**BRIEF REPORT**

The epidemiological enigma of gastric cancer rates in the US: was grandmother’s sausage the cause?

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Much has been written concerning the ‘epidemiological enigma’ of falling gastric cancer rates in the US. Up until the 1930s gastric cancer was the leading cause of cancer mortality in the US. Today it is eighth. This sharp decline during the 20th century remains an unexplained yet startling phenomenon.

The leading theories to explain this change concern the advent of refrigeration and infection with *Helicobacter pylori*. Refrigeration began in the early 1900s and gained widespread use by the 1950s. As a result the US diet began to include more fresh fruits and vegetables (high in anti-carcinogenic anti-oxidants) and less preserved meats (high in nitrites and carcinogenic nitrosamines). The temporal correlation between refrigeration and gastric cancer rates, however, has not held true for countries such as Japan, where widespread refrigeration noted in the 1960s has not resulted in a gastric cancer decrease. Infection with *H. pylori*. is currently regarded as the main contender to explain the enigma and studies have demonstrated a causal link between *H. pylori* infection, chronic atrophic gastritis, and the intestinal type of gastric carcinoma.

However, multifactorial causality is likely to be involved and other critical cofactors are yet to be identified.

The role of dietary nitrite and N-nitrosamines in the pathogenesis of gastric cancer has remained a matter of debate for over 30 years. N-nitroso compounds are potent carcinogens in primate animal models and result in a variety of tumour types. Such carcinogenic nitrosamines can be formed from the reaction of nitrite with secondary amines under acidic conditions (as occurs in the human stomach) as well as during the curing process used to preserve meats. Dietary sources of nitrosamines include US cured meats preserved with sodium nitrite as well as the dried salted fish eaten in Japan.

One aspect of nutritional epidemiology that has received minimal attention in the medical literature concerns changes in US meat curing practices that occurred in the 1920s. Prior to 1923 the level of nitrite detectable in cured meats was extremely high and variable. During that time meat was cured using potassium nitrate (or saltpetre). The conversion of nitrate (NO₃) to nitrite (NO₂) by nitrate-reducing bacteria during the curing process was responsible for the levels of nitrite found in the meats. Nitrite levels as high as 1400 ppm (1 ppm equals 1 mg/kg) nitrite in frankfurters and up to 960 ppm in ham were noted at that time. The average content was 185 ppm. There was no regulation of the amount of nitrite permissible in cured meat products and the process produced inconsistent results in terms of meat colour and flavour. In the early 1900s it was realised that nitrite, and not nitrate, was responsible for the preservation and characteristic colour/flavour of the cured meats. In 1923 the Department of Agriculture authorized experimentation using sodium nitrite (instead of nitrate) to cure meats. The experiments were deemed a success and resulted in the formal authorization of sodium nitrite as a meat curing compound. A 200 ppm maximal nitrite concentration was established and the use of nitrate for curing was discouraged.

As a result of this formal authorization in 1925, the amount of nitrite in cured meats was significantly reduced. By 1937 the average content had decreased to 56.7 ppm (i.e. a 326% reduction) and it has remained in this range. The effect that this nitrite reduction had on the nitrosamine content of the meats is not known since sophisticated analytical methods were not available. However, with such high nitrite levels present it is likely that high nitrosamine levels existed as well. Furthermore, since agents to prevent spontaneous nitrosamine formation (such as sodium ascorbate and sodium erythrobate) were not included in the meat curing process until the 1970s, it is reasonable to assume that cured meats of the early 1900s contained high nitrosamine levels.

The described change in US meat curing practice preceded the beginning of the gastric cancer incidence/mortality decline by about a decade. Examination of crude death rates from prior to 1930 shows that mortality from gastric cancer was increasing (US census data) and not until the 1930s did the rates begin their steep descent. This decline is noted simultaneously in
the age-specific death rates of all age groups (by decades of life), supporting a calendar period effect. Decreased nitrosamine content of cured meats in the US beginning in 1925 could, in part, explain this epidemiological enigma. Although no firm conclusions can be drawn from this historical relationship, the information does support the existing evidence that dietary nitrite, through nitrosamine formation, plays a role in the pathogenesis of human gastric cancer. Examination of historical changes in nitrite meat curing practices in other countries with declining gastric cancer rates could yield similar findings.

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KEY MESSAGES

- In the 1920s, a significant change in US meat curing practices resulted in a 326% decrease in average nitrite content. This event preceded the beginning of a dramatic decline in gastric cancer mortality.
- A possible causal link is postulated since age-specific mortality declined simultaneously for all age groups, suggesting a calendar period effect.

References