Diet and Prevention of Coronary Heart Disease and Cancer

Editors
Bo Hallgren
Östen Levin
Stephan Rössner
Bengt Vessby

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Fourth International Berzelius Symposium
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Editors

Bo Hallgren, M.D., Ph.D.
Professor
Swedish Nutrition Foundation
Göteborg, Sweden

Östen Levin, Ph.D.
Associate Professor
Margarinbolaget
Stockholm, Sweden

Stephen Rössner, M.D., Ph.D
Associate Professor
King Gustav V Reasearch Institute
Stockholm, Sweden

Bengt Vessby, M.D., Ph.D.
Associate Professor
Department of Geriatrics
Kungsgärdets Hospital
Uppsala, Sweden

David H. Ingvar, M.D., Ph.D.
Professor
Department of Clinical Neurophysiology
University Hospital
Lund, Sweden

Bengt Pernow, M.D., Ph.D.
Professor
Department of Clinical Physiology
Karolinska Hospital
Stockholm, Sweden

Lars Åke Pellborn, B.A.
Executive Director
The Swedish Society of Medicine
Stockholm, Sweden

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Preface

Cancer and coronary heart disease constitute by far the two most common causes of death in the western world. Both disease groups are highly heterogeneous, and a number of factors in the human environment may eventually lead to clinical manifestations. Diet is one such factor. During recent years, clinical, laboratory, and epidemiological research have considerably increased our knowledge of the relationship between our diet and these major diseases. These scientific achievements have implications for the development of national dietary recommendations. Sweden was one of the first countries to issue such recommendations; however, with increased research data available, such recommendations need continual scrutiny and reevaluation. *Diet and Prevention of Coronary Heart Disease and Cancer* gives some of the world experts on these topics an opportunity to present recent results and to challenge views.

THE EDITORS

Acknowledgments

In 1983, the Swedish Society of Medicine celebrated its 175th anniversary. This event inspired a fund drive to enable the society to hold international scientific symposia on important sociomedical problems. The society received many generous and substantial contributions to its 175th anniversary fund. The symposia were named after the famous Swedish biochemist, Jöns Jakob Berzelius (1779–1848), who was one of the founders of our society. This symposium on diet and prevention of coronary heart disease and cancer is the fourth Berzelius Symposium. The first dealt with drug effects on the brain, the second with brain injuries due to boxing, and the third with alcohol and the developing brain.

The symposium on which this volume is based was made possible by a special and very generous grant from the Swedish Nutrition Foundation. On behalf of the Swedish Society of Medicine, sincere thanks are expressed to the Foundation for this aid.

The society would also especially like to thank Professor Bo Hallgren who carried the great burden of organizing the meeting. The chancellary and technical staff, especially Mrs. May Hedqvist of the Society and Mrs. Kerstin Wennberg of the Swedish Nutrition Foundation, are thanked for their help with all the arrangements.

This volume is also included as No. XVI in the Series of Symposia of the Swedish Nutrition Foundation.

Foreword

This volume summarizes recent results within a number of relevant fields, from epidemiology to cell biology, concerning the relation between diet and cancer and coronary heart disease. Effects of dietary manipulations from experiments in laboratory animals to extensive intervention programs in large geographical areas are described.

In this presentation Richard Peto, Oxford, England, indicates that there are no data speaking for a general increase in the incidence of cancer, although there is an increase in the incidence of lung cancer. It is difficult to estimate to what degree cancer is associated with dietary factors. Figures varying between 10 and 70% have been published. Peto considers a mean value of 35% as likely.

Lars Wilhelmsen, Göteborg, Sweden, stresses that it is necessary to change the dietary habits of the whole population if one aims to reduce the incidence of coronary heart disease. The present situation is particularly alarming in Sweden where, in contrast to several other countries, there has been a slight increase in the incidence of coronary heart disease over the last few years.

Bruce N. Ames, Berkeley, California, reviews the future development of mutagen tests. Damage to DNA is likely to be a major cause of cancer, genetic birth defect, aging, and heart disease. Ames presents a simple method for identifying DNA-damaging agents by analyzing and quantifying DNA fragments in urine of subjects exposed to mutagens.

Ole Møller Jensen and Marianne Ewertz from the Danish Cancer Registry discuss the relationship between dietary protein and fat and cancer and underline that such relationships may not be causal. Epidemiological correlations between a high intake of dietary fat and protein and the frequency of breast and colon cancer possibly could be explained by the fact that fat and protein exert a promoting effect on tumors under growth, but there is no clear hypothesis that can explain the effects.

