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THE CHEMICAL MANIPULATION OF FOOD*

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The object of this lecture is to call attention to the great expansion and development of the treatment of food, during processing and production, by chemical substances foreign to the body. There are indications that this subject is now an important problem of public health, and unless controlled and wisely guided this practice may have a detrimental effect on the health of the country. It is particularly important that medical men should appreciate what is happening, for whatever is done to food ought to be dominated and decided by its effect on human health. It seems that the ordinary consumer often appreciates the changes in the aesthetic value of the food so treated even though such treatment may either lower its nutritional value or, in some cases, produce a toxic product. The consumer must be protected against himself and against the wayward choices of food into which his appetite leads him.

As matters stand at present the chemist holds the dominant position in developing and controlling the subject, and the great expansion of food manipulation is an indication both of his energy and of his success in this field of action. Chemists primarily engaged in this work are called "food scientists," a designation which is misleading, because they often have but little knowledge of the physiology and pathology of the animal body, nor do they in general grasp the significance or the difficulties and complexities of living processes. They are apt to view the reactions of the human body from the point of view of chemistry—a subject which is so highly developed, and so often lends itself to correct prophecy, that other scientific implications seem relatively easy. But the fact is that actions and reactions of the human body are so unpredictable, and knowledge of them so meagre, that the confidence and clear-cut views of the chemist may often be dangerous. That is why, if this subject is allowed to develop, medical scientists must play a leading part, especially before official decisions are made on the adoption and rejection of processes of chemical manipulation of food.

Present Practice

At the present time, both in the U.S.A. and in this country, it is possible for chemical substances to be used in food manipulation and production which ultimately prove to be harmful and deleterious. This does not mean that substances known to be harmful can be added to food but only that chemicals are often assumed to be harmless and, after being used for a longer or shorter time, are then proved to have harmful properties. This

kind of incident is constantly happening. It was stated at a recent inquiry in the U.S.A. that of 700 chemical agents at present used in food preparation 246 had not been studied enough from a toxicological angle to satisfy the Food and Drug Administration of that country that they were innocuous. Even when such chemical substances have passed through a battery of tests from the point of view of toxicology, unexpected harmful results have often ultimately been demonstrated.

Medical science often cannot give adequate answers to questions of toxicological action, not only as regards new compounds but even in the case of substances long in use. Indeed, to the medical man unpleasant surprises are constantly being revealed, in the case both of drugs and of chemicals used in food preparation. Many instances of such occurrences could be given, but two, in relation to drug action, which will be known to many medical men will be mentioned.

A series of cases of agranulocytosis often associated with septic throats (Vincent's angina) came to light about 1935-9 in which the individuals affected were found to have taken a well-known and extensively advertised patent medicine. The cause of the trouble in these cases was traced to the amidopyrine present in the patent remedy. As soon as the discovery was made and announced, many further instances turned up, and indeed a number of other chemical substances were later discovered to have a similar toxic action. This was a surprising poisonous action of a drug which had been long in use.

Another similar unexpected result casually observed quite recently has been the discovery that resorcinol, which has been a long-standing remedy as an antiseptic in skin disease, has the remarkable effect in some people of producing myxoedema and enlarged thyroid (Bull and Fraser, 1950).

It can be easily understood how these harmful effects have escaped detection by systematic toxicological inquiry in the past; but each discovery of the kind leads to an improvement in the technique of toxicology, and it is upon the still greater development of this subject that reliance must be made.

In this country there seems to be a special difficulty in controlling the situation, because the use of chemicals in food preparation is largely decided by the Ministries of Food and of Agriculture and Fisheries, whose main objectives must be the production of foodstuffs which are more abundant and acceptable to the consumer. It is undoubted that these Ministries also take into consideration the possible effects on the health of the consumer, but this aspect does not hold the commanding position that it clearly should. With the best will in the world these Ministries cannot, without the guidance of medical science, decide with knowledge and wisdom such questions affecting health. The duty of considering

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health officially devolves primarily upon the Minister of Health, and it would be more comforting if it were clear that all questions involving the addition of unnatural chemicals to food were more controlled and even dependent upon the decisions of that Minister.

Conditions in the U.S.A.

At the present time in the U.S.A. both Government Departments and the general public are keenly alive to the dangers of the position. The Food and Drug Administration has extensive laboratories and a large research staff engaged in the work, and official inquiries of a high legal and scientific standard are often held on specific matters of interest. At these inquiries experts are not encouraged to give their opinions only, but definite evidence on each point must be presented and filed as exhibits, so that the presiding officer can carefully examine and balance the evidence before coming to a decision.

