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The Transnational Tobacco Industry and Oral Health

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Objective: All tobacco products carry established or probable adverse oral health effects. This study highlights several examples of actions by transnational tobacco corporations to obscure those effects, including several in which they were aided by the oral health community.**Methods:** Information was derived primarily from a search of records in the Truth Tobacco Industry Documents Database, supplemented by other published material and the author's personal experiences. **Results:** Tobacco companies attempted to interfere with oral cancer research and dissemination of its findings the 1950s and 1960s. Philip Morris, Inc. partnered with the American Dental Association's periodontal research centre until 1973 and the Council for Tobacco Research supported its dental student research program until 1972. Swedish Match funded much of the Swedish research on oral health effects of its smokeless tobacco products and helped foster the current "tobacco harm reduction" strategy. Electronic nicotine delivery devices are the current focus of that strategy, though data on oral health effects are sparse. **Conclusions:** The transnational tobacco industry has a long history of deception, corruption, and devastation, and oral health was no exception. Organized dentistry may have unwittingly aided and abetted the tobacco industry during a critical period of history.

All tobacco products carry established or probable adverse oral health effects. Case-control studies that associated tobacco use with oral cancer appeared as early as the 1920s (Broders, 1920; Lombard and Doering, 1928). While evidence for smoking was sufficient to support causal conclusions for lung cancer aetiology in the early 1960s, both the 1962 UK Royal College of Physicians' report (1962) and the U.S. Surgeon General's Report on Smoking and Health (US Department of Health, Education, and Welfare, 1964) concluded that smoking and other forms of tobacco use may increase the risk of oral cancer, but the evidence was not yet sufficient to support a causal conclusion. It is now widely accepted that cigarette smoking is a major cause of cancers of the oral cavity and pharynx, responsible most of those cancers worldwide (International Agency for Research on Cancer, 2004; U.S. Department of Health and Human Services, 2004). Other combusted tobacco products, such as cigars, produce smoke that generally contains the same carcinogenic agents as cigarettes and have also been identified as risk factors for head and neck cancer (Munshi, *et al.,* 2015; Shanks and Burns, 1998). In addition, comprehensive reviews conducted by major health agencies have concluded that smokeless tobacco use is a cause of oral cancer (International Agency for Research on Cancer, 2007; U.S. Department of Health and Human Services, 1986).

The periodontal effects of tobacco use first appeared in the scientific literature more than 70 years ago (Pindborg, 1947). There is now consistent and compelling evidence that smoking is a major cause of chronic periodontitis (U.S. Department of Health and Human Services, 2004), and that cigar and hookah smoking may increase the risk for periodontitis (Albandar *et al.*, 2000; Krall *et al.*, 1999; Ramôa *et al.*, 2017). Oral surgical procedures generally have higher complication rates and poorer wound healing among smokers than among non-smokers (Tarakji *et al*., 2015; Sørensen, 2012; Javed *et al.*, 2012). Rapidly accumulating evidence consistently suggests that smoking increases the risk for dental implant failure (Alfada, 2018; Chrcanovic *et al.*, 2015; Strietzel *et al.*, 2007). Smokeless tobacco use is strongly associated with localized gingival recession and oral mucosal lesions, and may increase the risk for root surface caries (Greer, 2011).

Actions taken by the transnational tobacco industry over the past century hid or downplayed the negative oral health impacts of tobacco use and likely delayed the oral health community's responses to tobacco use. This study highlights several episodes in that history, including several in which the oral health community aided and abetted the tobacco industry.

Methods

Information on the tobacco industry was derived primarily from a search of records in the Truth Tobacco Industry Documents Database maintained by the University of California – San Francisco (https://www.industrydocumentslibrary.ucsf.edu/tobacco/). That database is a searchable archive of more than 14 million documents by tobacco companies about their advertising, manufacturing, marketing, scientific research and political activities. The search began with broad terms such as "dental", "periodontal", and "mouth cancer". It then narrowed as specific themes and organizations emerged. That search was supplemented by other published material and the author's personal experiences during the past quarter century.

