The Public Health Response to Toxic Shock Syndrome:
A Historical Review and Lessons Learned

Catherine N. Rasberry

Abstract

The toxic shock syndrome (TSS) crisis is a historical public health success story from which much can be learned and applied to contemporary public health issues. Following the first reports, multiple research teams initiated studies designed to ascertain the risk factors associated with TSS. Those studies evolved over several years – each building upon previous findings in an attempt to further understand both the nature and causes of toxic shock. After the first report of TSS in a May 1980 issue of the *MMWR*, multiple studies contributed to the body of knowledge that ultimately informed and facilitated interventions to reduce the incidence of TSS. Examination of the public health response to toxic shock syndrome highlights the effective use of epidemiological studies in successfully building a foundation for efficient responses to emerging problems and also highlights political and legal issues that remain for health professionals today.

The toxic shock syndrome (TSS) crisis is a historical public health success story from which much can be learned and applied to contemporary public health issues. The research that has emerged illustrates the efficiency with which public health professionals can react and initiate interventions. Many studies played important roles in gaining control over the growing incidence of TSS. These studies evolved over the course of several years–each building upon previous findings to further understand both the nature and causes of toxic shock. It was this persistent and intensive research that informed and facilitated interventions to reduce TSS incidence.

The Emergence of TSS

Toxic shock syndrome is a potentially fatal disease "characterized by sudden onset of fever, chills, vomiting, diarrhea, muscle aches and rash. It can rapidly progress to severe and intractable hypotension and multisystem dysfunction" (Centers for Disease Control and Prevention [CDC], 2003, p.1). The standard case definition used in initial CDC studies consisted of the following: "1) temperature greater than 102°F, 2) hypotension, 3) rash, 4) desquamation, and 5) abnormalities in three or more organ systems" (Schuchat & Broome, 1991, p. 105).

Reports of toxic shock syndrome first appeared in the *Morbidity and Mortality Weekly Report (MMWR)* on May 23, 1980, in response to growing concerns about the condition (CDC, 1997). In the months prior to publication of the *MMWR* article, health departments of two states, Wisconsin and Minnesota, received reports of toxic shock syndrome in young, menstruating women (Osterholm, Gibson, Mandel, & Davis, 1982). Since the first published report of TSS in 1978 was based on the manifestation of the condition in children (Todd, Fishaut, Kaprai, & Welch, 1978), unexpected reports of toxic shock in menstruating women prompted health departments to launch their own active investigations into the problem (Osterholm, Gibson et al., 1982).

Following the first reports, researchers nationwide initiated a series of studies designed to ascertain risk factors associated with TSS. Although the specific approaches and methodologies of the research projects varied, each contributed to the working knowledge of toxic shock. The years that followed brought increased understanding of the syndrome (Schuchat & Broome, 1991).

Epidemiological Evidence

Epidemiological data regarding factors associated with toxic shock syndrome were gathered by multiple teams of investigators using different methodologies over a span of many years. Following the first report of TSS in a May 1980 issue of *MMWR*, several studies were conducted. The Wisconsin study, the first CDC study (CDC-I), the Utah study, a second CDC study (CDC-II), the Tri-State study, national passive surveillance by the CDC, a third CDC study (CDC-III), and a fourth CDC study (CDC-IV) contributed to the growing body of knowledge of toxic shock syndrome and its risk factors.

Wisconsin Study

The Wisconsin study drew on a statewide surveillance of toxic shock syndrome conducted by the Wisconsin Division of Health. In January 1980, 3,500 physicians in the state were contacted through written correspondence describing the clinical features of TSS and requesting that all possible cases, whether previously or newly diagnosed, be reported. Once cases were confirmed, investigators

Catherine N. Rasberry, MS; Doctoral Candidate and Research Assistant, Department of Health & Kinesiology, Texas A&M University, Mail Stop 4243, College Station, Texas 77843-4243; Telephone: 979-862-8574; Fax: 979-847-8987; E-mail: crasberry@hlkn.tamu.edu; Chapter: Alpha Pi

interviewed 38 patients who had experienced the onset of toxic shock syndrome between September 1975 and June 1980 (Davis, Chesney, Wand, LaVenture, & Team, 1980). The study included 37 female cases, with 35 women experiencing menstrual toxic shock syndrome (defined in this study as onset during or in the 48 hours following the menstrual period), and these 35 were used in the case-control portion of the study. Control participants recruited from nonpregnant menstrual-age women at gynecological clinics in Dane County, Wisconsin, completed self-administered questionnaires. Three control participants were matched to each of the 35 menstrual TSS cases based on menstruation and age within two years (Davis et al., 1980).