We seem to have no such highly developed laboratory and examining mechanism in this country, and we are in the undignified position of having often to rely on the decisions arrived at in the U.S.A. before policy or action can be determined. If the questions at issue were small and of rare occurrence this situation might perhaps be regarded with more complacency, but this is not the case. Questions of great public interest are constantly cropping up, and the food and drug laboratories in America are very active. Is it right, therefore, that we should continue to be onlookers in this field of action, profiting by and dependent upon the hard work and the keen interest of another country? A beginning has been made here by the establishment of a toxicological research unit by the Medical Research Council, but this is far too small for work of the proposed type; and its objects are different from those of an officially developed testing department such as the Food and Drug Administration of the U.S.A.

It is of course true that in this field, as in most fields of scientific research, important contributions are sometimes made to the subject by private investigations here—such, for instance, as the carcinogenic properties of organic compounds of the coal-tar type and especially of the azo dyes—but, whereas we often look on such contributions, with passive equanimity, the U.S.A. seize on each discovery and by much labour apply it to the practical problems of food adulteration in relation to public health. Equally, their food manufacturers quickly and vigorously apply any new knowledge of chemical manipulation to the development of their products.

There is no question of apportioning blame in this problem. Food manufacturers and scientists, as well as official bodies, are undoubtedly anxious to do the right thing, and the question really resolves itself into the adoption of the best methods of dealing with the situation and the right angle at which to survey such problems. An enlightened public guided by good leadership, medical and scientific, will form the essential basis for proper action in such matters.

Changes in Disease Incidence

It may be asked if changes in the incidence of disease, especially in the past 50 years, afford any reason for suspecting that the modern practice of chemical manipulation of food is having any harmful effects on health.

This is not easy to answer, for there is nothing more difficult than guessing and forecasting in biological and medical problems, and in the present situation there are many unknown factors. Although most morbid conditions have rapidly diminished in highly developed Western countries in the present century there are a number which have increased, and this increase cannot wholly be explained on the basis of an ageing population. It is difficult to avoid the conclusion that some at least of these increases in disease are due to errors in living recently introduced or greatly expanded in modern times.

The present popular explanation of some is that they are largely of a psychosomatic origin, due to the modern stress of life. Such an explanation leaves the problems in the air from a research angle. Is this explanation sufficient to account for the great increase in abdominal trouble, and especially of gastric and duodenal ulcers, cholecystitis, and appendicitis? There are also diseases, fairly common in incidence, like hypertension, the leukaemias, and disseminated sclerosis, the aetiology of which has defied all investigation. The great increase in diabetes in modern times in the U.S.A., and in this country until the recent war, is also still an unsolved problem.

In most of these diseases there are great differences in incidence in different countries. For instance, there is almost a complete absence of disseminated sclerosis among the South-African-born white population, and the incidence of the above-mentioned alimentary disorders among the natives of tropical and subtropical countries is much smaller than in Western Europe and America. There is therefore good reason to believe that much disease in Western countries at present is due to errors of living introduced or greatly increased in modern times, and it may be that one of these errors is the ingestion of food treated by unnatural chemical substances. It is at least a subject worthy of inquiry, and might well be considered whenever a disease commonly found in countries which use these methods has resisted all efforts of the investigator to find a satisfactory aetiological basis.

There are therefore two main problems presented by this modern development of food processing and production affecting the consumer. One, the possibility of the introduction into food of substances which confer upon it toxic properties; and, secondly, the degradation of the nutritional qualities of food by the abstraction or reduction of some of its important constituents or by the dilution of its nutritional constituents by air and water. Of these two problems the second may be more difficult to combat.

Chemicals Used in Food Preparation and Production

Unnatural chemicals are used in food preparation and production for the following main purposes: (1) added to foodstuffs as fat-sparers (extenders) or spacers of other foods, to facilitate emulsification and as preservatives, antioxidants, sweetening, flavouring, and colouring agents, and as improvers and bleachers of flour; (2) to aid in the washing of utensils used in food production, processing, and wrapping; (3) as wax coatings, resins, plasticizers, and other ingredients of food-packing material; and (4) as pesticides, including insecticides, fungicides, acaricides, herbicides, and plant-growth regulators in the production of fruit and vegetables.

