Foods of the Future

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Future foods will be handled better, be cleaner, and have better quality and flavor. There will be increased flexibility in the choice of raw materials, including synthetic flavors and new protein sources, for fabricating foods. Computerized selection of food ingredients on a day-to-day basis will produce least cost standard products of high nutritional value and palatability. Foods will be engineered to be nutritionally complete without altering acceptability. Convenience foods will increasingly dominate the institutional and consumer markets. The away-from-home eating market will increase with a concomitant increase in the variety of available foods. Control of diet to prevent certain diseases, including obesity, will become prevalent.

It is, indeed, the height of folly to make predictions in this fast-moving world. We even doubt whether the kind of predictions that Jules Verne fictionalized, many of which came true, would be profitable.

But there is some point in attempting to make predictions. If the prediction extrapolates trends in technology, in social changes, and in the understanding and solution of social problems, one can define the boundary conditions for a variety of solutions. This will be our objective in a limited sort of a way. We will not consider foods as an independent outgrowth of the individual efforts of food scientists. Rather we will regard the nature of future foods as an interaction between social conditions and food science.

What will be the strains on our food supply and our ability to feed everyone in the world adequately? There are the old strains intensified and a new one, pollution. The old ones are war, population numbers, and poverty. War always disrupts food supply and has been a major cause of famine. Population growth in relation to the ability to produce food has always constituted a threat, but now constitutes a more intense threat. The fact that Malthus was wrong in his day does not free each generation from examining whether Malthus' time has come. The problem of poverty is being intensified. Although we are approaching an era of magnificent affluence in certain parts of the world, the spread between the affluent and the poor nations is increasing (Altschul, 1969). Finally, pollution is not really a new problem but our keen awareness of its existence is new. We are now aware that this is a finite world whose capacity to absorb the indignities of man-made waste is limited. And this affects the way we can use our land and our natural resources, which, in turn, affects the kinds of foods we can eat.

War and the threat of war always hang over man and his ability to take care of himself. A new dimension is that war is not the only threat. Even without war the ordinary unchanged course of events with the prevailing growth of population, the increase in the spread between the affluent and the nonaffluent societies, and the increasing problem of pollution could produce stresses of a magnitude which could lead to disaster. We, therefore, have to assume, as the basis for continuance of stable societies, that progress will be made in removing or lessening social and economic strains. Any predictions on food in the absence of assumed social progress are unrealistic indeed.

In the following sections we will list and discuss major trends and their effect on foods, and then try to take stock of where we might stand 10 to 15 years hence.

MAJOR TRENDS AND THEIR EFFECT ON FOOD

Public and Political Awareness of Nutrition. It is commonplace to hear that one cannot sell nutrition, that people buy foods primarily for their taste and appearance, and for the enjoyment they provide, rather than for nutrition. It is probably true that in the order of food priorities caloric requirements are first (man eats to fill his belly), food aesthetics and enjoyment are second, and need to be adequately fed is third. But the situation is changing. No one can deny the emerging interest in nutrition not only among all cross-sections of the population in the United States but also in the developing countries. We suggest that the following conditions will become more widespread. There will be an increased willingness on the part of the public and its government to pay the increased cost of good nutrition and to support activities which improve nutrition. There will be increased insistence by the consumer that good nutritional quality be built into foods and that labeling be adequate so that the consumer can evaluate the nutritional quality of the food being purchased. More and more nations will institute regular surveillance procedures to measure food consumption and health as related to nutrition. These surveys will be on a regular basis and will permit corrective measures to be undertaken and later assessed. More examples will be seen of large scale intervention in the food supply to provide deficient nutrients at the lowest possible cost. This will hold equally for societies with poverty-based malnutrition or for affluent societies. Examples of the kinds of intervention already practiced are iodization of salt, fluoridation of water, the fortification of bread and cereal products with amino acids, vitamins, and minerals, the fortification of milk and milk products with vitamins, and the widespread acceptance of nutritional supplements.

It is expected that every country with the burden of supplying enough protein for its population will adopt a cereals policy to maximize the protein content of its major cereal foodstuffs by fortification with amino acids and protein concentrates, by breeding more protein into the cereals, or by a mixture of the two procedures. Thus the major cereal foods will become almost complete foods in themselves (Altschul and Rosenfield, 1970).

