

## Editorials



### Reactions to food additives

Food additives are used in or on food (at any stage) to affect the keeping quality, texture, consistency, taste, odour, alkalinity or acidity, or to serve any other technological function in relation to food (Labelling in Food Regulations, 1984<sup>1</sup>). In other words, they make a food look, taste or smell better or improve its texture or keeping qualities (see Table 1). Some of these miscellaneous substances prevent the deterioration of food or its contamination with bacteria or fungi. Others, such as colouring agents, could be omitted without difficulty. The claim that all additives are harmful and unnecessary is not, however, tenable.

Since the safety and the usefulness of additives needs to be carefully assessed, this means that the regulating authority may have to evaluate about 350 preservatives, colouring agents and other substances together with perhaps 3000-4000 flavouring materials which are also known to be capable of provoking skin reactions but have yet to be studied in detail. It is also necessary to check on contamination with pesticides or veterinary drug residues<sup>2</sup>, which may persist from an early stage of food production.

Many widely used substances have a 'GRAS' status (generally recognized as safe) in the USA. New ingredients require much more rigorous testing, first by demonstrating the efficacy and need for a new substance, then by tests of biological safety which involve long term feeding studies in animals and may require the expenditure of several million pounds before the required approval is given by the EC Scientific Committee for Food and the United Nations Joint Expert Committee on Food Additives. Despite these rigorous precautions, concerns about reactions to food additives have increased. An additional safeguard has also been added, and an indication about the presence of additives is now required for the benefit of those who are known to be sensitive to particular additive substances. In the United Kingdom, the 1984 Regulations require that labels should indicate the presence of colouring agents, preservatives, antioxidants, emulsifiers, stabilizers,

sweeteners, and a host of other agents. Code numbers have been allotted, with the prefix 'E' if the substance has been approved by the European Community.

When the wrappers of food began to list the name and code number of additives, many members of the public became aware of them for the first time. E numbers came to be seen as representing an aspect of food technology which has since become the focus of concerted campaigns which have been highly critical of the steadily increasing use of these substances. Some critics estimate that the average intake of food additives now amounts to about 6-11 pounds each year (Ass CC Publications 1987).

#### Old or new?

The natural shelf life of most food is very short. Two traditional preservative methods, salting and pickling, go back some thousands of years. The first depends on reducing the water content of food by its high osmolarity, and this interferes with the microbial, chemical and enzymatic reactions which are the chief causes of food deterioration. The second depends on a direct antibacterial action and could be regarded as the forerunner of all the vast range of preservatives which have been developed since. Sucrose, glucose and more recently, propylene glycol, act in the same way as traditional salting methods. They have the effect of binding water and so making it less available to support bacterial growth.

The preservatives help to prevent food decay and the spread of food born infection. Traditional preservatives include ascorbic acid derivatives (E200-203), used mainly in cakes and baked foods; benzoic acid and the parabens (E200-E219) which are used in processed fruits, jams and soft drinks; and sulphur dioxide and sulphiting agents (E221-E227), which are now the most widely used of all.

#### Which additives have been shown to cause reactions

Sulphiting agents have been used for a hundred years to prevent the oxidation of oils and fat and to prevent enzyme effects from discolouring foods. It is now well established that in some people they can, however, cause flushing, itching of the mouth and skin, and asthma. About 5% of the asthmatic population can have an asthmatic attack provoked by sulphites, to a degree which may be life threatening<sup>3</sup>. The US Food and Drug administration has now banned their use in 'fresh' fruit and vegetables but substantial quantities are present in wine and other drinks, in shrimps and processed potatoes, and their use in nebulized drugs has also caused problems.

Other preservatives include the nitrates (E249-E252), which help to give preserved meats their pink colour but can also cause flushing and giddiness. Sodium nitrite is a vasodilator and a dose of 20 mg is reported to be capable of causing headache, skin rashes and gastrointestinal symptoms<sup>4</sup>. Twenty milligrams is within the range which might be encountered in food.