The study produced several important findings. First, 34 of 35 women with of menstrual TSS had used tampons during the menstrual period in which onset occurred; therefore, tampon use was significantly associated with onset of toxic shock syndrome. Second, differences in tampon brands between case and control subjects were not found to be significant, and third, control participants were found to be significantly more likely than case participants to have used some form of birth control (Davis et al., 1980). Preliminary results of this study and the Utah and CDC-I studies were included in the June 29, 1980, issue of the *MMWR* (CDC, 1980; Schuchat & Broome, 1991). Final results of this study were published in the December 18, 1980, issue of *The New England Journal of Medicine* (Davis et al., 1980).

CDC-I

This national case-control study, conducted by the CDC, was based on cases reported between publication of the first and second *MMWR* articles on toxic shock syndrome (May 23 to June 28, 1980). Of those cases, 53 met the clinicial case definition; 52 were cases of menstrual TSS. All 52 case participants and 52 controls matched for age and selected by the case participants were interviewed by telephone regarding use of sanitary products (Schuchat & Broome, 1991).

This study revealed several findings. Consistent with the Wisconsin study, CDC-I found tampon use to be significantly associated with onset of toxic shock syndrome; all 52 case participants (100%) had used tampons in the menstrual period of TSS onset compared with 44 control participants (85%). In addition, continuous use of tampons was significantly associated with onset of toxic shock. Researchers, however, did not find significant differences between cases and controls in terms of tampon brand or absorbency. Preliminary results of the study were published in the June 27, 1980, issue of the *MMWR* (CDC, 1980); final results were published in a 1980 issue of *The New England Journal of Medicine* (Shands et al., 1980).

Utah Study

Like the Wisconsin Division of Health, the Utah State Department of Health conducted an investigation into reports of toxic shock syndrome in its state. Preliminary results of the study were based on 12 cases of TSS and 40 controls matched by neighborhoods. Although the small number of participants did not yield statistically significant findings, results revealed that in 100% of TSS cases the women used tampons (compared to 80% of controls), and these results were included in the June 27, 1980, *MMWR* published by the CDC (CDC, 1980; Schuchat & Broome, 1991).

Final results were based on a case-control study of 29 case participants and 91 control participants, and revealed information regarding risks associated with use of particular tampon brands. The Utah study found that use of the Rely brand of tampons was associated with an increased risk of TSS (Kehrberg et al., 1981). These results, however, were not released and published until a second nationwide study had been completed by the CDC (Schuchat & Broome, 1991). Final results were published in a 1981 issue of the *American Journal of Epidemiology* (Kehrberg et al., 1981).

CDC-II

The second CDC study involved females whose onset of menstrual toxic shock syndrome during July or August 1980 had been reported to the CDC. A total of 50 case participants and 150 age-matched controls were included. Women were interviewed by phone regarding use of sanitary products and were later mailed self-administered surveys that collected additional information on sexual practices, use of birth control, socioeconomic status, medical history, contact with health care providers, and other factors (Schlech et al., 1982).

In keeping with previous studies, tampon use was significantly associated with onset of TSS; all 50 (100%) case participants had used tampons during the period of onset, as compared to 125 of the 150 control participants. Case participants were significantly more likely than control participants to have used Rely brand tampons; the relative risk of TSS development for use of Rely tampons compared to use of other brands was 7.7. Increased risk was not associated with any other brand, and absorbency was not found to be associated with TSS risk (Schlech et al., 1982).

Following conclusion of the study, the CDC reported findings to the Food and Drug Administration and the manufacturer of Rely brand tampons, Proctor and Gamble (Osterholm, Davis et al., 1982; Schlech et al., 1982). In September 1980, Rely tampons were voluntarily pulled from the market. Complete study results were later published in a 1982 issue of the *Journal of the American Medical Association* (Schlech et al., 1982).

Tri-State Study

In 1982, results of the Tri-State toxic shock syndrome study appeared in *The Journal of Infectious Diseases*. That study included all cases of TSS in Minnesota, Wisconsin, and Iowa women that were reported from October 1979 to September 19, 1980. Of the 80 cases that met the case

definition, 76 were menstrual TSS, and each case participant was grouped with two age-matched neighborhood control participants (Osterholm, Davis et al., 1982).