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Flexibility in Raw Materials. There will be increased flexibility in the choice of raw materials from which one can fabricate foods. Natural food polymers and other natural complex chemical substances which have been the mainstay of our textured foods, the precursors of many of our flavors, and the basis of most of our beverages will meet increasing competition from man-made cheaper raw materials. Hence we can expect that textured foods from oilseed proteins and other protein sources will take an increasingly large share of the market during the next decade. However, even if their total volume becomes relatively high, their impact on the markets for natural animal foods will probably be small. But it would be folly indeed to predict the slope of the growth curve of these new food ingredients.

The flavor chemist and the food scientist have made impressive strides in incorporating meat-like texture, mouth feel, appearance, and flavor into protein products. Meat analogs from plant protein are a reality. Products resembling beef, ham, and chicken are available (Odell, 1967). In time their quality will improve and their production will increase.

Oilseed proteins can supplement meat protein as well as replace it. It has been estimated that 30 million pounds of soy protein are being used per year to improve processed meats such as chili, spaghetti sauce, Sloppy Joes, and pizza toppings and in bacon-like products. Five years ago U.S. per capita consumption of soy protein was close to zero, now it is about 0.25 lb per year. Five years from now it may be 5 lb per year and in 20 years a conservative estimate may be 20 lb per year (Robinson, 1969).

Meat production, too, is undergoing technological changes. Breeding, animal selection, and feeding are developing animals that mature earlier and have less fat. Processes have been developed that preform boneless fresh meat to a predetermined fat content. Selected sections of meat may be reformed into more desirable shapes, such as chops or cubes of lean meat.

With further advances in both oilseed protein and meat technology, and with improvement in the control of texture and flavor, preportioned servings of meat analogs and extended meat products having a predetermined calorie content and protein value will become available. The label on a future meat purchase might tell not only the weight and price of the item but also the calorie and utilizable protein content. And, if the chemist's work in flavor and texture "pays off," a meaningful grade related to tenderness and flavor might also be included.

With the variety of meats, meat byproducts, and oilseed proteins that will be available to the processor, programming techniques will calculate on a day-to-day basis ingredient combinations to yield a standard product on a least cost basis. Thus, uniformity of product and greater price stability will be engineered into this class of foods.

We have limited our remarks to oilseed proteins because their technology is farthest advanced but, obviously, fish protein concentrate (FPC), microbial protein, etc., are all potential protein sources. The probability of widespread commercial use of proteins other than those derived from oilseeds and fish for human food within the time span of the next decade is probably less than 10% (Bird *et al.*, 1968). But this time scale may be shortened by intensive research and development in countries which lack adequate oilseed supplies. As for FPC, its competitive position *vis-a-vis* oilseed proteins is not clear. It may well prove out that fish protein may be a most important contributor to meeting protein needs but perhaps in a form other than FPC.

Just as meat proteins may be replaced by other protein polymers, coffee, tea, or cocoa may bow to the competition of man-made flavors. Such a development could have immense consequences for the economies of many countries that now depend on these as their major cash crops. This development can be likened in its economic impact to the effect of synthetic rubber on the existence of rubber plantations.

Engineered Foods. The history of the human race is a history of food modification. Hardly any "natural" foods are left. Bread is certainly not a natural food; the invention of bread is probably one of the great inventions of all time. And the invention of texture in protein concentrates is likely, in time, to occupy a similar place in history. Modification of foodstuffs is not new at all. What is new is the engineering or fabrication of foods for special nutritional purposes. And even this concept is not so new. At the beginning of this century the first steps were taken to develop infant food formulas. These have evolved into the sophisticated products available today for all types of infants, with their allergies and specific nutritional needs.

Processed foods intended to be a complete meal will provide all of the nutrients expected from them. Already baked products are available that, together with a glass of milk, supply a complete breakfast. All sorts of combinations will be available to make it easier to provide food easily and at lower cost to such sensitive populations as school children. Bizarre food habits will be converted into adequate food habits by modification of the foods. This will cause no problem to the food industry but will shake the foundations of those who insist on maintaining traditional food patterns.

