

Enamel Protective Factors in Food

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There is almost universal agreement that caries is a disease of westernized conditions,¹ although many of the data are uncritical or were collected inexpertly by archeologists and anthropologists. Although it is reasonable to assume that the chemical changes of the diet explain this effect of westernization, other aspects of feeding, such as, the timing of meals or the toughness of food or even nondietary differences, are difficult to exclude completely. There is no reason to believe that the same factors operate in all instances; eg, the traditional diet of the Eskimo contained no sugar and indeed virtually no carbohydrate, whereas the native diet of the African Bantu is high in carbohydrate, consisting largely of unrefined mealie meal.

Clinical Data on the Effect of Westernization

The clinical data of Osborn and Noriskin² on caries in the Bantus on native or European diets were carefully collected but do not show a really dramatic difference in incidence, eg, 43% of 143 who stated that they never had European food had caries, compared with 57% of 44 who ate European bread regularly. The data suffer from several defects, such as the ignorance of the Bantus about their own ages and reliance on their own testimony about the nature of their diet.

Turner and Vickery³ reported an attempt to study the effects of white and whole meal flour on caries. The DMF scores among a group of 94 British children between 1 and 18 years old who had always eaten whole meal bread were compared with those from several typical British groups (eg, the controls in the fluoridation studies). The results did show considerably less caries in the whole meal group: DMF scores for the 5-, 6-, and 7-year-old children were below three

in the whole meal group and between five and seven in the control groups. Unfortunately, these results cannot be taken at their face value, because 64 of the children were attending a "food reform school" at which the diet presumably differed from that eaten by the controls in several respects other than containing whole meal bread. The parents also stated that they "enforced significant control over the intake of sugar," which would obviously confuse the issue.

The effect of raw sugar cane on caries is even less substantiated. Most of the clinical data are impossible to interpret, because no comparisons were made between caries incidence in workers in sugar-cane plantations who ate much raw sugar and subjects who ate the same quantities of refined sugar with the same frequency during the day. It is not disputed that a high caries incidence can occur in sugar-cane eaters^{4,5} so that crude cane cannot exert dramatic over all protection but, in the absence of a suitable control, it is simply not known whether crude cane exerts any protective influences at all.

Animal Experiments on Protective Factors in Unrefined Foods

Earlier animal experiments in which refined or unrefined cereals or sugars were tested for cariogenicity were contradictory⁶⁻¹¹ but tended to support the presence of protective factors in the unrefined foods. These experiments were indecisive, however, because no evidence was presented on whether the diets were adequately matched for such factors as viscosity and taste or for the size and hardness of the particles, points which, it is now realized, could have had a crucial influence on cariogenicity.

The same criticism applies to some of the more recent work of Strålfors, which, on face value, suggested that cocoa¹² and "crys-

tallised brown sugar¹³ obtained from beet contained protective factors. König and Mühlemann¹⁴ repeated these tests with rats fed on a feeding machine; they used the same sugars used by Strålfors,¹³ in which the unrefined particles were coarser than the refined, and both sugars were ground to the same particle size. When the unrefined sugar was coarse, the reduction in caries score was similar to that found by Strålfors,¹³ but when both sugars were ground to the same particle size, no difference in score was found. The result was the same whether the diet was fed ad libitum or with the number of meals restricted (ie, a reduced food intake did not influence the results). They considered that the particle size of the unrefined sugar had affected the result. Since food intake had not been lower in the group on unrefined sugar, presumably the taste had not influenced the result. Strålfors¹³ did show, however, that when the sugars were dissolved in the drinking water, or included in cakes, the rats that received the unrefined sugar sustained a lower caries score. Since feeding cubes of the raw sugar beet did not reduce caries but tended to increase it, Strålfors¹³ concluded that cariostatic factors not present in the original beet are formed during the refining process.

König¹⁵ compared caries development in rats on white and brown bread and found consistently that brown bread produced slightly more caries than white bread, although the caries score on both was low compared with the score of rats on sugar diets. He explained this result on the basis that starch had a low cariogenicity and that the higher vitamin content of the brown bread slightly stimulated bacterial activity.