The possible effects of dietary fibers on colon cancer are analyzed by Michael J. Hill, Bacterial Metabolism Research Laboratories in Salisbury, England, who scrutinizes the present data suggesting that a high fiber consumption could be protective against colon rectal cancer. Hill does not find it indicated to increase the dietary fiber content in the diet with the argument that colon cancer affects a minor proportion of the population, and dietary changes that can adversely affect the remaining population are not warranted.

Diet and Coronary Heart Disease

The second part of this book concerns dietary factors and coronary heart disease. The relationship between nutrition and atherosclerosis was heavily

debated in 1984 when a number of important research projects, such as the Lipid Research Clinic's Coronary Primary Prevention Trial, indicated that reduction of serum cholesterol will indeed result in a reduced incidence of atherosclerotic manifestation. In contrast to this view, E. H. Ahrens, Jr., Rockefeller University, New York, vigorously indicates that pressures to publish dietary recommendations for use by the general public must be strongly resisted. In reviewing the recent trials, Ahrens concludes that only those members of the general population who are at highest risk for coronary heart disease should be advised to take appropriate action to reduce the risks.

Daniel Steinberg, San Diego, California, concludes that many different lines of evidence, ranging from studies in experimental animals to direct intervention studies in man, support the causative relationship between certain forms of hyperlipoproteinemia and premature arteriosclerosis. Steinberg indicates that it is now clear that the endothelial injury hypothesis and the lipid infiltration hypothesis are by no means mutually exclusive but, instead, can be regarded as two aspects of a unified hypothesis. Steinberg also notes the negative correlation between high density lipoprotein (HDL) levels and risk of atherosclerosis, but concludes that we still do not have adequate experimental or clinical studies to indict HDL levels as directly atherogenic.

In the United States, William E. Connor and Sonja L. Connor, Oregon Health Science University, Portland, Oregon, discuss the homeostasis the body attempts to maintain during ingestion of increasing amounts of dietary cholesterol. A variation in dietary cholesterol between 100 and 500 mg/day will result in varying concentrations in serum cholesterol. Above a certain ceiling, there is no further increase of low density lipoproteins (LDL) or total plasma cholesterol concentrations. The Connors also discuss the importance of the omega-3 fatty acids, found in particular in marine foods. They argue that these fatty acids, as well as linoleic and linolenic acids, should be regarded as essential fatty acids, in particular because of their role as prostaglandin precursors.

Michael A. Crawford, Nuffield Laboratory of Comparative Medicine, London, England, indicates that the food structure of today is greatly different from what man consumed 150 generations ago. Biologically, man is still a wild animal: The majority of wild foods have a relatively low content of saturated fats; their lipids are mainly membrane constituents and are therefore rich in essential polyunsaturated fatty acids.

Intervention Studies

Pekka Puska et al., National Public Health Institute, Helsinki, Finland, describe the North Karelia project where a multifactorial program was introduced in a population with a high incidence of coronary heart disease in an attempt to reduce serum cholesterol concentrations, smoking, and blood pressure. This intervention program has indeed resulted in sustained dietary changes, reduced

serum lipid levels, smoking, and systolic blood pressure, as well as a reduction of coronary heart disease, which was more pronounced in North Karelia than in the rest of Finland during the corresponding time period.

Ingvar Hjermann, Ullevål Hospital, Oslo, Norway, presents the Oslo Heart Study, a bifactorial dietary and antismoking study of healthy men between 40 and 50 years of age. A 47% reduction of coronary heart disease was found in the intervention group, compared to the control group, an effect that was primarily due to the dietary intervention.

The Lipid Research Clinic's Coronary Primary Prevention Trial testing the hypothesis that lowering plasma cholesterol concentration in hypercholesterolemic men would reduce the risk of coronary heart disease is presented by William Insull, Jr., Houston, Texas. With cholestyramine, an average plasma cholesterol reduction of 8.5%, compared to the placebo group, was obtained. This resulted in a 19% reduction in risk of definite coronary heart disease death or definite nonfatal myocardial infarction or both.

Conclusion

The relationship between diet and cancer and coronary heart disease is complex and in some respects still controversial. The discussion during the meeting on which this volume is based demonstrated the difficulties in conveying to the public one single and simplified message; however, there was agreement that the present Swedish dietary recommendations (not more than 35 energy % fat with a P/S ratio of at least 0.5) are adequate. The relationship between diet and cancer has as yet mainly been identified by epidemiological methods, whereas the relationship between diet and coronary heart disease is better defined and considered to be causal. There was agreement, however, that a change in diet of the same type as suggested to prevent coronary heart disease is without any risk, and has possible meaning with regard to the risk of breast and colon cancer.