One panel of the White House Conference (White House Conference, 1970) recommended that major foods should be made as nutritionally complete as is possible without altering acceptability to the consumer. The Panel suggested that each of the basic foods should be fortified with nutrients selected to a level such that if the food were consumed as the sole source of an adequate caloric intake, it would supply complete daily nutrient needs. Since consumption of food is controlled by caloric intake, this concept would prevent either excessive or deficient intake of critical nutrients. This is already being done in a few selected instances for wheat and corn flour in the U.S. domestic Family Food Programs.

Foods which have lesser impact, *i.e.*, provide a smaller proportion of calories in the diet, will likewise be engineered to eliminate malnutrition or to make it easier to do so. For example, it is conceivable that soft drinks will be engineered to be complete foods on the basis of their caloric intake. It may be that the most popular soft drinks of the future will either be those which have no nutritional content, that is will contain no calories for those who desire no calories, or will become close to complete foods for those who need more nutrients. The same rationale may also be applied to snacks, which are assuming a more important role in the diet.

There could be a tendency to over-fortify; this can be controlled by proper government regulations and by exercising good judgment. Fortification will be based on the totality of the food intake in order to take advantage of blending of foods eaten together.

Variety in the classical sense of a variety of food commodities will become less significant as a means of achieving good nutrition in the face of increased consumption of complete meals made up of processed foods. This will provide an added incentive to engineer for better nutrition.

Food Processing and Preparation. In general, techniques will resemble those of today. Conventional and improved methods of canning, freezing, and dehydration will continue to play dominant roles. Freeze-drying will continue to grow in popularity. Freeze-dried products need no refrigeration. In many instances flavor is superior to that of spray-dried or roller-dried products, since the removal of water at low temperature prevents the loss of flavor volatiles. The reconstituted product is often indistinguishable in taste and smell from the fresh product. Meats, shellfish, dairy products, eggs, vegetables, fruits, desserts, even salads can be freeze-dried and later rehydrated to yield products of excellent acceptability (Bird *et al.*, 1968). The commercial success of freeze-dried coffee is a forerunner of things to come (Bird, 1969).

Currently freeze-drying is expensive, but more efficient methods and improved equipment and handling procedures will lower costs (Brockmann, 1970). There are built-in economic advantages to freeze-drying that counterbalance higher processing costs, *e.g.*, fruits and vegetables may be produced under ideal growing conditions, freeze-dried near the growing site, and transported cheaply to faroff population centers since 70% or more of the product in the form of water may be left at the point of origin.

Boil-in-bag food (Bird *et al.*, 1968) is an example of convenience plus improved acceptability. Centrally-processed vegetables are precooked, surrounded by a medium such as a precisely formulated, flavorful cream sauce, and packaged in a sealed plastic bag. The vegetable is cooked by immersing the bag in hot or boiling water. Since the pouch is sealed, cooking odors are eliminated; further, the product is not burnt or overheated. The technique is of course not limited to vegetables; the consumer buys, in addition to the fully prepared food, extra flavor, cleanliness, and convenience. Some problems of stability of the products in-the-bag may require further technological improvements and very careful quality control.

Thus, as a result of improved techniques in packaging and in the preprocessing of foods prior to their final preparation step, we can expect our future foods to be more complete and to be more easily processed at home.

Legislation to minimize pollution of our environment and our food will have an impact on food processing and food utilization. Obvious examples are solid waste disposal associated with feed lot operations and clean-up of effluents associated with canneries, dairies, slaughterhouses, etc. Techniques to remove organic colloids and solutes from aqueous media need to be improved, and, equally important, techniques to utilize the recovered waste products need to be developed. One can foresee that such cleanup procedures need not prove costly. Just as the electrolytic refining of copper pays for itself in the gold and silver recovered as byproducts, the cleanup of plant wastes may also yield valuable byproducts.

Built-in Services. Food companies, to increase product sales, have been building more services into the foods which they market. And the consumer for reasons of convenience and because of requirements of new life styles is accepting them. There is little doubt that increased convenience and variety will characterize the new generation of foods. "Convenience" foods will increasingly dominate the institutional and consumer markets. Convenience foods will be equally important in the developing world. A homemaker in the United States, if that is her sole job, may enjoy spending some time on food preparation. A woman in a less developed country, beset with an endless number of daily chores, may find any degree of labor- and time-saving in food preparation, even at some added cost, to be more than welcome.