As a follow-up of some indecisive suggestions in the Vipeholm experiment¹⁶ of an anticaries effect of chocolate, Strålfors reported experiments in which 20, 10, 5, and 2% of cocoa¹² and 20% of milk or dark chocolate¹⁷ were included in the diet of hamsters. Large reductions in caries were found (of 84, 75, 60 and 42%, respectively, with the cocoa and 35 and 73% with the chocolate). The effect was not caused by the fat in the cocoa, since it was still present with de-fatted cocoa; furthermore, 15% cocoa butter added to the diet had no protective effect but increased caries. Aqueous extracts of cocoa and the extracted residue were both

active, which indicates the probable presence of two factors, some properties of which were studied. Food consumptions were not measured in most of these experiments, but body weights showed no difference, except in the group that received 20% cocoa, which indicates that there was no gross interference with the amount of food consumed. However, the possible effects of a different eating pattern or differences in the extent to which the diet was held in the mouth were not eliminated.

Strålfors¹⁸ also showed that several constituents of cocoa (0.2% theobromine, 0.2% xanthine, 0.05% vanillin, and 0.01 to 0.05 tannic acid) all reduced caries at the indicated concentrations, which did not affect food intake (higher concentrations of some of them did reduce food consumption). Aqueous extracts of cocoa have a definite effect on the solubility of apatite but negligible antibacterial activity, and an apparent small effect on acid production was for the most part accounted for by the buffering power of the extract.¹⁹

A number of investigators have reported that the inclusion of hulls from oats, rice, cottonseed, peanuts, and pecan all reduced caries in rats.^{9,20-22} The effect of the oat hulls was believed to be chemical rather than mechanical, because the anticaries action was increased, rather than reduced, by grinding the hulls finely. Nor could it be accounted for by a mere dilution of the sugar, because the addition of an equivalent amount of an inert diluent, cellulflour, had no effect. Autoclaved rice hulls had lost much of their cariostatic activity, which again suggests a chemical rather than physical effect.

Nature of the Protective Factors in Foodstuffs

After clinical observations, Osborn, Noris-kin, and Staz²³ demonstrated that unrefined cereals and sugar-cane juice contained substances that reduced the solubility rate of whole teeth when incubated with saliva without altering acid production. This has been confirmed by others,²⁴⁻²⁷ who have also shown that phytate, like other organic phosphates, possesses this property and can account for the *in vitro* effect of unrefined cereals, which are known to contain this substance. Osborn²³ suggested that organic phosphates might account for the protec-

tive effect that he observed, but he concluded (at least at one stage of his work) that these substances were broken down by enzymes of the salivary bacteria and that the inorganic phosphate released was the active substance. Andlaw²⁵ also concluded that inorganic phosphate explained the reduced solubility of the blocks of enamel that he tested in unrefined flour-saliva mixtures. This conclusion was based on the fact that extracts of wheat bran and wheat germ possessed activity after ashing, but this result may be an artifact. Not only would ashing convert organic phosphate to the inorganic form (thus raising the inorganic phosphate to much higher levels than the original extract), but some of the inorganic phosphates would be converted to pyrophosphate. Both the orthophosphate and pyrophosphate would, by different mechanisms, reduce enamel solubility (orthophosphate by a common ion effect and pyrophosphate by binding to the enamel crystals). This conversion of orthophosphate to pyrophosphate by ashing is an important potential source of error in dietary research and may have confused the results of some experiments on caries (eg, that of Nizel and Harris²⁸).

Since uncooked flour was used by Andlaw,²⁵ the enzymes of the cereal (including phytases) would be active, and the concentration of phytate would be falling and that of phosphate rising throughout the experiment. The reduction in solubility rate is about the same in experiments of this type in which cooked cereals are used, as it is when buffers are used as a solvent in place of saliva with its bacterial enzymes. Thus neither enzymic release of phosphate nor reductions in acid production are an essential part of the *in vitro* effect.²⁴ Most organic phosphates have been found to reduce solubility, but of those tested phytate is the most active, in the sense that it can work at greatest dilution because its effect is detectable at concentrations as low as 0.01 mM (ie, about 1% of the concentration of inorganic phosphorus with a similar effect). Organic phosphates appear to act by becoming adsorbed on to the enamel surface and perhaps acting as a "kink poison." After exposure to phytate, a tooth can be shown to have retained a lower solubility after thorough washing; phytate is also detectable chemically on calcium phosphate

after it has been shaken with phytate solution and washed in water. Several animal experiments have confirmed that 1 to 2% of phytate added to the diet can have a considerable effect in reducing caries,²⁹⁻³² although a negative result has also been reported.³³