Let us now briefly examine some of the chemical agents used for the above purposes. In the first place I shall deal with the evidence which shows that some of these substances, a number of which have long been in extensive use, are harmful to animals. As regards the toxic action of these adulterants it is obvious that if substances can be shown with certainty to have bad effects they are unlikely to continue in permanent use. This question of degree of toxicity is often difficult to decide, and instances will be mentioned in which the use of substances has continued and is continuing although there is evidence that they are harmful, because such evidence or deductions made therefrom are not unanimously accepted.

Sweetening Agents

One of the simplest instances of chemicals used in food preparation is that of sweetening agents. These substances are valuable as substitutes for sugar in the diet of diabetics, but are also extensively used for normal consumption in the soft-drink industry and in baking and in the manufacture of confectionery. Of these, four compounds have been used: (1) saccharin, (2) dulcin, (3) P 4,000, and (4) sodium cyclohexylsulphamate. These substances have been tested from the point of view of chronic toxicity by Fitzhugh and Nelson (1950), and interesting and unexpected results have come to light.

Dulcin (paraphenetolurea) had been used as a sweetening agent for 50 years before the chronic toxicity tests on animals showed it to be harmful. In animals fed at dosage levels of 0.1% and above, large liver tumours were produced. At higher levels of feeding (0.5-1%) growth was retarded and the mortality rate increased. At 1% the blood picture became abnormal, including a reduction in the red-cell count and the appearance of normoblasts. P 4,000 (2-amino-4-nitrophenylpropyl-ether), which received its descriptive name because it has about 4,000 times the sweetening power of cane sugar, was first reported from Holland as non-toxic. It is, however, a local anaesthetic as well as a sweetening agent, and has recently been shown to produce pigment changes in the thyroid gland and kidney damage (Fitzhugh and Nelson, 1950). Under the same experimental conditions saccharin and sodium cyclohexylsulphamate were apparently harmless. Thus of the four sweetening agents that have been or are in use, two (dulcin and P 4,000) are clearly too toxic for human ingestion.

Colouring Matter

By far the most commonly used chemical substances for colouring belong to the azo-dye group. In the U.S.A. and Canada those azo dyes which can be used as food colourers are specified, but in this country only those dyes are named which may not be used. (In 1947 five of the coal-tar colours were officially included in this group, but the number may have increased since then.) In recent years, and especially since the great activity which followed the discovery of the carcinogenic action of polycyclic aromatic hydrocarbons and simple derivatives of these substances, the azo dyes have come under suspicion as being potentially toxic agents. These latter observations had their origin as long ago as 1906, when Fischer described the cell proliferation produced by the azo dye scarlet red, an observation later developed when this substance was used to accelerate the healing of wounds.

However, in 1932 Yoshida found that the addition of a related azo dye (*o*-amino-toluene) to the diet of rats produced malignant tumours of the liver. Even more potent as a liver carcinogen was another azo dye, *p*-dimethylamino-azobenzene, which had long been used as a food-colouring agent under the name of butter yellow. Cook *et al.* (1940) examined a large number of azo dyes for their carcinogenic properties and found a few to have this undesirable action. Kirby and Peacock (1949) showed oil orange E to be carcinogenic. The following azo dyes have been shown to have carcinogenic action, in most cases producing hepatomas when fed to rats: *o*-amino-azobenzene, *p*-dimethylamino-azobenzene (butter yellow), *p*-monomethylamino-azobenzene, *p*-amino-azobenzene, 2:2'-azonaphthalene, 1:1'-azonaphthalene, and benzene-azo naphthol (oil orange E).

Although the use of azo dyes in food preparation, especially those proved to have carcinogenic action, sounds unpleasant, there is probably no great cause for alarm. Primary hepatic carcinoma, which some of these dyes have been shown to produce in rats, is a rare condition in this country. In some tropical and subtropical countries, however, this morbid condition is common, although the amount of azo dyes consumed is probably *nil* or negligible. There is indeed evidence that in these latter countries hepatomas are the result of malnutrition, and seem to be associated in some way with a low-protein diet deficient in riboflavin. Thus the incidence of primary liver carcinoma throughout the world gives no support to the view that azo dyes in the food can be incriminated as a direct cause of the disease in man. While this is true, the only practical method of dealing with the problem is surely to exclude from human diet the dyes which are known to have such effects on animals, and it would also be advisable to have other dyes tested on animals *before* they come into use and not after their adoption.