Convenience foods for the affluent countries and for the developing world are as far apart as their technologies. In the U.S. it may mean "popping" an entire meal into a microwave oven. In Guatemala it may mean the purchase of a preground and prepackaged tortilla mix made from high lysine or fortified corn. In both instances convenience is equally welcome.

One countertrend to convenience foods may well emerge. As affluence and leisure time play an increasing role in our lives, more people will seek pastimes combining play and utility. Gourmet cooking is developing into one such endeavor. Specialty shops and organizations designed to bring exotic foods and drinks from around the world to amateur clients may become an expanding leisure-time business. And time spent in food preparation, home cooking, and concocting of flavorful sauces and desserts may become an all-absorbing avocation for at least some.

Institutional Feeding. There will be an increase in the "away from home" eating market. With increasing affluence, more and more meals are consumed in restaurants, cafeterias, hotels, etc. One estimate is that by 1975 thirty-five billion dollars will be spent within the U.S. for food away from home (Bird *et al.*, 1968). And if the growth rate in population and income increase as in the past 10 years, a 50% increase can be anticipated by 1985. With so great a market, incentives for innovation abound.

It is not difficult to envision a completely automated restaurant of the future. The customer will indicate his food choices by proper notation on a data card. The data will be analyzed by computer, preportioned items will be selected, cooked, then assembled and delivered to the proper table in a time sequence determined by the customer as the meal proceeds; all steps will be automated and free of human intervention.

Institutions, where the final preparation of thousands of meals per hour is required, demand more of innovation than the home. It is not merely a difference in the number of meals served that differentiates the home from the institution. The institution presents an entirely different concept. The institution must provide meals as attractive and nutritious as individually-prepared and served home meals. Yet for most institutions, except high-priced restaurants, individual preparation is no longer practicable. This puts a serious demand on technology to preserve flavor, color, and texture throughout the chain of events in institutional foods: factory-made, stored, delivered (often over long distances), reconstituted, and reheated. But there are some advantages: there is a greater flexibility in choice of food ingredients over home-made foods. And there is a greater flexibility in the choice of nutrients and control of cooking conditions to minimize damage during preparation. Hence, foods in institutions could approximate the best nutrition achievable by current practice and knowledge.

We will look on institutional feeding, whether it is private or public, as a natural outgrowth of our way of life, of increased population, of increased urbanization, and of increased modernization. Rather than rail against it and wish for the good old times, the better policy will be to utilize food dispensing institutions as a means of providing food and eliminating malnutrition under the best possible circumstances achievable. There should be no excuse for malnutrition among any school age population exposed to school lunches.

And school lunches will not only be a simple way of providing a meal but will be part of intervention programs to furnish any deficient nutrients revealed by surveillance.

Sophisticated Selection of Foods. Flexibility in ingredient composition and the trend toward production of complete foods will allow greater use of computers. Such techniques are indispensable for producing low-cost nutritional meals and for developing specifically tailored diets. Miller and Mumford (1970) described an approach to both of these problems.

Thus, to develop diets high or low in nitrogen, sodium, fat, and carbohydrates, appropriate foods are selected by the computer from basic data from food composition tables such as those published by the U.S. Department of Agriculture (Watt and Merrill, 1963) or by FAO (1970). Not all combinations make for an appetizing meal. To formulate a palatable diet from a listing such as this, there must be an interaction between the dietitian and the computer. The dietitian roughly constructs a diet from the selected foods to meet the individual's requirement. The items are then fed into the computer which, in turn, calculates the exact nutrient content, notes deficiencies or excesses, and suggests foods to correct these. The dietitian then amends the diet accordingly and thus builds up a palatable mixture of desired composition. The entire process can be carried out at the computer keyboard.

Least cost diets can be prepared by a similar approach (Miller and Mumford, 1970). As might be expected the major expenditures are for calories and protein; vitamin and mineral requirements can be met for a few pennies a day. Nutritionally satisfactory least cost diets must be modified to achieve consumer acceptability. At a conservative estimate, 25% of the cost even of the most economical diet is for nutrients and 75% is for palatability.