As in previous studies, tampon use was significantly associated with risk of toxic shock syndrome; 75 of 76 case participants had used tampons compared to 123 of 152 control participants. The odds ratio for tampon use compared to non-use was 18.01 ($p< 0.001$). In addition, use of Rely brand tampons was found to significantly increase risk of TSS; risk associated with use of Rely tampons was 2.49 times higher than TSS risk associated with the other brands. Several other brands, however, were associated with a risk higher than that experienced with no tampon use (Osterholm, Davis et al., 1982).

Furthermore, the Tri-State TSS study produced a finding that had not emerged in previous research. In addition to use of Rely tampons, results indicated that tampon absorbency also increased TSS risk. The study suggested that women using higher absorbency tampons were at greater risk than those using lower absorbency tampons (Osterholm, Davis et al., 1982).

CDC National Surveillance

After the initial CDC publication about toxic shock syndrome in May of 1980, additional articles appeared in the *MMWR* in June and September of 1980 requesting cases of the syndrome be reported. In October of that year, the CDC provided copies of all case reports to state health departments and encouraged reporting future cases. Through this system, the CDC was able to record all reported cases and keep state health departments informed. Upon request, the CDC provided practitioners with packets of TSS information, report forms, and address labels for the appropriate state health department (Reingold et al., 1982).

In the summer of 1981, a listing of all toxic shock syndrome cases was sent to each state health department to be checked, and if necessary, corrected. All cases meeting the full CDC case definition were labeled "confirmed." Two aspects of the case definition were changed slightly in 1981, but surveillance continued in accordance with the updated definition (Reingold et al., 1982).

The passive surveillance (reliant upon case reporting by patients or health care providers) revealed a decrease in menstrual toxic shock syndrome cases in the years following public awareness and response to the disease. Although some skeptics questioned whether the passive surveillance was a true reflection of the disease patterns in the country, the work of several researchers support the findings. It appears the decrease in TSS was likely real and not the result of less thorough reporting. Reviews of records, charts, and hospital discharges were conducted on different occasions to verify the validity of the national surveillance. In all but one case (Minnesota), the examinations were consistent with passive surveillance (Schuchat & Broome, 1991).

CDC-III

Once additional questions surfaced regarding characteristics of tampons such as composition and absorbency, the CDC undertook a third study using data collected from passive surveillance in 1983 and 1984 and a mailed, self-administered survey completed by a nationally representative sample of 34,712 participants. In this study, the CDC confirmed that toxic shock syndrome was associated with tampon absorbency. As absorbency increased by 1 gram, TSS risk increased by 37% (Schuchat & Broome, 1991).

CDC-IV

In response to continuing concerns that national data from passive surveillance was underestimating the actual incidence of disease, one last active surveillance project was initiated in 1986 (Gaventa et al., 1989; Schuchat & Broome, 1991). This project was conducted with populations in Missouri, New Jersey, Oklahoma, Tennessee, Washington, and Los Angeles County, which totaled approximately 34 million (Gaventa et al., 1989).

The incidence of TSS (menstrual and nonmenstrual in females and in males) in the entire population was 0.53/100,000 individuals. The incidence of menstrual toxic shock syndrome was 1.05 cases/100,000 females between the ages of 15 and 44. This rate was considerably lower than rates calculated from active surveillance in 1980 that ranged from 6.2/100,000 to 12.3/100,000 (Gaventa et al., 1989). Those results further substantiated the validity of the TSS decrease observed through passive national surveillance (Schuchat & Broome, 1991).

Current State of TSS

Toxic shock syndrome has been a nationally notifiable disease since 1980; therefore, data are collected on the disease each year. An update on TSS, published in 1999, examined toxic shock syndrome data between 1979 and 1996. Of 5,296 cases reported in that time frame, only 1,035 (19.6%) occurred from 1987 to 1996. That review supported findings published elsewhere that described a decrease in incidence rates. In addition, the transition from 1979 to 1996 was characterized by an increase in the percentage of nonmenstrual TSS cases (Hajjeh et al., 1999). Furthermore, the Summary of Notifiable Diseases, which provides one of the most current records of disease cases, documented 109 reported cases of toxic shock syndrome (menstrual and nonmenstrual) in the United States in 2002 (CDC, 2004).