Table 1. Examples of food additives

Function	Category	E numbers
Keeping properties	Preservatives	E200-E321
	Antioxidants	
	Acidity regulators	
Improved appearance	Colours	E100-E180
Modified consistency and texture	Emulsifiers	E322-E495
	Stabilizers	
	Thickeners	
	(Sweeteners)	

Colouring agents include the coal tar dyes, such as the well known tartrazine (E102), sunset yellow (E110), amaranth red (E123), brilliant blue (E133) and erythrocin (E127), of which about 60 tons are manufactured each year in the United States. Tartrazine can undoubtedly provoke urticaria and this has been confirmed in double blind studies of patients with the chronic form of the disease<sup>5</sup>. This is relatively uncommon, however. After extensive testing Murdoch and his colleagues<sup>6</sup> could find only two cases in which tartrazine or other azo dyes were capable of provoking an attack. There is no evidence in Sweden, where the use of tartrazine has been banned, that there has been any reduction in the prevalence of urticaria, asthma, or the conditions which have attracted the most sensational claims in respect of tartrazine - that is, hyperactivity and the childhood behaviour disorders.

A number of other additives can cause adverse reactions. Butylated hydroxyanisole and butylated hydroxytoluene are antioxidant substances that prevent food becoming rancid. They aggravate urticaria in occasional cases<sup>7</sup>. Benzoates can do the same<sup>8</sup>, and children who smear benzoates or ascorbic acid-containing food around their faces sometimes have local skin reactions in the contact areas<sup>9</sup>. High concentrations of the flavour enhancer monosodium glutamate can also cause problems<sup>10,11</sup>, although the central chest pain which has been linked with Chinese restaurant food is probably due to the high concentration of an irritant substance rather than an allergic reaction.

On investigation, most of the reactions which have been described appear to be due to irritant or pharmacological effects. Evidence of a classical IgE-mediated allergic reaction is rare. Nevertheless proteins, such as the proteolytic enzymes which are used as meat tenderizers, are certainly capable of causing immunological reactions<sup>12</sup>. It is possible that a number of flavouring substances may also act through an immunological mechanism when they provoke an exacerbation of a pre-existing eczema<sup>13</sup>. The flavours which have been identified in this context include a number of natural substances, especially balsams and resins (including ginger resinoid), cinnamon, vanilla, lovage, and oils of juniper, spearmint and caraway. Since they are often present in chocolate and other beverages, flavoured ice cream and toothpaste, sausages (containing oil of juniper), and confectionery, drugs and tobacco (containing lovage), their potential effects in eczematous patients deserve to be more widely known, especially as they are not as yet identified specifically on a food contents label.

Allegations concerning food additive reactions are nevertheless more often false than true. Aspartame, which was thought to be responsible for two urticaria cases<sup>14</sup>, may have been falsely accused, since Garriga<sup>15</sup>, who screened 61 individuals suspected of suffering from aspartame-provoked symptoms, was unable to confirm this suspicion in any of these cases by means of challenge tests. Despite the negative results of this further investigation, the potential for causing public anxiety and the emotive aspect of food additive reactions were underlined by this report. The sales of aspartame plummeted, and those concerned with the marketing of other sweetening agents may well have derived some comfort from the suspicions cast upon their rival.

### Estimates of prevalence

There have been numerous errors in estimating the prevalence of reactions to food additives, and those who consider that they themselves have reacted to a food additive are seldom proved right. When Kerr and his colleagues<sup>16</sup> were concerned about the adverse effects of monosodium glutamate, they designed a questionnaire which listed 18 food-associated symptoms, of which chest tightness, facial burning and numbness were thought to be suspiciously associated with the adverse effects of this agent. Of those who answered, 6.6% gave positive replies which appeared to justify an enquiry about a second set of specific symptoms, and they were also asked if they had heard of the 'Chinese restaurant syndrome'. The same respondents gave answers suggesting that in 31% of cases there were adverse effects related to restaurant food. A subsequent study which avoided the use of leading questions<sup>17</sup> reduced the figure of 6.6% with 'possible Chinese restaurant syndrome' to 1.8%. Of this smaller number, 2.3% (instead of 31%) were convinced that they had adverse effects related to restaurant food.