Support is given to the concept that organic phosphates have protective properties by the promising reductions in caries obtained in the Australian clinical trial of calcium sucrose phosphate³⁴⁻³⁶ as an additive to sugar and the findings that calcium glycerophosphate has anticaries properties in rats³⁷ and monkeys.³⁸

It is, of course, not proved that in these clinical and animal experiments calcium sucrose phosphate or phytate reduced caries by lowering solubility, although this seems the most likely explanation, since no other property of these substances is known that could account for an anticaries effect. In none of these animal experiments were unspecific effects, such as reduced food intake, eliminated. Two reports do cast doubt on this mode of action of organic phosphates, however. McClure³⁰ found that 1:6 fructose diphosphate was the most highly effective organic phosphate in reducing caries, whereas this substance has low solubility-reducing powers *in vitro*, except in high concentrations. The second reason for doubting the mechanism of action of these substances arises from results of Tatevosian and Jenkins³⁹ on the entry of the substances into the plaque when used as additives to sugar. Subjects with 24 hour accumulation of plaque sucked sugar lumps that contained 1% of calcium or sodium orthophosphate, calcium sucrose phosphate, phytate or calcium glycerophosphate, or no additive (in the controls). Inorganic, and organic phosphates in plaque were analyzed before and two minutes after sucking the sugar. The results showed that only calcium phosphate or calcium sucrose phosphate appeared to enter the plaque in detectable concentrations under the conditions of the experiment. However, when the sugars with additives are present during plaque formation, it is possible that they may become incorporated into a developing plaque but cannot readily diffuse into a preformed plaque. With sodium phosphate, the probable reason for its failure to enter plaque is that by the time the saliva has dissolved

the sugar, it has so diluted the phosphate additive (and the phosphate of the saliva also falls with increasing rate of flow) that its concentration outside the plaque is below the already rather high concentration in plaque.

How may the positive results of phytate in animal experiments be reconciled with König's¹⁵ negative findings with animals that received brown flour? A likely explanation is that the phytate added to diets was in a soluble and available form, whereas the phytate in flour is present inside insoluble particles of bran. It is doubtful whether the food would stimulate a sufficiently brisk flow of saliva to extract the phytate and make it available to contact the tooth surface within the few seconds that it remains in the mouth. An implication of this is that phytate trapped in unrefined foods may not play a part in the low caries incidence of primitive communities but, as a soluble additive to carbohydrate, might have an application in modern caries control. More work on these substances is needed.

Thanik and Bibby⁴⁰ tested the decalcification of radioactive enamel blocks in white flour extracts and saliva with or without the addition of extracts of wheat germ or bran. The results showed that the extracts of unrefined materials reduced solubility, but there was no exact proportionality between the concentrations of calcium and phosphorus in the cereals and the reduction in solubility. This was not surprising, since the extracts would be expected to contain protective factors other than inorganic ions; although, as in Andlaw's²⁵ experiments, the uncertainties were introduced by enzymic release of phosphate and corresponding reduction of organic phosphate concentration.

Khanna and Bibby⁴¹ found that cereal products from different geographic regions differed in their powers of reducing decalcification, but the effects did not correspond with known variations in regional caries prevalence.

SUGAR PRODUCTS.—The existence of factors that reduce solubility rate in cane juice and molasses has been confirmed,⁴² although the results with molasses are confused by the presence of about 0.5% calcium, which arises from the lime added during refinement and not from the original plant. The position with crude sugar and

honey is more complicated. In buffers, honey reduces the solubility rate of enamel, but the active constituent (probably an organic phosphate) is destroyed during incubation with saliva. The powerful effect of crude sugars on enamel solubility in buffers is observed after four hours' incubation with saliva but is much reduced or abolished after 24 hours. The active constituents are probably calcium and traces of copper and iron, which are present in the crude sugar and which can simulate its action in buffers. These are less effective in saliva, especially after 24 hour incubations, because the different conditions found during prolonged incubation—lower pH and the chemical nature of the acids produced—tend to counteract the effects of these solubility-reducing actions. In addition, the greater buffer strength of the incubations containing crude sugars, compared with controls, may tend to nullify the solubility-reducing action.