Lessons Learned

There are several important lessons of contemporary relevance to be learned from a historical look at the public health response to menstrual toxic shock syndrome. Public

health officials must respond to an emerging problem quickly, and at times, action must be taken based on limited evidence from initial studies. When taking action, health officials must be aware of the role that political power has in shaping the response, and must be able to react accordingly. Finally, the response to toxic shock syndrome set a precedence of legal protection for participants in studies designed to shape public health responses.

One of the most important lessons from the epidemiological investigations of menstrual toxic shock syndrome is the "speed and effectiveness" with which health professionals and scientists responded to the crisis (CDC, 1997). After the first report of nonmenstrual toxic shock syndrome appeared in 1978 (Todd et al., 1978), state health departments in Wisconsin and Minnesota began noticing cases of TSS in menstruating women (Osterholm, Davis et al., 1982). The initial report of menstrual toxic shock syndrome appeared in the *MMWR* in May 1980 (CDC, 1997). Three of the five studies that followed found increased risk of TSS for users of Rely brand tampons (Davis et al., 1980; Kehrberg et al., 1981; Osterholm, Davis et al., 1982; Schlech et al., 1982; Shands et al., 1980). Although the studies were not published until 1981 and 1982, sufficient evidence existed to prompt the voluntary removal of Rely brand tampons from the market in September of 1980 (Schlech et al., 1982). Approximately four months passed from the initial published report of the problem to an intervention.

The investigations of TSS are an excellent example of the way epidemiological data do not always provide immediate answers to why or how some factors affect risk for disease; however, as illustrated in the case of TSS, it often is possible for intervention recommendations to be made based on sound evidence but limited explanations. In fact, study authors commented that in spite of the lack of understanding of why tampons (or certain tampons) were associated with TSS risk, there was sufficient evidence to support tampon use recommendations (Osterholm, Davis et al., 1982). For example, the role of absorbency in the development of TSS was not clearly understood, but despite this lack of understanding, researchers had determined that high-absorbency tampons were associated with greater risk of TSS (Osterholm, Davis et al, 1982). Women, therefore, were encouraged to use lower-absorbency tampons instead. That type of recommendation (as well as the removal of Rely tampons – already determined to increase TSS risk) helped public health officials reduce the incidence of TSS.

Another important lesson of the epidemiological examination of toxic shock syndrome is related to political power that influences the work of public health officials. For example, the Utah study described an association between toxic shock syndrome risk and the use of Rely brand tampons. Preliminary results were available in the summer of 1980, and although the CDC published parts of the results in a June 1980 issue of the *MMWR*, that particular aspect was not included. In fact, the report stated, "The finding that no particular brand of tampon is associated with unusually high risk reduces the likelihood that the tampon carries or introduces the causative agent and suggests that the tampon acts as a cofactor" (CDC, 1980, p. 298). Despite the apparent importance and usefulness of such a finding, results of this study were not released until after the completion of another national study (Schuchat & Broome, 1991).

That is especially interesting considering that in the first CDC study, Rely tampons were used more by the greatest number of tampon-using case participants. The difference in tampon brand, however, was not statistically significant in the CDC-I study, possibly due to distribution characteristics of tampon brands used. It was not until the CDC conducted a second study that results were published implicating a link between increased risk of TSS and use of Rely brand tampons (Schlech et al., 1982). It is also interesting to note that while the tampon brand was identified, the manufacturer's name, Proctor and Gamble, was not mentioned in initial articles describing the Utah study or the CDC-II study results (Kehrberg et al., 1981; Schlech et al., 1982).

An additional noteworthy result of the study of toxic shock syndrome came in the form of judicial rulings that provided legal protection for study participants (CDC, 1997). As women began to file lawsuits against one tampon manufacturer, the company attempted to force the CDC to release identifying information on participants in the case-control studies. The manufacturer argued it had a right to identify and even cross-examine women who served as sources of information that became evidence against the company. A federal appeals court ruled access to identifying information would not be granted to the manufacturer, and that such disclosure would be detrimental to the types of research which require voluntary disclosure of personal information that plays a key role in protecting the nations' public health (CDC, 1997). The ruling was based, in part, on the idea that participants had "a reasonable expectation of confidentiality even in the absence of express promises that their [the women's] names would not be revealed" (O'Neil, 1996, p.40); and furthermore, it was determined that freedom of information laws did not require the CDC to release personal identifiers (Curran, 1986). The court ruling set a legal precedence that remains applicable for researchers today by providing greater protection for participants in government-conducted public health research.