After taking account of the problems of self diagnosis and making allowances for those who failed to respond to an initial questionnaire, Young *et al.*<sup>18</sup> (personal communication, 1992) identified individuals whose symptoms were sufficiently suggestive of adverse reactions to food or food additives to justify proceeding to double blind challenge tests. Only three (out of a sampling population which initially consisted of 30 000 people) had reactions which they were able to confirm by challenge testing. While this figure was regarded as an underestimate, they subsequently found that adverse reactions to common foods occur in 1.4-1.9% of the population, representing a considerably higher prevalence than the reactions to food additives which they were able to identify.

Negative double blind challenge tests results with food additives do not entirely exclude the possibility that an earlier adverse reaction may have occurred. It is known that patients whose initial challenge tests give positive results may lose their reactivity or at least develop a reduced sensitivity<sup>19</sup>. The adverse effects of food additives may also require the potentiating effect of exercise, psychological tension or, in the case of asthma, the inhalation of an additional irritant substance<sup>20</sup> before they can be demonstrated. Definitive tests for the diagnosis of food additive reactions, whether IgE-mediated or not, have yet to be developed.

### Conclusion

The food industry has begun to respond to public concerns about the unnecessary additive content of food products, and regulatory authorities have also insisted on a reduction of the use of sulphites (in the USA) and tartrazine (in Scandinavia). For the general public, however, permitted food additives have a substantial safety margin. There is no evidence to support the claim that these substances cause a large number of illnesses in the population at large which could be avoided by 'natural' foods. On the contrary, the removal of additives which improve the keeping properties of food can add to the increasing dangers of food-transmitted infection, which are still several thousand times more frequent than reactions provoked by food additives.

Food labelling can be of great value to those with a degree of sensitivity which makes it necessary for them to avoid particular substances, and further studies are certainly needed to identify the nature of the reactions which occur. There is no justification, however, for the alarmist advice which has led vulnerable people with vague symptoms to adopt inadequate, restricted diets which are themselves a cause of disease. It is a matter for concern that parents who are worried about behaviour disorders in their children or what they consider to be hyperactivity can sometimes be led to impose an obsessional dietary regimen on an already disturbed child. While increased parental attention may be beneficial in such cases, food prohibitions on the basis of an unconfirmed diagnosis cannot be justified.

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#### Diet and coronary heart disease: why blame fat?

The article by Gorrings<sup>1</sup> reminded us that coronary heart disease (CHD) is one of the diseases associated with affluence, and that it is more prevalent in populations with a high standard of living than in those with a low standard. This is reflected in the higher prevalence of CHD in countries where cigarette smoking is high and where many people have motor cars, radios and television.

Gorrings properly points out that such statistical evidence from populations does not prove cause, but it is not only in populations that they occur. Individuals that smoke have a higher risk of developing CHD than do non-smokers. And people with cars, radios and televisions are likely to be less active physically than those who do not, and physical activity is now also accepted as a risk in developing CHD.

As regards diet, differences between wealthy and poor populations are so numerous that it has become necessary to try and isolate those items and processes that are harmful; the current view is that it is dietary fat, especially the saturated fats, that are the dietary cause of coronary heart disease.

A more careful examination of the diets is needed in order to ensure that we have isolated the true positive items.

There are two characteristics of coronary heart disease that have to be considered in seeking a dietary cause of the disease. These are: (1) the abnormalities in the blood and (2) the clinical relationship between coronary heart disease and other diseases.

It is common to point to the raised blood concentrations of cholesterol as being the underlying cause of CHD. Other blood abnormalities include an increased concentration of glucose, triglyceride, uric acid and insulin; there is also a decreased concentration of high density lipoprotein<sup>2,3</sup>. Other changes are a reduction in glucose tolerance, an increase in insulin resistance,