ANTIBACTERIAL FACTORS IN UNREFINED CEREALS.—Taketa and Phillips²⁰ reported that alcoholic extracts of oat hulls contained antibacterial factors, partly identified as polyphenols, and assumed that they were responsible for the action against caries in animals. Neither they or others who had studied various seed hulls on animal caries investigated their action on enamel solubility, but Jenkins and Smales¹⁹ demonstrated that they all possessed water-soluble constituents that reduced the solubility rate. These authors suggested that these substances were more likely to be effective *in vivo* than antibacterial factors, which are insoluble in water or require an extraction procedure far more drastic than is likely to occur to food in the mouth. Of the materials tested in animals, only pecan nut hulls contain water-soluble antibacterial factors.

Madsen and Edmonds⁴³ found that feeding a diet containing 25% rice hulls to weanling cotton rats for as short a time as ten days reduced caries as effectively as feeding the diet throughout the whole experimental period. This high dose of what, in any case, cannot be regarded as a food, makes this a somewhat academic experiment but suggests a possible systemic effect. Could an antibacterial effect exerted over a short time have a prolonged action on caries? This is possible, since Jay⁴⁴ has

shown that drastic reduction in carbohydrate eating for two weeks can alter the oral flora for some time. It is even possible that substances that reduce solubility bind to the tooth surface and exert a prolonged reduction in solubility, a process that may or may not resemble an increase in the normal post-eruptive maturation.

Action of Major Food Constituents

ROUGHAGE.—The cellulose roughage of plant foods probably has some mechanical effect in removing plaque, and eating raw vegetable matter (eg apple, carrot, or celery) has long been recommended as a caries preventive measure. Although it is easy to observe that plaque on the smooth surfaces is removed by these procedures, personal observations agree with Lindhe⁴⁵ in showing that the procedures have little effect on cervical or interstitial plaque, which is presumably most relevant to caries. Only one clinical trial on caries appears to have been carried out, that of Slack and Martin⁴⁶ on apple rings. The results gave indications of reduced caries but were not entirely convincing, because of initial variations between the caries score of the apple and control group. Apples are a strongly acidic food (which led Stephan¹¹ to suggest that they might be a cause of erosion) and even when mixed with rapidly flowing, and therefore alkaline, saliva, the pH of the mouth contents is usually around 3.9 to 4.2 (Jenkins, unpublished results). Other tough foods (such as raw celery or carrots) have a similar mechanical effect and, although not such a powerful saliva stimulant, observations show that the pH of mouth fluids when these foods are chewed is much higher (from 6.1 to 6.50). This result suggests that celery and carrots might be more valuable in caries control than apples.*

PROTEINS.—Milk and proteins from milk and other foods have been found to reduce enamel solubility even after the teeth treated with these proteins were thoroughly washed.⁴⁷⁻⁵⁰ Presumably, the protein becomes adsorbed on to the surface and acts as a barrier between acid and apatite. Both enamel powder and blocks of enamel with the outer layer removed have been used,^{48,49}

as well as thoroughly brushed whole teeth in which pellicles were presumably intact.⁵⁰ Both groups observed a 20% reduction in solubility rate. It is not surprising that protein should become attached to the exposed apatite of ground enamel but it is unexpected that whole teeth, which must have been exposed to proteins for years in vivo, should still be influenced by in vitro treatment. Either the protein is not bound under in vivo conditions or it is readily removed even by toothbrushing. In any case, it would seem that protein can be adsorbed by pellicle as well as by apatite. Pearce and Bibby^{48,49} suggested that the higher nitrogen of early caries and possibly the greater decalcification in early caries of the deeper layers of enamel (less accessible to proteins in the oral fluids) may arise from this adsorption of protein by enamel. Whether quantitative or qualitative variations in protein intake could influence caries by the formation of these layers is unknown.