One major medical advance will be the increasing importance attached to preventive medicine. Insofar as knowledge permits, control of diet to prevent certain diseases will become more prevalent. It will be possible for a person to select a diet from specially engineered foods to meet any nutrition-engendered disease. For example, obesity is a major problem of the affluent society. It should be possible to control obesity by providing low calorie foods with built-in texture and flavor. In fact, it should prove possible to separate the enjoyment of food from nutrition—just as the enjoyment of sex can now be separated from procreation.

Properly tailored diets should provide control of metabolic defects involving nutrition. Here the problem involves limiting the intake of specific substances which cannot be metabolized, but at the same time supplying a relatively satisfactory diet. In some instances this can be done relatively simply, in others such as phenylketonuria (PKU), where phenylalanine must be restricted, the problem becomes more difficult.

It is difficult to define a normal diet. In addition to metabolic defects and allergies, we have individuals with anemias, malabsorption problems, diabetes, renal malfunctions, high cholesterol, etc. For each one of these individuals specific nutritional requirements must be met. The more we learn about the relationship between nutrition and disease the more specific we can be in defining the nutritional needs of the individual (Hegsted, 1970).

Better Professional Practice of Nutrition and Food Science. We suppose that included in a discussion of new foods should be what might be expected of the people who are responsible for the new foods. It is quite clear that greater sophistication will be required in the practice of both nutrition and food science. The demands for the kinds of activities listed above can only be met by the highest type of professionalism in both of these areas. Much more information will be necessary in order to make possible the proper intervention and control of our food supply. One example is the need for better methods of testing populations for existence of protein deficiency problems.

Entirely new concepts of testing additives for safety are needed to replace the time-consuming and expensive methodologies now employed, which make it almost impossible to think of developing new kinds of foods or new concepts in foods without enormous expense. Moreover, the present methods are not always satisfactory in predicting what might happen in the human being. More fundamental studies will be required to determine the metabolism of new foods and food additives, and to try to relate this information to possible metabolic effects in the human. There will need to be better methods for total surveillance of population and for monitoring new foods and additives so that changes can be made in accordance with new knowledge. Everyone rejects the notion of experimentation on human beings. Yet, in spite of all efforts taken to anticipate what might happen to humans from experience with prior experiments on animals (and sometimes with volunteers), the final experimental animal on a new food or for that matter on an old food under new conditions is the human being himself. More attention will have to be given to the epidemiology of new foods and of old foods so that, continuously, information will be made available on what foods are doing for humans under real-life conditions. All this requires new knowledge and new technology.

More knowledge is needed on the role of nutrition in improving performance of humans of various ages, and much more is needed on the role of nutrition in the etiology of specific diseases.

Food scientists will have to learn more about design of texture and flavor so as to be able to increase flexibility and utilize to the fullest extent the new raw materials that will become available for incorporation into foods.

DISCUSSION

There is no question that our foods have improved, no matter how you look at it. The handling is better; they are cleaner, quality and flavor are better; uniformity is greater; quality standards and quality assurance are better. The cost of foods has risen less rapidly than other costs of goods or services.

There have been regressions. Flavors of certain artificially-ripened fruits and vegetables do not compare with the same products harvested under ideal conditions. For those who preferred the stronger flavors of farm-fed poultry of 50 years ago to the bland and uniform flavor of the computer-fed and factory-produced poultry of today, this might be a regression. Nero Wolf (a favorite gourmet of one of the authors) once extolled the virtues of ham made from peanut-fed hogs. But this is a delicacy available to just a few. And there will be other regressions forced by higher labor costs, increased problems of pollution control, and increased problems of transportation and marketing.

But balanced against these, for example, is the disappearance of seasonal foods. Fruits and vegetables are available all year around from all parts of the world, preserved by advanced techniques, and flown to the market. The acceptability and pleasurability of foods is in a dynamic state.

Advances in breeding and in agricultural practice, and newer knowledge about ripening, will improve our ability to market perishable items with least deterioration. We must not rule out the possibilities that flavors can be improved over what we now have or what we assume to be "natural" (Hornstein and Teranishi, 1967). We conclude that food science can cope with the increasing problems superimposed by a more complex society, and even get ahead.

Complaints are being voiced about nutritive quality of some classes of foods. Some foods which at first provided an insignificant proportion of the caloric intake have become, for certain age groups at least, important foods so that their nutritive value becomes an important consideration. There have been complaints about overstatement of virtues of certain foods. And there have been complaints about inadequate information on the labels. Above all these activities are symbolic of the greater awareness and interest in nutrition by the consumer, which we cited earlier. With this greater awareness will come more frequent expressions of satisfaction and dissatisfaction with the procedures and products of the food industry.

