in the presence of a cellophane membrane in a liquid medium. He outlined the factors most responsible, emphasizing increased adsorbing surface area. By introducing a membrane into an experimental system, a second variable is introduced. Both the tampon and the membrane can separately produce TSST-1 dependent upon the physicochemical conditions inherent to each product. In addition, another variable is introduced—synergy, an enhancement caused by the tampon working in concert with the membrane for more than a simple additive effect of the two variables. This is bad science because in a well-planned scientific experiment, there should only be one operative variable, in this case the tampon. The bad science explains the outrageously high levels of TSST-1 that Schlievert produced in all-cotton tampons compared with non–all-cotton products.

The physical and chemical conditions that enable TSST-1 production are dependent on the material used and the ecologic environment created [3]. Our data and those of others suggest that absorbing and adsorbing surface area, P02, PCO2, pH, temperature, protein concentrating ability of fiber, ionic strength, viscosity, leachable chemicals, interspecies competition and cooperation, and the in vivo versus the in vitro environment along with host factors govern the production of TSST-1 [3, 5]. A constellation of these factors affects toxin levels at any timepoint and may result in disease expression. Throughout my 15 years of research on TSS, Schlievert has espoused the safety and efficacy of three other synthetic tampon fibers (carboxymethyl cellulose, polyester, and rayon polyacrylate), only to have been proven wrong (manufacturers had to remove these fibers from tampons because of their inherent danger). His observations are even ignored by the manufacturer, who quote his work in litigation but don’t use it for product changes; in fact, one manufacturer has just announced it is introducing an all-cotton product line at the start of this new year [6]. Several others are about to join with similar products.

Lastly, if what Schlievert has shown is true, then we should see a greater incidence of TSS with users of all-cotton tampon versus users of synthetic or mixed fiber tampons. Time will be the final judge of our work. Thus far, over the last 15 years, time has continued to verify my observations.

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References

Reply

To the Editor—In the early 1980s, I presented a seminar on toxic shock syndrome (TSS) at the national meeting of the Infectious Diseases Society of America. During the question and answer period that followed and in no fewer than five subsequent publications, my colleagues and I have discussed an oxygen theory for the role of tampons in TSS as outlined below. In [1], we showed that the cultural conditions necessary for production of TSST-1 (TSST-1) include animal protein (glucose catabolite represses toxin production), neutral pH, elevated body temperature, and oxygen. These studies have been confirmed by many subsequent investigations. Since the vagina is considered to be relatively anaerobic, I proposed that tampons, particularly those of highest absorbency, must introduce sufficient oxygen into the vagina to allow TSST-1 production and subsequent illness.

In 1984, Wagner et al. [2] demonstrated that tampon insertion greatly increases vaginal oxygen levels. In a subsequent study, my colleagues and I [3] showed that many of the tampons most associated with TSS, notably those containing polyacrylate rayon, inhibit production of TSST-1 and in many cases prevent growth of Staphylococcus aureus. Mills et al. [4] later showed this inhibitory activity resulted from Mg2+ chelation by those tampons, such that microbial growth and toxin production were altered. Also, the “reference standard” epidemiology data obtained in the Tri-State Toxic Shock Syndrome Study [5] indicate that risk of development of TSS associated with tampon use increases directly with increases in tampon absorbency. With only a few exceptions, the risk of TSS is independent of tampon composition. These findings were confirmed by subsequent studies. Considering our data [3] and that of the Tri-State Study [5], I proposed and maintain today that tampon-associated TSS occurs most likely as a result of oxygen introduction into the vagina by tampons, not as a result of S. aureus growth within tampons, but rather as a result of growth and toxin production at vaginal sites separate from the tampons.