FAT.—Dietary fat reduces caries in animal experiments, but there is no clear evidence of this in man. Nevertheless, this possibility leads to a complication in interpreting certain experiments in man (eg, the Vipeholm experiment¹⁶): if carbohydrate is restricted, fat is increased to maintain the calories, thus introducing another variable. The mechanism of action of lipids is unknown, but it is speculated that they may surround bacteria and carbohydrate food, thus keeping them apart, or form an impermeable barrier on the enamel surface. Foods with a high fat content are retained in the mouth in smaller amounts than similar foods low in fat.⁵¹ Certain fatty acids (eg, palmitic) inhibit some oral bacteria, although it is unlikely that the weak lipases in saliva would be able to hydrolyze fat in the food (although the lipase activity of plaque has not been studied).

FRUIT JUICES.—Gross decalcification, usually of the maxillary incisors, that leads to rampant caries has been reported after the consumption of acid fruit juices in comforters, in "dinkie feeders," or whenever allowed to remain in contact with enamel for long periods or move over it slowly.⁵² The exact course of events is not known but it might be speculated as follows: the high acidity of the juice (pH 3 is common) dissolves the outer surface of the enamel, plaque accumulation is favored and allowed

* Since this was written, Reece and Swallow (*Brit Dent J* 128:55, 1970) have shown that eating carrots after the midday meal did not produce a statistically significant reduction of caries in schoolchildren.

to penetrate more deeply than usual into the enamel, and, perhaps supplemented by acid produced bacterially from the sugar in the juices, gradually forms the penetrating lesion characteristic of caries.

Blackwell and Fosdick⁵³ found that sugar tended to reduce the amount of enamel dissolving in acid buffer solutions and that the effect was much greater with sucrose than with the other sugars tested. It is possible, therefore, that the sucrose in fruit juices may have two contradictory effects: to reduce the action of the acid in the juices and to provide a substrate for the bacterial activity, which may be necessary to convert a superficial erosion into a penetrating cari-ous lesion.

It must be emphasized that this condition arises only from the misuse of these fruit juices; when consumed in the normal way or as directed by the manufacturers they have no adverse effect on the teeth.

There are cases on record of damage to teeth by habitual eaters of fruit, such as lemons, especially when sucked or eaten in such a way as to prolong contact with the teeth, but this is chemical erosion, induced presumably by the combined acid and chelating effects of the citrate in the fruits rather than caries.^{54,55} Stephan¹¹ found erosion from apples in rat caries and considered that any fruit with a pH below 4.5 was potentially harmful.

Interactions Between Sucrose and Enamel

It has been suggested by several investigators that sucrose may have a direct effect in dissolving enamel and thus lead to caries without the intervention of bacteria.^{56,57} After one inadequately described experiment, Blackwell, McMillan, and Fosdick⁵⁸ published electron micrographs that showed etching on replicas of the enamel surface by sucrose solutions at a pH of 11.0, which gives some support to this possibility. It is well established that compounds known as saccharates can be formed between sucrose and calcium. Tatevossian and Jenkins³⁹ have confirmed previous work in showing that sucrose readily combines with $\text{Ca}(\text{OH})_2$ at pH 11.0 but have found no conditions under which it solubilizes $\text{Ca}_3(\text{PO}_4)_2$ or enamel. They concluded that direct interaction of sucrose in favoring caries is most unlikely and that the one reported result

of Blackwell, McMillan, and Fosdick⁵⁸ remains unexplained.

Masticatory Stress and Caries

Neumann and DiSalvo⁵⁹ state that the one factor common to populations with a low caries incidence is major tooth compressions, produced either in eating or use of teeth as tools. They have speculated about the ways in which stress might build up a resistance and suggest reorientation of enamel crystals⁶⁰ or changes in hydration of the organic matter analogous to the thickening of the epidermis caused by habitually walking barefoot.⁶¹ Neither of these effects would seem to be obviously related to caries prevention, although the possibility cannot be dismissed. Two clinical trials did show that chewing sugar cane or a hard gum was associated with a reduction in caries,^{62,63} but several interpretations are possible in addition to those suggested by Neumann's group.⁵⁹⁻⁶³

Although of considerable theoretical value, this effect, even if fully confirmed, would have limited application in view of the reluctance of most contemporary young people to chew vigorously.

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