Results

The tobacco industry and oral cancer research

As evidence mounted during the 1940s and 1950s that smoking increased the risk of oral and pharyngeal cancer, tobacco companies sought to control the information or at least gain early access to it in order to refute it. For

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example, starting in July 1951, Reynolds Tobacco Company made a series of cash donations to the Memorial Center for Cancer and Allied Diseases to "further enable the compilation of data on the possible effects of tobacco as they are related to mouth cancer" (Rhoads, 1951). The industry was keenly aware of the cancer research that Ernest Wynder was conducting at that institution, which was part of New York University's Sloan-Kettering Medical Center. As was revealed in other internal tobacco industry documents, these contributions were intended to influence the institution's research and its reporting and to provide the industry with early warning of potentially damaging research findings. One internal document summarized some of the industry's motivation for these financial contributions: "*Mr. Hanmer's* [H.R. Hanmer was Director of Research for the American Tobacco Company] *recommendations were to offer up to $30,000 in additional funds to Damon Runyon* [a cancer research fund established in 1947]*, let the other representatives of industry know about the contribution, cultivate Rhoads* [C.P. Rhoads, MD, Director of the Memorial Center for Cancer and Allied Diseases] with the object of finding *out what he has in mind and "what he will do if we comply with his recommendations", attempt to persuade the N.Y.U. group to correct some of the "scientific fallacies", develop means for following closely all developments in the field of cancer research…commence a critical study of Wynder's work and if bias is shown make this information available…While Mr. Hanmer believes that he would have recommended that the Company support the N.Y.U project, on the basis of assurances that Wynder would be "controlled"*". (Unknown, 1954).

In fact, the Memorial Center for Cancer and Allied Diseases had been receiving financial contributions from tobacco companies to support research on oral cancer since at least 1946 (Clarke, 1946), when Camel Cigarettes donated support to Dr. Hayes Martin's research on tobacco and oral cancer. A draft manuscript by Martin titled "Tobacco in the Etiology of Mouth Cancer" was found in the files of Reynolds Tobacco Company in discovery for the 1990 lawsuit brought against the major U.S. tobacco companies by the State of Minnesota (Martin, 1946a). The study includes 1,318 cases and 1,059 controls, and concluded, "The degree of tobacco addiction in all forms of mouth cancer is higher than in the control group" and "The greatest difference between the mouth cancer group and the control groups is the percentage of heavy and excessive smokers." Curiously, that manuscript was apparently never published and therefore not included in the 1964 U.S. Surgeon General's Report. In addition, Dr. Martin was somewhat dismissive of tobacco as an independent risk factor for oral cancer in his 1946 paper, Mouth Cancer and the Dentist (Martin, 1946b): "*In most cases of mouth cancer, however, one can find evidence of more than one form of chronic irritation; therefore it is erroneous to ascribe the lesion in any given case to tobacco simply because the person smokes. Further investigation often proves that the patient also has syphilis and suffers from avitaminosis*."

The Tobacco Industry and the American Dental Association

The tobacco industry had connections with the American Dental Association (ADA) over at least 50 years. In the 1930s through 1950s, those connections primarily involved tobacco advertisements in the *Journal of the American Dental Association* and exhibits at the ADA Annual Meeting (American Dental Association, 1936; Philip Morris & Co., 1936; Brown & Williamson, 1941). By the mid-1950s, that relationship began to change.

On October 1, 1956, the ADA included a session on oral cancer during its annual meeting in Atlantic City, NJ. Dr. Harold Hillenbrand, Secretary of the American Dental Association, sent a letter dated August 30, 1956 and a preliminary copy of the program for that annual session to Robert C. Hockett, Associate Scientific Director of the Tobacco Industry Research Committee, addressed as "Dear Bob" (Hillenbrand, 1956). The Tobacco Industry Research Committee (TIRC) had been established in 1953 by the largest American tobacco companies, in partnership with a public relations firm, in response to evidence linking tobacco smoking to lung cancer, heart disease, and other diseases (Brandt, 2012). The primary function of the TIRC was to cast doubt on mounting evidence of tobacco's harm and to allow the industry to claim that it was supporting research to ensure the safety of its products. TIRC was little more than a public relations effort, and leading researchers on the health effects of tobacco use at the time realized as early as 1954 that TIRC had no intention of funding research designed to reduced disease and death caused by smoking (Ochsner, 1954). In a September 20, 1956 letter, Hockett (1956) asked Hillenbrand for advanced copies of the papers that were to be presented at the conference. An internal memo suggests that several TIRC employees obtained advance drafts of the ADA press release on that conference and convinced the ADA communications people to change its contents (Thompson, 1956). The headlines in the next day's major newspapers downplayed any possible role of tobacco in the development of oral cancer (Unknown, 1956).