Chemical Substances used in the Preparation of Bread and Cakes

These foodstuffs are so largely eaten that they demand particular attention, especially as they are probably more treated by chemicals than any other articles of dietary. Many of the chemical agents used seem to make the end-product more palatable to the average man or confer some benefit on the food. Some of these benefits, such as anti-staling and anti-rancidity, are of real value, while others only increase the aesthetic qualities of the product to the consumer.

Bleachers and Improvers

The following substances are used as bleachers and/or improvers: Nitrogen trichloride (NCl₃), chlorine dioxide (ClO₂), nitrosyl chloride (NOCl), nitrogen peroxide (NO₂), chlorine (Cl₂), potassium persulphate, ammonium persulphate, potassium bromate, benzoyl peroxide (C₆H₅CO)₂O, calcium acid phosphate, calcium sulphate, ascorbic acid, succinic acid. Some of these substances (for example, NCl₃ and ClO₂) are both bleachers and improvers, some are only bleachers (NO₂, benzoyl peroxide), and some are only improvers (ascorbic acid, ammonium persulphate, potassium bromate).

The use of bleachers is claimed to be directly due to the preference of consumers for white rather than coloured bread. The same reason is offered for the preference for bread made from flour of low extraction,

as in this case the coloured portions of the grain—namely, the germ, aleurone layer, and bran—are eliminated. Although there may be some doubt about the direct and indirect harm bleaching does to the nutritive value of flour, there is no doubt that the removal of the germ and aleurone layer definitely lowers the value. As regards bleaching, the only observation I can make is that in my experience some bleached flour has a smaller amount of vitamin-A precursor, probably carotene, than unbleached flour. The amount of vitamin-A precursor in flour is very small in any case, and for people on a mixed diet its loss is probably of little significance. As for white flour of low extraction, it must be stated that, apart from any aesthetic attraction to the consumer, the miller has strong economic reasons for advocating it, for the wheat offal has a high value as an animal feeding-stuff.

From the point of view of the State the question of bleached flour reduces itself to the practical one, Would the non-fulfilment of the preference of the average man for white bread by supplying him with a nutritionally better but slightly coloured loaf be harmful? Surely the answer to the question was supplied during the war, when bread, even though it was made of flour of 85% or higher extraction, and was distinctly coloured, was eaten with pleasure by the vast majority of a remarkably healthy population.

The question of the use of flour improvers is also difficult. These substances make the loaf lighter by allowing more air and gas to be incorporated in it. Thus loaves of unit volume made from improved flour will contain less flour and more air and water than loaves made from untreated flour of similar size. It is said that the loaf volume is increased by improvers by 15–20%. Here again many people prefer these lighter loaves, as they are more easily masticated and pleasant to the mouth. If people prefer to eat bread which contains less sustenance and nutritional value per unit volume, it is difficult to see what can be done about it apart from official action. Both the producer and consumer seem satisfied—the one because he can make more loaves out of a given quantity of flour, and the other because he is prepared to buy bread of less nutritional value which he likes. The lower nutritional value of the improved loaf will alone cause the consumer to buy more bread to satisfy his needs. I shall return to this point later.

Toxic Effects of Agenization

How about the possible toxic effects of such chemical additions to flour? Although several official inquiries on this subject have been made in past years, it has only recently become one of great public interest, since the discovery that agenzized flour (treated with NCl_3) causes hysteria or running fits in dogs. In the U.S.A. this discovery has led to an official decision on the part of the Government to exclude the use of agene as an improver—a decision which was quickly acted upon. Although a similar decision was made in this country some years ago, it has not yet been implemented, but no doubt in the future the agene process will also disappear from the United Kingdom, and it may be replaced by some other method of improving flour. In the U.S.A. nitrogen trichloride as a flour improver has been replaced by chlorine dioxide. Many tests have been made with ClO_2 -treated flour, and up to the present no harmful effects have been observed in animals. No decision

seems to have been made in this country regarding the improver to be used as a substitute for the agene process.