STEPHAN RÖSSNER
Editor
The Swedish Society of Medicine

Contributors

E. H. Ahrens, Jr.
The Rockefeller University
New York, New York 10021

Bruce N. Ames
Department of Biochemistry
University of California
Berkeley, California 94020

J. E. Bakke
Metabolism and Radiation Research Laboratory
State University Station
Agricultural Research Service
U.S. Department of Agriculture
Fargo, North Dakota 58105

Åke Bruce
Swedish Food Administration
Box 622
S-751 26 Uppsala, Sweden

Sonja L. Connor
The Section of Clinical Nutrition and Lipid Metabolism
Department of Medicine
The Oregon Health Sciences University
3181 S.W. Sam Jackson Park Road
Portland, Oregon 97201

William E. Connor
The Section of Clinical Nutrition and Lipid Metabolism
Department of Medicine
The Oregon Health Sciences University
3181 S.W. Sam Jackson Park Road
Portland, Oregon 97201

Michael A. Crawford
Nuffield Laboratory of Comparative Medicine
The Zoological Society of London
Regent's Park
London NW1 4RY, England

Christian Ehnholm
Department of Epidemiology
National Public Health Institute
SF-00280 Helsinki, Finland
Mannerheimintie 166

Marianne Ewertz
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
Landskronagade 66
DK-2100 Copenhagen, Denmark

J.-Å. Gustafsson
Department of Medical Nutrition
Karolinska Institute
Huddinge University Hospital
S-141 86 Huddinge, Sweden

Michael J. Hill
Bacterial Metabolism Research Laboratory
PHLS-CAMR
Porton Down
Salisbury, Wiltshire, SP4 OJG England

Ingvar Hjermann
Oslo Study
Ullevaal Hospital
Oslo 1, Norway

Jussi K. Huttunen
Department of Epidemiology
National Public Health Institute
Mannerheimintie 166
SF-00280 Helsinki, Finland

William Insull, Jr.
Department of Medicine
Baylor College of Medicine
The Methodist Hospital
6535 Fannin
Houston, Texas 77030

Ole Møller Jensen
Danish Cancer Registry
Institute of Cancer Epidemiology
Danish Cancer Society
Landskronagade 66
DK-2100 Copenhagen, Denmark

Martijn B. Katan
Department of Human Nutrition
Agricultural University
De Dreijen 12
6703 BC Wageningen, The Netherlands

Aulikki Nissinen
Department of Epidemiology
National Public Health Institute
Mannerheimintie 166
SF-00280 Helsinki, Finland

Richard Peto
Nuffield Department of Clinical Medicine
Cancer Studies Unit
Radcliffe Infirmary
Oxford OX2 6HE, England

Pirjo Pietinen
Department of Epidemiology
National Public Health Institute
Mannerheimintie 166
SF-00280 Helsinki, Finland

Pekka Puska
Department of Epidemiology
National Public Health Institute
Mannerheimintie 166
SF-00280 Helsinki, Finland

Jukka T. Salonen
University of Kuopio
P.O. Box 6
SF-70211 Kuopio, Finland

Daniel Steinberg
Division of Endocrinology and Metabolism
Department of Medicine
University of California, San Diego
La Jolla, California 92093

Jaakko Tuomilehto
Department of Epidemiology
National Public Health Institute
Mannerheimintie 166
SF-00280 Helsinki, Finland

Jarmo Virtamo
National Public Health Institute
Mannerheimintie 166
SF-00280 Helsinki, Finland

Lars Wilhelmsen
Department of Medicine
Östra Hospital
S-416 85 Göteborg, Sweden

Contents

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Cancer Around the World: Evidence for Avoidability

Richard Peto

Nuffield Department of Clinical Medicine, Cancer Studies Unit, Radcliffe Infirmary, Oxford OX2 6HE, England

The fundamental evidence that cancer is avoidable comes from the comparison of different human populations.

We can compare people at different times; we can compare the past with the present. We can compare people in different countries with each other or within one country; we can compare people who live in different areas with each other and within one area. We can compare different individuals with each other; we can compare the rich with the poor. We can compare the parous with the nonparous. We can look at smoking, sexual activity, and various personal characteristics.