In the last 15 years, Tierno et al. [6] have proposed myriad explanations for the association of tampon use with TSS, some of which Dr. Tierno cites in his letter [7]. Some of these merit further discussion. In a study of carboxymethyl cellulose (CMC), Tierno et al. [6] proposed that the association of the Rely tampon with TSS resulted in part from microbial degradation of CMC, yielding glucose that stimulates S. aureus growth and production of TSST-
1. On the surface this seems plausible, but it is filled with flaws. First, the microbial flora of the human vagina, including *S. aureus*, have little if any capacity to degrade CMC. Second, the end product of digestion is glucose, but it repression of production of TSST-1. Finally, CMC has been used in Rely tampons and in tampons that are the least associated with TSS, again emphasizing the importance of absorbency rather than composition.

In his letter, Tierno [7] indicates that polyacrylate had to be removed from tampons because of its inherent harmful effects. He fails to mention that polyacrylate was removed because of a jury verdict against Playtex rather than on the basis of scientific merit. According to this way of thinking then, as scientists, let us never doubt what the legal system tells us is true. Based on its microbial inhibitory properties combined with its high absorbency properties, I maintain that a very small polyacrylate tampon may reduce the risk of TSS. Such a tampon would introduce the least amount of oxygen into the vagina compared with presently available products, yet could provide sufficient absorbency to control menstrual flow. The tampon could have the additional benefit of inhibiting toxin production, which incidentally is a major area of research today in tampon development.

In our 1984 study [3], cotton fiber (as used in Kotex tampons) was evaluated for its effect on growth and TSST-1 production of *S. aureus*. Cotton had no effect either on growth of *S. aureus* or on production of TSST-1. Thus, I was skeptical when the recent study by Tierno and Hanna [8] suggested that all-cotton tampons nearly completely prevent toxin production and further that any toxin made is considered to be adsorbed by cotton, thus rendering it unavailable for TSS causation. The logical extensions that can easily be drawn from the Tierno and Hanna study both by tampon manufacturers and women who use tampons are that cotton tampons of any absorbency can be marketed and used, since cotton prevents toxin production, and that women who use cotton tampons need not worry about developing menstrual TSS. Indeed, why have TSS warning labels at all on cotton tampon products?

I believe that both of these extensions are absurd on the basis of the Tri-State TSS Study findings and on the oxygen theory for tampon involvement in TSS. I [9] recently attempted to reproduce as closely as possible necessary aspects of the Tierno and Hanna study [8] and included other test systems, since there can be disagreement over which is the "best" in vitro system to use. In his letter, Tierno [7] cites differences between my study and the one he did with Hanna [8]—a different inoculum size, "2% higher CO₂ tension, 25 mL greater flask volume, a concentration technique that was not described, only three extant tampon brands and styles, and only regular-absorbency products" and lack of use of a prewashed experimental set. I do not believe any of these differences affect the conclusions of my study. It is important to remember the objective of my study was not to "de-bunk" the Tierno and Hanna study but rather to compare selected cotton versus cotton/rayon tampons for effect on toxin production. In no instance in my experiments did cotton tampons perform better than cotton/rayon tampons.

I was asked by the reviewers of my manuscript [9] to provide possible explanations for the differences between my data and those of Tierno and Hanna [8]. I did not then and still do not know what size containers Tierno and Hanna used for testing tampons. Certainly, degree of exposure of tampons above the aqueous surface can have significant effects on toxin production, as I noted [9]. It is also noteworthy that the manufacturer of the concentrating device used by Tierno and Hanna indicates the device is for qualitative, not quantitative, purposes. I used ethanol precipitation in my studies, which we previously showed is a quantitative method to concentrate TSST-1.

Finally, and most importantly, neither cotton nor cotton/rayon tampons prevent production of TSST-1 by *S. aureus*. Thus, it is prudent to continue to follow the Centers for Disease Control and Prevention recommendations: If women choose to use tampons, those of lowest absorbency to control menstrual flow should be used, and women should read the tampon box labels and warning inserts concerning TSS. If signs of TSS develop, tampon use should be discontinued and medical attention sought.

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References