Lessons from the story of n–3 fatty acids¹,²

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ABSTRACT The discovery of the effects of n–3 fatty acids came about as a result of contacts between scientists in different countries and disciplines who followed up some unexpected observations. There are probably other fields of research in which discoveries of similar importance await the application of lessons from this story. Am J Clin Nutr 2000;71(suppl):397S–8S.

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The growing body of evidence on the effects of n–3 fatty acids makes it increasingly clear that fish is a much more important food than had previously been supposed. Fish played an important part in the fortunes of the seafaring nations. During the Middle Ages the wealth and power of the Hanseatic League rested on its domination of the North Sea herring fishery. In 1486 the Dutchman Willem Beukels discovered that fish could be preserved for long periods if they were gutted as soon as they were caught and immediately pickled in brine. This discovery led to the rise of the Dutch herring industry and overseas trade and, in consequence, the emergence of the Netherlands as a major maritime power. The English were drawn to North America because of the cod they found off the coasts of Newfoundland and Labrador.

International harmony has not uniformly characterized matters relating to fish. In 1429 the Battle of the Herrings occurred when the French attacked a convoy of herrings bound for the English army at Rouen. In the seventeenth century, rivalry over fishing rights led to 3 Dutch wars (involving England, France, and the Netherlands in different combinations) and a serious attack on the Dutch fishing fleet by France in 1703. The 20th century’s “cod wars” and other fishing disputes have been relatively mild affairs. The frequency of these disputes may explain why Switzerland is the only European country with which Britain has never been involved in a war on either side.

By contrast, the discovery of the benefits of marine fatty acids resulted from the collaboration of workers in many different countries. In 1929 the essential fatty acids were discovered by Evans and Burr in the United States. The British physiologist Hugh Sinclair visited Evans in 1937 and became interested in the possibility that deficiency in some fatty acids might account for the rise in Western diseases such as ischemic heart disease. In 1944 he undertook his first visit to Eskimos, where he noted their freedom from any trace of arcus senilis and their liability to epistaxis. His views were set out in a long letter to Lancet in 1956, “Deficiency of essential fatty acids and atherosclerosis, etcetera” (1). Danish investigators Bang and Dyerberg (2, 3) investigated the rarity of ischemic heart disease in Greenland Eskimos and attributed this to their marine diet. They showed the distinctive plasma lipid pattern and hemostatic function of Greenland Eskimos, consistent with their low incidence of myocardial infarction. They also drew attention to the rapid fall in ischemic heart disease incidence and mortality in Norway that occurred in parallel with dietary changes (ie, more fish, less meat) consequent to German invasion in 1940 (4). Studies of Japanese populations with different intakes of fish confirmed the findings in Eskimos (5).

There are several lessons from this story. From them, I propose that the following suggestions would be helpful in other fields of research:

1) Seek out populations that have unusual disease patterns and unusual diets and visit them. If Sinclair, Bang, and Dyerberg had not taken the trouble to investigate the Eskimos at first hand we would probably be quite unaware of the relevance of n–3 fatty acids to heart disease. There must be other populations among whom equally valuable discoveries could be made.

2) Look out for natural experiments. It is not feasible to arrange for populations to change their eating habits drastically, but sometimes the circumstances impose such a change (as happened in Norway during World War II). Migrant groups have been studied to a limited extent, but more useful work might yet be done in these populations, studying both long-term and short-term migrants. There are many people who spend part of the year in one country and part in another, either because of their work or to escape from cold weather, whose diets change in a predictable manner.

3) In another type of opportunistic research, use data that were originally collected for a different purpose. A good example is the Zutphen study: when the original dietary information was recorded in 1960 there was no particular interest in the cardioprotective effect of fish but the cohort was available for testing that hypothesis (6). Similar cohort studies were then examined in the same way. There must be other bodies of data that could be put to equally good use.

4) Look out for observations that do not fit in with the received wisdom. Sinclair’s 1956 letter to Lancet drew attention to the fact that the evidence from Eskimos conflicted with the

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accepted view that dietary fat of whatever kind was related to atheroma. He ended the first paragraph of this long letter with the words “Your readers with stereotyped minds should stop reading at this point” (1). He drew attention to the word “etcetera” in the letter’s title and pointed out that there is probably a range of diseases that are affected by the essential fatty acids. Observations that do not accord with the present state of knowledge are likely to be particularly illuminating if they are properly investigated.

5) Look outside your field of research for ideas. The story of n–3 fatty acids shows the value of collaboration among workers in laboratories, hospital, and the community. The health effects of these fatty acids would never have been discovered by studies confined to any one of these areas. Far too many research workers have little or no contact with scientific disciplines other than their own. It is most important for clinicians, biochemists, physiologists, and epidemiologists to meet together and exchange ideas.

6) If you can, be a subject in your own study. You will gain valuable insights and be confident about the compliance of at least one subject. Sinclair put himself on a diet of seal meat and fish for 100 d in 1976 and achieved record bleeding times as a result.

7) Perhaps the most obvious lesson of all is that research can be enjoyable. It leads to a broadening of the mind as contacts are made with a wide variety of people in different scientific disciplines, and a variety of places and cultures are visited.

REFERENCES