MEDICAL PRACTICE

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Nitrites—to ban or not to ban?

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Washington, DC—Science tends to assume a pained expression when it is invoked by Government to justify an action that predictably will be unpopular. A current example is seen in the United States, where a regulatory proposal would make a great change in what people eat.

The Government wants to remove nitrite that is added in the curing process to hot dogs, bacon, ham, sausage, cold cuts, smoked fish, roe, poultry, some imported cheeses, and even canned dog food. The proposal is based on a new study from the Massachusetts Institute of Technology, which raises the possibility that ingestion of nitrite by rats is associated with the development of lymphomas and other lymphoreticular system changes.

The importance of the MIT study depends on who is describing it. The Food and Drug Administration, which sponsored it, says that the findings "constitute confirmation that nitrite is an animal carcinogen," that it "induces cancer when ingested by laboratory rats." Paul M Newberne, of the MIT Department of Nutrition and Food Science, who conducted the study, reported only that "While the results do not permit assigning nitrite a proximate carcinogenic role in the induction of lymphoreticular tumors, an enhancing effect is evident."

But we diverge. The FDA's receipt of the study report last spring set in motion a typical series of bureaucratic actions designed to culminate in ruling the offending substance off the market. The addition of a substance to food during its processing falls in the regulatory purview of both the FDA and the US Department of Agriculture, which together began planning a co-ordinated programme to ban nitrite in the curing of foodstuffs.

A regulatory flinch

Both agencies doubtless had a foreboding that a ban on nitrites would cause unhappiness in some quarters. Nitrite-treated meats, poultry, and fish make up about 7% of the US food supply and constitute a business worth an estimated $12·5 thousand million a year. The FDA sent a letter to Joseph A Califano, jun, secretary of the Department of Health, Education, and Welfare, apprising him that the nitrite issue had some sensitivities to it. In response, Mr Califano is reported to have written, "Don't let it become another saccharin," or words to that effect, thereby preparing the way for a regulatory flinch of no mean proportions.

Saccharin was the last previous additive in widespread use that the FDA proposed to remove from the food supply, most alarmingly from "diet" soda drinks, and even from toothpaste. That proposal was made in the spring of 1977 on the strength of a Canadian study, which suggested that saccharin-laced drinking water caused bladder cancer in rats. By November 1977, Congress passed a law prohibiting any of Mr Califano's many agencies from pulling saccharin off the market for a period of 18 months. During that time, the National Academy of Sciences is to conduct a detailed examination of food safety in America, including, of course, the saccharin issue.

In Government regulatory circles, then, "saccharin" is a code word for what can happen when the findings of science prompt an unpopular action on behalf of the citizens' health and well-being: Congress can pass a law and halt the action. There are a lot of low-cal constituents out there. Probably the only reason that FDA got away with banning the non-nutritive sweetener cyclamate in 1969 was that the food manufacturers still had saccharin. Even the cyclamate ban, however, was

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appealed against through legal and regulatory channels for nearly a decade.

Mr Califano's cautioning not to let nitrite become a similar cause led to a bureaucratic exercise of studying risks versus benefits, legal aspects of regulation, alternatives to nitrite processing, and contribution of the processing to the total human burden of nitrites. The agencies also composed a thorough restatement in lay language explaining why rats can be used to study the danger of cancer to man, why huge doses of a suspect substance are legitimate in such a study, and refuting a popular notion that one can feed almost anything to laboratory animals and produce cancer if the quantities are great enough.

Cancer or botulism

The outcome of all this activity was a joint FDA-USDA proposal that was unusual for its lack of regulatory crispness: nitrite causes cancer, but nitrite is so valuable as a food preservative to prevent botulism that its addition to foods will only be ended "over a period of time." How long a period depends on "the time needed to implement on a national scale measures to prevent problems of botulism." It may also depend, although the proposal does not so state, on how gingerly the phase-out can proceed so as to avoid affront to the food industry and, therefore, the Congress, and, at the same time, how effectively brisk it can appear to ward off more lawsuits by environmental or consumer organisations who want nitrites banned.

The only previous government actions to reduce the amount of nitrite in cured meats were based on an entirely different aspect of nitrogen compounds as carcinogens. It has long been known that nitrite can combine with amines from dietary protein to form carcinogenic nitrosamines. The discovery of nitrosamines in crisply cooked bacon raised the likelihood that high heat was producing the nitrite-amine combination before the bacon was ever eaten, so the Government reduced the amount of nitrite that could be added to bacon or poultry.

Until recently, however, nitrite has not been implicated as a direct carcinogen. Toxic in relatively large quantities, yes, but not an agent to accomplish malignant transformation. The study by Newberne and associates at MIT changed all that, at least in the view of the Government.