Overall, the epidemiological studies of toxic shock syndrome provided important information to inform public health officials' response to the problem of menstrual TSS. Researchers responded quickly to an emerging disease and were able to identify alterable risk factors as points of intervention for improving public health. Multiple studies were necessary to explore the initial hypotheses of investigators, but ultimately, toxic shock syndrome was brought under control. In addition, a historical review of studies that focused on TSS highlights political and legal issues that remain applicable for health professionals today.

References

Centers for Disease Control and Prevention. (1980). Follow-up on toxic-shock syndrome–United States. *Morbidity and Mortality Weekly Report, 29,* 297-299.

Centers for Disease Control and Prevention. (1997). Epidemiologic Notes and Reports: Toxic-shock syndrome-United States. *Morbidity and Mortality Weekly Report, 46*, 492-495.

Centers for Disease Control and Prevention. (2003). Toxic shock syndrome. Retrieved August 7, 2005, from http://www.cdc.gov/ncidod/dbmd/diseaseinfo/toxicshock_t.htm

Centers for Disease Control and Prevention. (2004). Summary of Notifiable Diseases-United States. *Morbidity and Mortality Weekly Report, 51*, 1-84.

Curran, W. J. (1986). Protecting confidentiality in epidemiologic investigations by the Centers for Disease Control. *The New England Journal of Medicine, 314,* 1027-1028.

Davis, J. P., Chesney, P. J., Wand, P. J., LaVenture, M., & Team. (1980). Toxic-shock syndrome: Epidemiologic features, recurrence, risk factors, and prevention. *The New England Journal of Medicine, 303*, 1429-1435.

Gaventa, S., Reingold, A. L., Hightower, A. W., Broome, C. V., Schwartz, B., Hoppe, C., et al. (1989). Active surveillance for toxic shock syndrome in the United States. *Reviews of Infectious Diseases, 11*(Suppl. 1), S28-S34.

Hajjeh, R. A., Reingold, A., Weil, A., Shutt, K., Schuchat, A., & Perkins, B. A. (1999). Toxic shock syndrome in the United States: Surveillance update, 1979-1996. *Emerging Infectious Diseases, 5*, 807-810.

Kehrberg, M. W., Latham, R. H., Haslam, B. T., Hightower, A., Tanner, M., Jacobson, J. A., et al. (1981). Risk factors for staphylococcal toxic-shock syndrome. *American Journal of Epidemiology, 114*, 873-879.

O'Neil, R. M. (1996). A researcher's privilege: Does any hope remain? *Law and Contemporary Problems, 59*(3), 35-49.

Osterholm, M. T., Davis, J. P., Gibson, R. W., Mandel, J. S., Wintermeyer, L. A., Helms, C. M., et al. (1982). Tri-state toxic-shock syndrome study. I. Epidemiologic findings. *The Journal of Infectious Diseases, 145*, 431-440.

Osterholm, M. T., Gibson, R. W., Mandel, J. S., & Davis, J. P. (1982). Tri-state toxic shock syndrome study: Methodologic analysis. *Annals of Internal Medicine, 92*, 899-902.

Reingold, A. L., Hargrett, N. T., Shands, K. N., Dan, B. B., Schmid, G. P., Strickland, B. Y., et al. (1982). Toxic shock syndrome surveillance in the United States, 1980 to 1981. *Annals of Internal Medicine, 96*, 875-880.

Schlech, W. F., Shands, K. N., Reingold, A. L., Dan, B. B., Schmid, G. P., Hargrett, N. T., et al. (1982). Risk factors for development of toxic shock syndrome: Association with a tampon brand. *Journal of the American Medical Association, 248*, 835-839.

Schuchat, A., & Broome, C. V. (1991). Toxic shock syndrome and tampons. *Epidemiologic Reviews, 13*, 99-112.

Shands, K. N., Schmid, G. P., Dan, B. B., Blum, D., Guidotti, R. J., Hargrett, N. T., et al. (1980). Toxic-shock syndrome in menstruating women. *The New England Journal of Medicine, 303*, 1436-1442.

Todd, J., Fishaut, M., Kaprai, F., & Welch, T. (1978). Toxic-shock syndrome associated with phage-group-1 staphylococci. *Lancet, 2*, 1116-1118.

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