Those who favour the retention of the agene process or think that there is no need to hurry its ban from the milling industry point to the absence of evidence that agene-treated flour has a toxic action on man. It is quite certain that different species of animals differ greatly in their susceptibility to agenzized flour, but it is equally true that no species of animal yet tested with the active principle—methionine sulphoximine—has failed to show severe toxic symptoms of the central nervous system when these tests have been systematically made; and it would be remarkable if man were an exception, especially if the dosage were raised. Monkeys are said to have about 100 times the resistance of dogs to methionine sulphoximine, and it is possible that man has a similar resistance as regards acute reaction to this substance. Nothing is known of the chronic toxic effects of agenzized flour, and it may well be a matter of some importance to individuals who have been living on bread made from agenzized flour over periods up to 25 years.

We certainly have enough chronic degenerative diseases of the nervous system of unknown aetiology to suggest that this matter is worthy of consideration. The present apparent official complacency to the ingestion of agenzized flour in this country is disturbing, not only in itself, but because it indicates a reluctance to consider seriously the wider problem of chemical manipulation of food and its relation to health and disease. As agenzized flour was widely consumed for nearly 30 years before its toxic action was discovered, it is very difficult to exonerate other improvers, even if in their case no harmful effect has yet been discovered. As stated previously, it is the unexpected that so often happens in matters of this kind.

Apart from the question of direct toxic action of the chemical improvers and bleachers added to flour or of any toxic agent they may produce in their reaction with the constituents of the flour, there is an aspect of the subject which does not seem to have been investigated. I refer to the possibility of the production of substances in these reactions whereby the availability or physiological use of essential factors in bread is modified. On the agenzized flour analogy, where the NCl_3 clearly destroys some or much of the methionine of the gluten in the development of the toxic methionine sulphoximine, it would not be surprising if, for instance, it were found that others of these improvers and bleachers destroyed or modified one or more of the essential amino-acids of flour protein so that they became physiologically unavailable.

It may be added that one of the difficulties in dealing with this subject is that both millers and bakers use improvers—the millers generally under controlled conditions, the bakers sometimes in a more haphazard and indiscriminate way to produce a particularly desired property in the loaf according to the kind of flour at their disposal. The end-result is that by the time the loaf reaches the consumer its earlier chemical treatment and the results thereof must often be a matter of conjecture.

Probably enough has been said about improvers and bleachers of flour to suggest that the chemical manipulation of flour still requires further investigation, and that this practice should not be accepted uncritically as a safe and desirable food-processing treatment.

Replacement of Natural Fats in Food by Chemical Emulsifiers

One of the most remarkable groups of chemical substances introduced into food processing is that of "surface active" agents or emulsifiers. These fall into four classes: (1) mono- and di-glycerides of natural fatty acids; (2) a class of compounds produced by the reaction of sorbitol (a sugar alcohol) with a fatty acid; (3) compounds formed by the reaction of a sorbitan ester of a fatty acid with polymerized ethylene oxide; and (4) polyoxyethylene monostearate (by varying the fatty acid or the length of the polymerized ethylene oxide chain many compounds can be formed).

It was found in 1937 that by the use of the mono- and di-glycerides bread, buns, cake, and other sweet goods became more "tender." In 1947 the polyoxyethylene monostearate type of compound began to compete with the mono- and di-glycerides as bread softeners. In addition to their shortening and anti-staling effects, these substances are used as emulsifiers in preparing cake mixes and ice-cream, and also as dispersing agents in flavours, essential oils, and polyvitamin preparations.

As regards possible toxic-action, no evidence of any such effect has been ascribed to mono- and di-glycerides even when ingested in large quantities. In the case of polyoxyethylene compounds there has been much controversy about their safe use in foods. This will be referred to only briefly, as the experimental evidence seems so conflicting. Polyoxyethylene glycols of molecular weight 1,250-3,600 have been used both in foods and in cosmetics. No ill effects were produced in rats when large quantities (20 g. per kg. per day) were included in the diet over a period of three months (Smyth *et al.*, 1942). Dogs were found to excrete the substance unchanged, so that it is evident that they do not depolymerize the compound into the poisonous ethylene glycol (Shaffer, Critchfield, and Carpenter, 1948). The same facts were shown to hold also for rabbits and man (Shaffer, Critchfield, and Nair, 1950).

The danger in such cases is the presence of the polymers of ethylene glycol in the less pure preparations. Here in fact is one of the many instances in food and drug work which show how essential it is to use chemicals of the highest purity; otherwise the effects may be disastrous. Medical men will need no reminder of the many deaths which resulted from the brief life of elixir of sulphanilamide when diethylene glycol was used as the solvent. This is a lesson which needs emphasizing in the case of all food adulterants.