That study employed 1381 Sprague-Dawley rats in various experimental groups and another 573 as controls. Variations in diets and dosage of nitrite for different groups of animals made the study the equivalent of six different studies. As related in the lengthy statement by FDA and USDA in explaining their position, "The results of the study show that nitrite produced a statistically significant increase in cancer of the lymphatic system . . . The combined incidence of lymphomas in the groups that were *not* fed nitrite in their diets was 7·9%; the incidence in the combined nitrite-treated groups was 12·5%."

The government statement also took into account some changes in the experimental animals short of frank lymphoma. "If the observed instances of immunoblastic cell proliferation (considered to be a precancerous state) are added to the lymphomas, the overall incidence of cancerous and precancerous lesions in the combined control groups was 15·7%, and in the combined nitrite-treated groups it was 23·9%."

In his own summary of the study, Paul Newberne mentioned immunoblastic cell proliferation as a "yet unsupported assumption" when he totalled those with lymphomas. He found a "somewhat less than convincing case that nitrite is lymphomagenic in Sprague-Dawley rats," but said "one cannot escape the distinct impression that nitrite does affect the lymphoreticular system of the rat." And he conceded that, while "the data are only suggestive and the biological significance of nitrite-associated lesions of the lymphoreticular system is unclear," the study was enough "to raise questions about the widespread use of relatively high concentrations in our food supply."

Nitrite is added to foods, as the Government statement said, to prevent the germination of spores of *Clostridium botulinum*, which then grow and produce the toxin that causes botulism. The food industry contends that it has no other similarly effective additive against the spores, which, if not germinating, are harmlessly present in many samples of meat, fish, and poultry. Adequate refrigeration, thorough cooking, ionising radiation, and other alternatives can control botulinus spores, but the nation's food processing and marketing system is not regarded as able to employ those alternatives effectively. "An immediate ban on the use of nitrite," the Government states, "could lead to many cases of botulism and to many deaths." The Government paper raises the spectre of undercooked hot dogs and summer-warmed bologna sandwiches felling hundreds of picnickers and beach party groups.

Sausages or saliva?

Nitrite was not originally added to foods to prevent botulism, however. It was to give meats a pleasingly red colour. Without nitrite, for instance, ham is grey. Nitrite also imparts a characteristic flavour that we tend to associate with smoked meats although most of us probably have not tasted meat that actually has been smoked: the process does not lend itself readily to bulk commercial food preparation.

By the Government's estimate, based on the MIT rat figures, a human being who eats one hot dog a day imposes on himself a lifetime risk of developing lymphoreticular cancer of between one in 16 700 persons and one in 3700 (a risk of 0·6 to 2·7 per 10 000 population). Greater exposure poses greater risk, and the Government estimates that a citizen who eats three slices of bacon at breakfast, two bologna sandwiches at lunch, and two hot dogs at dinner has a lifetime cancer risk of 3·1 to 13·5 per 10 000 from cured meat alone.

The proposal of a rather massive and protracted upheaval in industrial and personal practices and habits relating to cured meats, however, would address only about 20% of the problem with nitrites. Eighty per cent of the nitrites that reach the stomach are formed in saliva from the nitrates that naturally occur in vegetables, water, and soil, and that are enhanced in quantity by the use of more than 11 million tons of nitrogen fertiliser used last year on American farmland.

Now *there's* a challenge to regulation.

Is there any recognised disorder of the tensor tympani muscle that can give rise to tinnitus? If so what are the aetiology and treatment?

The aetiology of tinnitus associated with contractions of the middle ear muscles has been studied extensively. Clinical observation of the tensor tympani in a subject who was able to contract this muscle voluntarily showed a temporary audiometric loss for low tones associated with subjective tinnitus.[1] Studies of patients recovering from peripheral facial nerve palsies from varied causes showed a temporary threshold shift during contraction of the stapedius muscle. This was synchronous with tinnitus that could be abolished by section of the stapedius tendon.[2] More recent computer analysis of the intra-aural muscle reflex together with studies of human temporal bones have led to the view that although the stapedius is the initiator of the reflex and the primary contributor to ossicular chain fixation, the tensor tympani is responsible for the major observed response. The proprioceptive feedback mechanisms located within the stapedius muscle and tendon permit or initiate, or both, tensor tympani contraction during acoustic stimulation.[3] Hence probably the contraction of the tensor tympani is responsible for the tinnitus and the latter may contribute to the auditory threshold shift. As to alleviating the tinnitus by section of the tendon of stapedius further studies are needed to exclude hearing loss due to increased vulnerability to noise hazards.[2]

[1] Smith, H D, *Archives of Otolaryngology*, 1943, **38**, 369.
[2] Watanabe, I, Kumagami, H, and Tsuda, Y, *ORL; Journal for Oto-Rhino-Laryngology and its Borderlands*, 1974, **36**, 217.
[3] Love, J T, and Stream, R W, *Laryngoscope*, 1978, **88**, 298.