Within one area, we do not get such large contrasts of behavior as when we compare, e.g., the rich world with the poor. It is more difficult to pick up differences within one area than it is to pick up differences between different countries. Conversely, however, it is often possible to make much more reliable inferences by the comparison of one time with another, of different parts of one country, e.g., the towns with the surrounding countryside. However, comparisons could generate a lot of wrong conclusions if they are used incautiously.

DIFFERENCES IN CANCER INCIDENCE BETWEEN COUNTRIES AND CHANGES IN INCIDENCE ON MIGRATION

There is a relationship between colon cancer incidence and meat consumption in different countries (Fig. 1): New Zealand, United States, and Canada have high rates for colon cancer; Japan and Finland have low rates. The rates were age-standardized in that people of similar ages in different countries were compared.

Such a graph could just as well have been plotted against fat consumption, sugar consumption, number of telephones, and a variety of other things. We do not really know if meat consumption is particularly hazardous. All that the graph is intended to suggest is that there are large differences between one country and

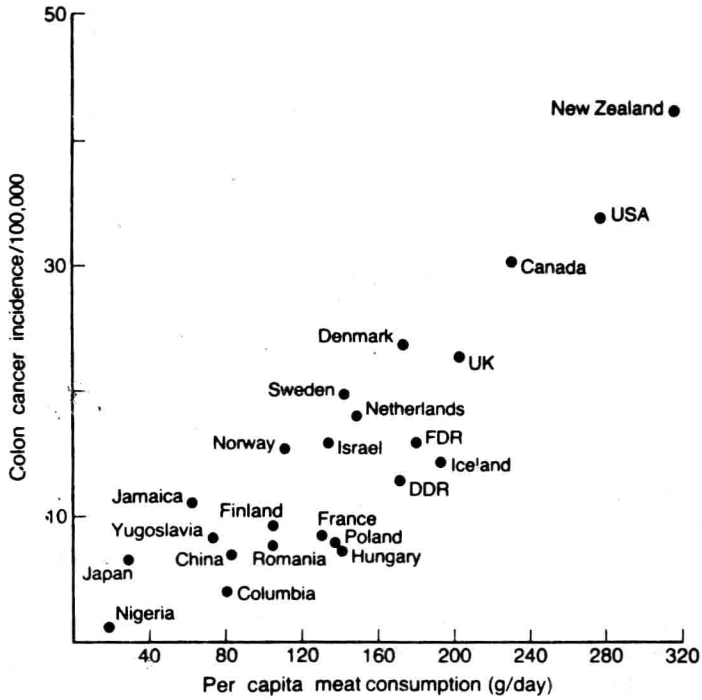

FIG. 1. Relationship between meat consumption in various countries and the risk, in those countries, of developing cancer of the colon. (The colon is the part of the large intestine where most cancers arise.) In FIGS. 1 and 2, each point represents one country (and the cancer rates per 100,000 women relate to women of similar age, and so are not materially affected by the greater risks of premature death from other causes in poor countries). The (generally prosperous) countries where meat or fat consumption is highest are those where women of a given age are at greatest risk of developing cancer of the colon or breast. But, although the explanation of this remains obscure, this is *not* strong evidence that either fat or meat are important causes of these cancers, merely strong evidence that these cancers have causes (1).

another. That suggests that most of the cancers occurring in New Zealand could have been avoided if people there lived as people in Japan lived, and that about 90% of the difference might represent avoidable risks for colon cancer. This is true, of course, only if these differences are due to the way in which people live and not to genetic factors. This is one point where the correlation is useful, because if it was due to genetic factors one would not expect these rather striking and impressive correlations.

The second piece of evidence is that if we look at migrants from Japan who move to the United States, we can compare Japanese living in the United States with, e.g., Caucasians living in the United States. We find that the rates among Japanese in the United States are quite different from the disease rates of the Japanese in Japan and much more like the rates of Caucasians in the United

States. When we compare blacks from, e.g., Nigeria with blacks living in the United States, we find that the United States blacks have colon cancer rates that are very similar to those of the United States whites and quite different from the West Africans who are still living in West Africa, which is where most of the blacks in the United States originated. These studies on migrants show that colon cancer is largely an avoidable disease.

When we compare different countries with each other, we find the same for breast cancer. In Fig. 2 the correlation has been plotted against total dietary fat intake. There are striking differences between countries. There is a general correlation and this suggests that a great deal of breast cancer might be avoidable if we could find out what it is about the Japanese way of life that results in Japanese in Japan having much lower breast cancer rates than Japanese in Hawaii or in California.