Polyoxyethylene sorbitan monolaurate has been given to rats as 0.5-2% of their diet during their lifetime without obvious toxic effect, and 1 g. daily has been given to four monkeys without producing toxic effects (Krantz *et al.*, 1948). When the monostearate was incorporated at levels of up to 25% in the food of young rats, nasal haemorrhage, gangrene of the tail and legs, severe diarrhoea, and vesical calculi developed. At the level of 12.5% the rats were unaffected (Harris, Sherman, and Jetter, 1950). Evidence, however, has been more recently forthcoming to show that polyoxyethylene monostearate fed to hamsters at a level of only 5% of the diet was harmful in that some of the animals died, and in the surviving animals the growth was less than in the control animals given lard (Schweigert, McBride, and Carlson, 1950). Erosion of the mucous membrane of the intestinal

wall was one of the pathological lesions produced (Wang, McBride, and Schweigert, 1950).

Coppock (1950), reviewing the evidence of the recent U.S.A. Bread Hearings, states that many of the polyoxyethylene compounds, including polyoxyethylene sorbitan mono-oleate and polyoxyethylene stearate, do not give rise to any obvious acute symptoms after oral administration, but that there is some evidence, both from animal experiments and from human studies, that gastrointestinal disturbances occur. On the basis of the available evidence the Committee on Food and Nutrition of the U.S.A. has recommended that, until a uniform material is produced which conforms to a specification known to relate to a non-toxic product, these substances should not be used in the making of such a staple dietary product as bread.

According to the *Federal Register*, August 8, 1950, the U.S.A. Food and Drug Administration has proposed that lecithin and the mono- and di-glycerides of fat-forming fatty acids alone shall be permitted in the shortening used in American bread. The amount of the glycerides is restricted to a maximum of 25% by weight in the fat. No other surface-active compounds are recommended. Polyoxyethylene stearate, sorbitan esters of fatty acids, polyoxyethylene sorbitan esters of fatty acids, and the glycerides of acetylated tartaric acid are specifically excluded. Again we must await the official British reaction to the U.S.A. decision.

Reduction of the Nutritive Value of Food by Chemicals

Some of the actual and potential toxic actions of chemicals used in food preparation having been briefly discussed, let us now turn to the second problem—namely, the reduction of food value by these substances. There are instances in which chemical adulterants interfere with the absorption of essential factors of the diet, but this is not the type of case to be discussed now. The point to be considered is the situation caused by discoveries that some chemical agents of no use nutritionally to the body can confer on food preparations pleasant and acceptable gustatory properties which have previously been given to food by natural ingredients. The substitution of saccharin and other chemicals for sugar has already been mentioned.

Up to 1945 mineral oil was widely used throughout the country as a substitute for fat. For many years it had been used as a substitute for olive oil and other natural vegetable fats in salad dressing. During the war it became a popular ingredient of cakes as a fat substitute, and undoubtedly improved their texture and made them more acceptable than otherwise would have been the case. Mineral oil is for the most part passed through the alimentary canal unchanged and is a popular laxative. Its use in the U.S.A. was forbidden as a food adulterant not because it had no food value or because it was a laxative, but because it interfered with the absorption of vitamin A and caused in some infants a lipoid pneumonia. No doubt similar reasons formed the basis of its official rejection here. At the present time the use of mineral oil is confined to the greasing of baking-tins so as to prevent sticking.

But the introduction of polyoxyethylene derivatives and other substances as fat-sparers has raised this aspect of food treatment to a major issue. The Director of the Fats and Oils Branch of the Production and Marketing Administration of the United States Department of

Agriculture recently testified that the pre-war average use of fat per pound (454 g.) of flour in the baking industry was about 4% for bread and rolls; and that after the war and the introduction of emulsifiers the evidence indicated that the proportion was reduced to 1.5 to 2%. With the 2% figure this would amount to a reduction in the use of fat by the baking industry in the U.S.A. of about 160,000,000 lb. (72,575,000 kg.) annually. The proportionate reduction in fats used in baking by these fat sparers is probably not so large in this country, because bakers do not usually use the high amount of fat in bread-making as in the U.S.A., but still the principle is the same.

