps, showing some abnormalities of lipid metabolism.

DR. HOLMAN: The best answer I can give to your question is that the majority of the patients with fibrocystic disease which we studied were receiving pancreatin therapy; with this they absorb up to 75 per cent of ingested lipid.

We were concerned at one point with the possibility that chronic infection—which these patients always show—might be an important factor. However, patients with other types of chronic infection do not show such a low incidence of aortic involvement.

To me, an attractive possibility is that the progressive segmental occlusion of the pancreatic ducts in this disease might lead to damming back of lipase and the es-

cape of lipase into the blood, where it might facilitate removal of lipid from the arterial wall. We do not, however, have any direct evidence to support this hypothesis.

DR. STANLEY M. GARN (*Yellow Springs, Ohio*): Dr. Holman, would you comment on sex differences in your data? I remember about ten years ago that Dr. Dock reported an almost male-specific incidence of early plaque information.

DR. RUSSELL L. HOLMAN (*New Orleans, Louisiana*): At that particular time, Dr. Dock was describing the microscopic intimal thickenings in the coronary arteries in infants. Our studies are on the lipid-rich lesions, studied on the basis of gross appearance of the aorta. With our methods, we found that the aorta of the white female was least involved with fatty streaking, the Negro male most involved, and the Negro female and white male were intermediates. Thus, there is a slight difference in favor of males, but nowhere was this as great as Dr. Dock found in the coronary arteries.

DR. S. E. SNYDERMAN (*New York, New York*): I would like to add another factor which may influence serum cholesterol levels in infants. In our studies on amino acid requirements of infants we use a complete synthetic diet in which a mixture of eighteen l-amino acids is the source of nitrogen, and corn oil provides the fat. Omission of a single essential amino acid very frequently results in a marked reduction of the cholesterol level, from a control range of 135 to 150 to below 100 mg. per 100 ml. When the missing amino acid is once more included in the diet, the cholesterol immediately returns to normal control levels. These studies have been carried out in infants under four months of age.

DR. SARETT: I would like to supplement the information that Dr. Pomeranze gave on the serum cholesterol levels of infants. In other unpublished experiments, it has been found that the cholesterol levels are high in breast-fed infants and in those fed evaporated milk diets, in contrast to lower levels found when unsaturated fats are substituted for butter-fat in milk diets.

DR. CALVIN WOODRUFF (*Nashville, Tennessee*): We have some preliminary observations also on serum cholesterol levels in breast-fed infants and evaporated milk-fed infants. By the age of six weeks, the cholesterol levels in the breast-fed infants are slightly higher than in the infants fed evaporated milk, with average levels of 161 mg. per 100 ml. for breast-fed infants and 154 mg. per 100 ml. for evaporated milk-fed infants. This difference is found only in the female infants.

Dr. Sam Fomon* has a paper in press, using similar feedings and with essentially similar results. In our infants, the dienoic acid (linoleic acid) level in the blood is twice as high in the breast-fed infants as it is in the artificially-fed infants.

It would appear, at least in the six-week age group, that the correlation between low cholesterol levels and high dienoic acid levels which occur in adults may not

* *J. Dis. Child.*, 99: 27, 1960.

exist. The breast-fed infants at six weeks have much higher dienoic acid concentrations than evaporated milk-fed infants but they do not have lower cholesterol concentrations. This brings up the question that Dr. Pomeranze referred to, namely, that in breast-fed infants where there are qualitative and quantitative changes in the fat eaten by the mother, to what extent can one use such infants as the desirable norm?

DR. L. E. HOLT, JR. (*New York, New York*): I would like to put in a word of caution about breast milk fat in this connection. Nobody has called attention to the fact that breast milk fat varies enormously with the diet of the mother. This was pointed out by German pediatricians more than fifty years ago and has been verified by a number of other workers since then.

If one feeds the mother a diet high in unsaturated fat, her milk fat shows this very promptly in a matter of hours.

DR. E. H. AHRENS, JR. (*New York, New York*): Dr. Holman, in regard to fatty streaks you have described an increase in incidence and severity which is directly proportional to age in years, while for fibrous plaques there is a sudden rise in incidence after twenty-five to thirty years of age. Do you not think that this argues against the concept that fatty streaks are the precursors of fibrous plaques? What direct evidence can you cite which shows that fibrous plaques are formed from fatty

streaks? It seems to me this point is central in the disagreement between your concept of atherogenesis and that of Dr. Duguid and the English school of pathologists.

DR. HOLMAN: I would like to disregard these fatty streaks completely and say they have nothing to do with atherosclerosis. It would simplify the whole problem. But you cannot look at these blood vessels day after day and believe that. All sorts of transitional stages are seen. We have never found a fibrous plaque without a fatty streak. The question hinges on the fate of a fatty streak. Our studies indicate that by age forty, roughly one-third of the fatty streak has disappeared, one-third of it remains status quo, and one-third of it has progressed to a fibrous plaque.

We are acutely aware of the problem you raised, but there is just too much evidence of a real relationship between the fatty streak and the fibrous plaque.

To discuss briefly the second part of your question, namely, the question of fibrin incrustation as the mechanism for fibrous plaque formation: I mentioned that fibrin incrustation was one of the mechanisms by which fatty streak could become a fibrous plaque. We get the impression, however, that most of the transformation of fatty streak to fibrous plaque is due to reactive fibrosis, and I believe that this is the most important process involved.