It is not our function to weigh the pros and cons of the arguments. But it is worth mentioning that the positive response of the American food industry to the challenges of the White House Conference on Food, Nutrition, and Health (1970) is an impressive social phenomenon and may be one of the important social developments of the last few years. An entire industry publicly recognized its share of responsibility for the nutrition and health of the American community and took specific steps, each company according to its ability and interests. In the Follow-up Conference held in February, Mr. James P. McFarland, (1971) speaking for the industry, summed up as follows: "As I look over the past year, I am impressed by what has been accomplished. It has been innovative, it has been constructive, and it has been substantial. And as I view where we are today, I am once again impressed—this time by how much more demands to be done. None of us in industry views today's session as anything more than a brief respite, a breathing spell that gives us the chance to make a progress report. Tomorrow, like yesterday, we'll be back on the firing line and working toward the full attainment of those goals we set for ourselves one year ago."

The present climate encourages the cooperation of government and industry to stimulate food innovation for social benefit. This uniquely favorable situation is a challenge to the leadership of both government and industry.

What will the foods of the future look like? We cannot rule out the appearance of entirely new and novel forms and flavors. These have appeared in soft drinks, breakfast foods, and in snacks. But, by and large, the appearance will be the same and the tastes or flavors more or less the same, even if the composition, processing, handling, stability, and packaging will differ.

Nutrition will become less a matter of chance. One anthropologist, when asked about foods of the future said, "A person will take a pill in the morning and eat whatever he likes the rest of the day." This observation reflects an important and accepted part of our modern food culture: micronutrients are not just found in natural surroundings; they are equally available in pills, capsules, wafers, or liquid concentrates and the like. Affluent malnutrition which arises from lower calorie intakes, less variety in the nutritional sense, and a greater proportion of food eaten as processed food will be overcome by proper design of foods and food systems. The strategies will include utilization of nutritional supplements, proper engineering of foods, and fortification. And control of poverty-based malnutrition will be more easily attained, and at lower cost.

One could possibly be wildly optimistic that we are approaching a relationship of food to society undreamed of.

But this could all be a dream. The time has passed that technology alone can overwhelm and transform societies regardless of other trends or conditions. No longer is there automatic acceptance of technological innovation. And food is no exception.

The public climate must be responsible and understanding. Violent fluctuations in interest and position, and religious devotion to food fads could delay progress for years or decades. One committee at the follow-up conference to the original White House Conference was moved to express itself as follows: "A. *Balance between Knowledge and Action.* In all of the food and health problems facing our society, we should recognize the need for a national balance between action and knowledge. We do not know all we need to know about nutrition or safety, yet we must make decisions about new foods, old foods, additives, pesticides and environmental contaminants. At any moment, our decisions should be balanced and sophisticated, recognizing that our knowledge is incomplete and that we must, therefore, choose among risks that cannot fully be known. (For example: Shall we choose at the moment persistent pesticides or current supplies of food and fiber?) We should recognize the relation between decisions on food and nutrition and other elements of our social fabric and should be reluctant to make extreme decisions of acceptance or abandonment without full and informed consideration of the consequences of such decisions" (White House Conference, 1971).

The ever-widening gulf between the affluent and poor nations continues to be a major cause of world instability; localized differences within a country contribute to national instability. Technological improvements alone could further widen the gulf and exacerbate the instability. Whether or not we come closer to achieving the zenith of nutrition and food enjoyment that we can expect on the basis of knowledge and technology will depend on how well we solve all the rest of our problems. It is not likely that society can get too far ahead of itself in any one aspect.

Conversely, new technology can stimulate new social effort and instill a sense of optimism. Surely, most of the food problems cannot be solved without the intervention of new technologies. When the new technologies appear, they stimulate hope and action. This influences action and rhetoric by governments in the field of the particular technology, but there is also some spillover to the other fields and problems.

New food technologies could be a generator of general social action and hope. And this might be the most important contribution of all.