In addition these surface-active emulsifiers have the same property of increasing the size of the loaf as the improvers mentioned above. Thus Coppock found that, whereas the average volume of a loaf made without the addition of substances of the glyceryl monostearate type was about 1,358 c.cm., when these substances were added to the extent of 0.3% of the same flour weight the volume of the loaf increased to about 1,480 c.cm.—a reduction of 9% in the nutritive value per unit volume of the loaf. Coppock also found that by the use of polyoxyethylene stearate (0.5% of the flour weight) the average volume of the loaf was increased from 1,364 c.cm. to 1,651 c.cm.—that is, a reduction in the nutritive value per unit volume of loaf by about 20%. It is clear, therefore, that, quite apart from any question of toxicity, these anti-staling and crumb-softening agents have two actions which can be used to reduce the nutritive value of the loaf or other baking products. In the first place, as anti-staling and shortening agents they can replace fats, and, secondly, by increasing the volume of the loaf they reduce the food value per unit volume by a significant amount.

Summing up all these effects of flour treatment on the ultimate constitution of the loaf, we see that improvers used by millers might be expected to reduce the total energy value per unit volume of loaf by about 15 to 20%, and the baker's use of anti-staling agents by 9% up to 20%. In addition there is the possibility, just discussed, of substituting for fat in many foods the new emulsifiers. To this might be added the 10% reduction in protein value of flour by the proposed lowering of the extraction rate from 85% to 72%, together with the loss of mineral elements and of vitamins and probably many other unknown essential food factors. Many of these effects are additive and will undoubtedly result in products which are lighter, whiter, and more easily masticated, but of considerably reduced food value.

A worker in this field recently suggested that the ultimate goal of this general trend would probably be reached when a bread substitute made up primarily of starch, air, water, polyoxyethylene stearate, and a little saccharin was found acceptable to the general consumer. This exaggerated statement at least suggests the magnitude and importance of the present problem, and the time has come when the question of depressing the nutritional value of food as against the benefits brought by the use of chemical agents, even harmless chemical agents, will have to be decided.

Pesticides and Food Crops

Although there is general agreement that most food crops require the use of pesticides, the recent introduction into agriculture of some very toxic and effective substances of this class has raised much misgiving among

health authorities. These include D.D.T., the first of the chlorinated hydrocarbon insecticides; chlordane, another insecticide of the same class which is four to five times as toxic as D.D.T.; and selenium compounds. Phenyl mercury compounds are used as fungicides on fruit and vegetable crops. It has been pointed out that as little as $2\frac{1}{2}$ parts of chlordane per million in the diet produces pathological changes in the liver in rats, that 3 parts of the selenium compounds per million in the diet will produce cirrhosis of the liver and, if continued, cancer of the liver in animals; and that in the case of phenyl mercury compounds as little as 0.5 part of mercury per million in the liver in the form of phenyl mercuric acetate leads to measurable storage in the kidney with damage to that organ in animals.

The great drawback to the use of D.D.T. is that it is absorbed and stored by the body in the fatty tissues, and above a certain point of accumulation it injures the animal. Five parts in a million in the diet of rats produces definite liver injury (Laug, Nelson, Fitzhugh, and Kunze, 1950). Cows sprayed with D.D.T. or given silage which has been sprayed with it, or even housed in a barn in which it was sprayed, accumulate D.D.T. in their fat and eventually excrete it in the milk. The recent report from the U.S.A. that considerable quantities of D.D.T. have been found in the fat removed at operation from ordinary citizens is disturbing (Laug, Prickett, and Kunze, 1950).

But none of the above-mentioned chemical agents used as insecticides and fungicides have the intense toxicity of the organic phosphorus insecticides, the discovery of which as poison gases by the Germans led afterwards to their introduction to agriculture as insecticides and present extensive use throughout the world. Pharmacologically they are of great interest because they have an anti-cholinesterase action. While much is known about the acute toxic symptoms they produce, we have no information about the chronic effects. They are very useful in the control of a wide variety of pests such as aphides and red spider, and are of particular value against insects which may be resistant to D.D.T. and the older insecticides. As the action of many of these new insecticides depends on their absorption by the growing plants, the question of the effect on the consumer of eating such plants and their products, together with their spray residues, is clearly one of great importance. Sometimes the residues remaining on fruit and vegetables after spraying are high, and become particularly dangerous when they penetrate their skin. Thus it is said that selenium compounds accumulate in the apple in amounts up to 3 parts per million, a concentration which is known to be dangerous.

This subject is too big to discuss further here, but it may be stated that the official world that considers these matters must be cognizant of the dangers, because many people engaged in the preparation and use of these substances as insecticides have already been killed or injured by them (Bidstrup, 1950). The question is, What happens to the consumer?

