A recent issue of the *Journal* included an excellent and interesting paper by Wernli et al. (1) supporting the concept that exposure to organic dust that contains endotoxin has beneficial effects against cancer. We would like to comment on the commonly suggested confounder associated with lower rates of cancer in workers exposed to organic dust—smoking—and expand on the mechanism by which endotoxin in dust may be responsible for the observed benefits as related to this exposure.

Historically, a few reports suggested that dust reduced the rate of lung cancer (2), although most investigators dismissed this finding and inferred that this was a methodological issue relating to lower smoking rates in exposed populations. However, studies by this research group (3–5) investigating Chinese cotton textile workers, as well as other investigations of textile (6, 7) and agricultural (8) workers, specifically dairy farmers (9, 10), now support the position that this effect of a lower-than-expected rate of cancer is not a result of differences in smoking rates between study and control populations. A 1973 study by Henderson and Enterline (11) collected data on the smoking rates of cotton textile workers and reported that the rates were slightly higher (51.9 percent) than those of the control population (51.2 percent). A recent evaluation of smoking rates of cotton textile workers (12) also suggests that the rate for this population is higher than or similar to that for controls and the general population.

This study (1), as have others (2, 9), suggests that the mechanism for the lower rates of cancer is a result of endotoxin, a lipopolysaccharide constituent of the Gram-negative bacterial cell wall. Previous investigations (13, 14) have shown that many occupational groups are exposed to high levels of airborne dust containing endotoxin. Wernli et al. (1) suggest that the endotoxin results in stimulation of the immune system, which causes macrophages to become antitumor/carcinogenic. We previously suggested a mechanism for this antitumor activity through the involvement of toll-like receptors and cytotoxic mediators, such as cytokines.
(e.g., tumor necrosis factor, interleukins) (9, 10, 15). In combination, these result in cellular activation of apoptosis pathways resulting in death of the cancer cell. It has been suggested that toll-like receptors 2 and 4 are involved, which activate the signaling pathway involving MyD88 and in turn result in the activation of TRAF6 (15). This action then signals one or more of the following: nuclear transcription factor kappa B, p38, and mitogen-activated protein kinases such as the c-Jun-NH–terminal protein kinase, which act on apoptosis (12, 15). It is even possible that other known cellular signaling systems, such as ERK, and others that are not known are involved.

It is suggested that the mechanism is similar for each organ system reported to benefit from exposure, including cells associated with the stomach and esophagus. We propose that other organ systems have similar effects in lowering cancer rates and that this process is occurring in other occupational groups (e.g., sewage workers) (16) besides cotton textile and agricultural workers.

Additional research on observed lower-than-expected rates of cancer is warranted. Traditional explanations of methodological causes (e.g., confounders) for lower rates can no longer be used to account for these observations.

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REFERENCES


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Editor’s note: In accordance with Journal policy, Wernli et al. were asked whether they wanted to respond to this letter, but they chose not to do so.

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