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END OF SYMPOSIUM ON THE CHEMICAL ASPECTS OF NUTRITION NEEDS

Additional papers given at Symposium are:
"Aspects of Vitamin 'A' Nutrition in Man," by J. E. Canham, E. M. Miller, D. L. Wallace, N. Raica, H. E. Sauberlich, and R. E. Hodges

"The Protective Action of Vitamin E Against O_2 Toxicity," by S. L. Kinzey, C. L. Fischer, and C. A. Mengel

Acetylcholinesterase Inhibition by Substituted Phenyl *N*-Alkyl Carbamates

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Acetylcholinesterase (AChE, EC 3.1.1.7) inhibition constants (binding, carbamylation, reactivation, and overall bimolecular rate constants) were studied for selected substituted phenyl *N*-alkyl carbamates. *N*-Methyl carbamates were better inhibitors than larger *N*-alkyl carbamates. AChE from different species of animals showed remarkable species specificity toward these inhibitors. *N*-Ethyl carbamates were the least potent inhibitors toward bovine erythrocyte AChE, while *N-n*-butyl or *N-n*-hexyl carbamates were the least potent inhibitors toward AChE from housefly (*Musca domestica* L.), honeybee (*Apis mellifera* L.), and house cricket (*Acheta domestica* L.). Thus, short chain *N*-alkyl (*N*-methyl to *N-n*-propyl) carbamates favored the inhibition of insect AChE, while longer *N*-alkyl (*N-n*-butyl and up) carbamates favored the inhibition of bovine erythrocyte AChE. AChE inhibited by short-chain *N*-alkyl carbamates recovered its activity faster than the long-chain *N*-alkyl carbamates. Bovine erythrocyte AChE inhibited by carbamates recovered its activity much faster than insect AChE, especially when the inhibition is made by long-chain *N*-alkyl carbamates. Insecticidal activity was decreased when *N*-alkyl chain length was increased.

Acetylcholinesterase (AChE, EC 3.1.1.7) inhibition by carbamates is analogous to acetylcholine hydrolysis which may be expressed as

$$\underline{\text{EH}} + \underline{\text{CX}} \underset{}{\overset{Ka}{\rightleftharpoons}} \text{EH}\cdots\text{CX} \xrightarrow{k_2} \underline{\text{E—C}} \xrightarrow{k_3} \text{EH} \qquad (\text{EH} + \text{CX} \xrightarrow{k_i} \text{E—C})$$

in which EH is free enzyme; CX, the carbamate; EH···CX, the enzyme-inhibitor complex; E-C, the carbamylated enzyme. Main (1964) has described a procedure to measure the binding constant Ka, carbamylation constant k_2, and overall bimolecular rate constant k_i. The decarbamylation rate constant k_3 can be determined by the method of Wilson *et al.* (1960).

Almost all insecticidal carbamate inhibitors studied are *N*-methyl or *N,N*-dimethyl. It is generally realized that *N*-ethyl carbamates and *N*-phenyl carbamates are poorer inhibitors than *N*-methyl carbamates (Kolbezen *et al.*, 1954). However, no good explanation has appeared to explain this phenomenon. Therefore, several series of substituted phenyl *N*-alkyl carbamates were prepared. Main's analysis for inhibition constants (binding, carbamylation, and overall bimolecular rate constants) for AChE from housefly, honeybee, and bovine erythrocyte were studied in order to analyze the factors which cause the decrease of the inhibitory potency due to the increase of *N*-alkyl chain length.

The *in vitro* decarbamylation rate constants k_3 of AChE have been studied by Hellenbrand (1967), Kunkee and Zweig (1965), and Wilson *et al.* (1961). It is generally regarded that *N*-methyl or *N,N*-dimethyl carbamates behave as reversible inhibitors due to their fast decarbamylation rates. However, there are some variations in decarbamylation rates in regard to the *N*-methyl or *N,N*-dimethyl groups for AChE from different species of animals. Thus, k_3 of AChE from housefly and bovine erythrocyte are greater for *N*-methyl than for *N,N*-dimethyl carbamates. The opposite is true for honeybee AChE. Wilson *et al.* (1961) reported that k_3 of electric eel AChE decrease in the order of $-NH_2 > -N-Me_2 > -NH-Me$. There is no study extended to longer *N*-alkyl carbamates. Since bis-carbamates are known as irreversible

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