Conclusion

Although it has been possible to consider only a few instances of the use of chemicals in food preparation and production, enough may have been said to show the vastness and importance of a problem closely bearing on the public health. The triumph of medical science in the prevention and control of disease during the present century has been impressive, and care must be

taken that, at the time of gaining such control, new habits of living which cause ill-health should either be prevented or, if they arise, be controlled. Such errors in living are undoubtedly developing at the present time, and it is the duty of medical science to find out their relative disease-producing importance. The chemical manipulation of food may well be the basis of some of these errors, and the problem requires investigation.

Official inquiry—both laboratory and judicial—and control want strengthening. There ought to be a practical counterpart in this country of the Food and Drug Administration of the U.S.A., in the form of either a public institute for such work or an extensive and close liaison with other institutions capable of making the necessary investigations. Official direction and control of, and responsibility for all such matters should ultimately be placed with the Ministry of Health, as this is fundamentally a medical problem. Apart from chemicals long in use, a decision ought to be made on whether any new chemicals should be allowed in food processing and production before they have been adequately tested for their toxicological effects. No use of chemicals based on effective aesthetic or even practical advantages conferred on food by these substances should be countenanced if they have harmful effects on animals; and, apart from questions of toxicity, the present trend of lowering the nutritive value of extensively eaten food such as bread, both by chemicals and by other forms of manipulation, demands attention.

One final suggestion is that if people want bread which has not been chemically treated in any way they ought to be able to purchase it. This is no doubt possible in the case of wholemeal bread, but the same ought to apply to bread made of flour of lower extraction. At least untreated flour of this kind ought to be freely available so that persons can bake their own bread if they wish.

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ACUTE TUBERCULOUS SEPTICAEMIA
WITH LEUCOPENIA

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Acute tuberculous septicaemia presents as an obscure clinical picture, with pyrexia, severe leucopenia, and a rapid downhill course. No case so far recorded has been diagnosed during life, but in view of the possibility of chemotherapy an early diagnosis is very desirable. Three cases will be described. They were observed on the same medical unit within four years, which alone suggests that this form of tuberculosis is commoner than is usually believed.

Case 1

A plasterer aged 54 was admitted on April 17, 1946. He had been well until three weeks previously, when he developed rigors followed by severe sweating. The personal and family histories were not significant. On examination he was very ill. He had herpes labialis, a furred tongue, and petechiae on the chest. There was an impaired note with diminished breath sounds at the right base. No abnormal signs were present in other systems.

White cells numbered 925 per c.mm. (neutrophils 72%, lymphocytes 21%, monocytes 5%, eosinophils 2%). The white cells rose later to 1,100 and 1,450, with 86% neutrophils on each occasion. Haemoglobin, 89%; red cells, 4,400,000; colour index (C.I.), 1.0. Sputum gave a growth of *Staph. aureus* and pneumococci. No tubercle bacilli were seen. X-ray films of chest showed some consolidation at both bases.

His temperature was irregular up to 101° F. (38.3° C.). A diagnosis of pneumonia with leucopenia was made, and he was treated with penicillin and liver extract. He steadily became worse and died on April 24.

Summary of Necropsy and Histological Findings

(For anatomical details, see Blair and Pagel, 1947.) The main feature was the presence of extensive naked-eye changes in the spleen, liver, and mesenteric lymph nodes. There were areas of necrosis full of acid-fast bacilli and devoid of the classical tuberculous cells. The shadowy preservation of the organ structure in the necrotic areas suggested that it was an example of "direct necrosis." (For definition, see Case 3.)

Careful dissection and post-mortem radiography failed to detect any traces of old or fresh tuberculous changes in the lung. Extensive fresh caseation of the mesenteric lymph nodes, however, suggested that the intestinal tract was the portal of entry.

The numerous areas of necrosis full of tubercle bacilli which were present in the marrow of the sternum and the femur were regarded as the cause of the leucopenia.

There was haemorrhagic consolidation of the basal part of both lower lobes. The alveolar exudate was full of cocci, but no acid-fast elements were seen.

Tubercle bacilli of human type were recovered from a mesenteric lymph node.

Case 2

An insurance agent aged 56 was admitted on May 5, 1947. He had been well until one month previously, when he had fainted in the street and bruised himself. He later developed a rash on his face, arms, and legs, and twitching of the face.