The breakthrough in cancer epidemiology came when people started to treat cancer, in terms of causes, as being many different diseases. As soon as it was subdivided into different diseases, it started to make sense. Talking about total cancer is as nonsensible as talking about infectious diseases—we cannot add

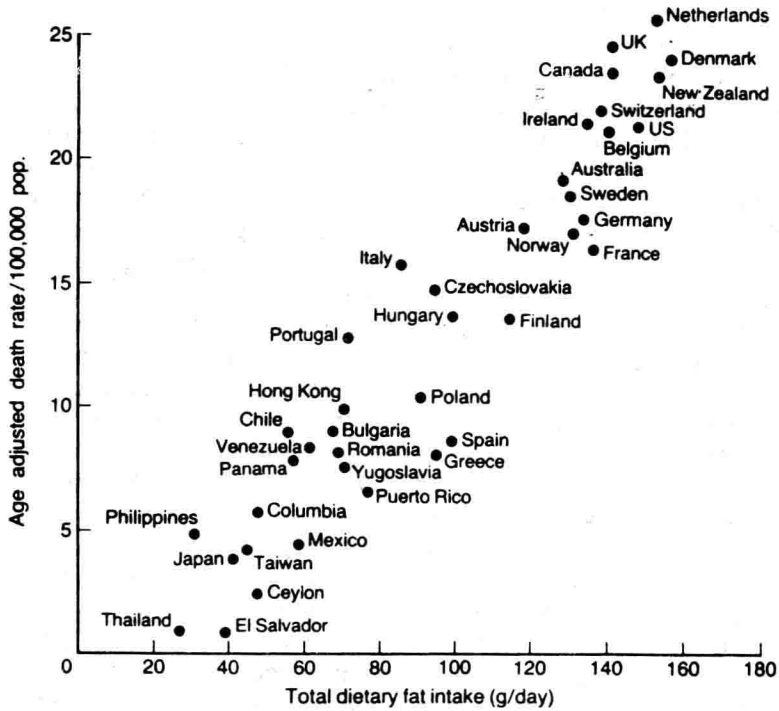

FIG. 2. Relationship between fat consumption in various countries and the risk in those countries of death from breast cancer (see Fig. 1 legend) (1).

syphilis and cholera together and talk about them as one disease. We have to treat the different types of cancer, breast, stomach, or colon, as being diseases that are as different from each other as the different infective diseases are.

DIFFERENCES IN CANCER RATES WITHIN ONE COUNTRY

Comparisons within one country show differences in cancer rates. The data on the migrants, e.g., the colon cancer rates in black Africans in Africa, blacks in the United States, and Caucasians in the United States demonstrate the 10-fold difference between countries, and the similarity between the blacks and the whites in the same country. The data for stomach cancer in Great Britain show big differences between different parts of the country. This has been true for 50 years and the explanation is still unclear. This also emphasizes some of the dangers of trying to use geographic correlations in a search for causes. There are some interesting hypotheses that nitrate is related to stomach cancer, so David Forman at Oxford went to some of the high-incidence areas and tried to look at the nitrate levels in saliva. He went to low-incidence areas and did the same and found that the nitrate levels were much higher in the low-incidence areas. In other words, the relationship was the opposite of what had been predicted. This does not mean that nitrate protects you against stomach cancer, but it does mean that that kind of geographic correlation is an unreliable source of information.

The county areas of Great Britain have a low incidence of lung cancer and the urban areas (London, Southampton, Birmingham, Liverpool) show high lung cancer death rates. An obvious conclusion is that the cause is air pollution, but this is wrong. Air pollution does have a contribution to make, but it is not a large contribution. The chief reason is that there is a long delay between cause and effect in cigarette smoking, and the smoking of manufactured cigarettes is a habit that spread a few decades ago from the cities to the surrounding countryside. Consequently, what we are now seeing is largely the result of the delayed effects of past differences between town and country in cigarette consumption. And, in fact, you will see the same urban role of difference in, e.g., Finland. You will find that the differences between Helsinki and the surrounding countryside in lung cancer is as marked as the differences between Birmingham and the surrounding countryside. Yet, Helsinki has never been a polluted city and there certainly has been no large difference caused by air pollution there. Again, this emphasizes the dangers of trying to make inferences based on purely geographic correlations. Sometimes, as, for example, with the old studies of cholesterol and heart disease, we will get the right answer from the international correlations, but sometimes we will not. They are not a trustworthy source of information. They are an excellent source of hypotheses, but a very poor source of tests of hypotheses.

The trouble with England is the small variety—the English people are to a great extent the same—and so the differences between one part of England and another are not large enough to be really exciting. If you want to be really excited you