If the ADA might be forgiven for its warm relations with the tobacco industry in the 1950s, when the adverse health effects of tobacco use were not yet well established, the relationship was less understandable a decade later. The ADA established its Periodontal Pathology Research Center in 1968, supported primarily by the Clark Gum Division of Philip Morris, Inc. [American Dental Association, 1968]. That partnership emerged four years after the U.S. Surgeon General's landmark report established smoking as a cause of cancer in humans [U.S. Department of Health, Education, and Welfare, 1964]. Why would Philip Morris be interested in supporting this ADA initiative? For its contributions, internal memos reveal that Philip Morris executives felt the affiliation with ADA would boost the company's corporate image, build goodwill with the ADA, gain early access to research and therefore early notice of potentially damaging findings, and curry favour with the ADA if Philip Morris later decided to pursue the ADA Seal of Acceptance for the line of oral hygiene products it was developing (Echeandia, 1968). Furthermore, Philip Morris executives felt that "*Dr. Tieke* [Richard W. Tieke, Director of the Periodontal Pathology Research Center] *would become a "de-facto" consultant, stating "We fully expect that as areas worthy of further investigations become apparent from the studies and compilations, we would get first notice…Via Dr. Tiecke,*

we would know what is going on at other public institutions. The elimination of the lag time (6 months to 1 year) between research and publications could be our greatest benefit." Philip Morris maintained its affiliation with the Periodontal Pathology Research through 1973.

The ADA also established a Dental Student Research Fellowship in 1966, which was fully supported by the Council for Tobacco Research – USA (formerly the Tobacco Industry Research Committee) from 1966 through 1972 (Hillenbrand, 1966). There is evidence that at least one dental school dean expressed concern about this source of funding, but relented after assurances from the ADA that the awards were made with "no strings attached" (Ingle, 1967). Research reports from this fellowship program were passed along to the Council for Tobacco Research, fulfilling one of the tobacco industry's main objectives for supporting such research programs in addition to currying favour with the ADA.

Smokeless Tobacco and Industry Deception

On April 19, 1995, I found myself sitting around a conference table with attorneys from several major tobacco companies. At the time, I was an epidemiologist with the Office on Smoking and Health, part of the U.S. Centers for Disease Control and Prevention (CDC), and among other duties I was responsible for overseeing smokeless tobacco manufacturers' response to several requirements of the Comprehensive Smokeless Tobacco Health Education Act of 1986 (U.S. Government Printing Office, 1986). Among the provisions of that law, manufacturers of smokeless tobacco were required to report "the quantity of nicotine contained in smokeless tobacco products." In 1989, the smokeless tobacco industry requested and received permission from the U.S. Department of Justice for collaboration among the manufacturers to develop a uniform analytic protocol to measure nicotine levels in their products. The industry submitted that protocol to CDC in 1993, which then sought peer review. In response to peer reviewers' comments on the draft protocol submitted by the ten major U.S. manufacturers of smokeless tobacco at the time, the Office on Smoking and Health (OSH) requested that the manufacturers revise the protocol to include product pH. Why did we ask for data on pH? As was revealed during a product liability court case a decade earlier in which a young consumer of smokeless tobacco died from oral cancer, *Marsee v. U.S. Smokeless Tobacco*, smokeless tobacco manufacturers can and do manipulate nicotine dosing of their products in order to develop low-dose "starter" products for novice users and higher dosage products for users who have developed greater nicotine tolerance and progressed in the nicotine addiction process (Connolly, 1995). One manufacturing process that smokeless tobacco companies employ to control nicotine dosing is adjusting the product's pH: at acidic or neutral levels, the proportion of nicotine in its more bioavailable unprotonated (un-ionized) form is relatively low and nicotine absorption across oral mucosa is fairly slow. However, at more alkaline levels, increasingly high levels of nicotine are unprotonated and the rate and amount of nicotine absorption increases dramatically, as does nicotine's physiologic effects (Fant *et al.*, 1999). This relationship between pH and nicotine bioavailability had been documented in the scientific literature for at least a century with animal experiments that clearly established the role of pH on nicotine's physiologic effects published as early as 1940 (Travell, 1940). Manufacturers add alkaline buffering agents such as sodium carbonate and ammonium carbonate to increase the pH of smokeless tobacco products and thereby enhance the rate and amount of nicotine dosing.

In response to this request from OSH to include product pH in manufacturers' protocol and subsequent data submissions, the tobacco industry lawyers balked. In a May 9, 1995 letter to OSH from U.S. Smokeless Tobacco Company, the nation's largest manufacturer of smokeless tobacco products, the company denied that pH has any effect on "so-called 'free nicotine'". The company based its claim on a company-commissioned, but unpublished, review paper that concluded, "In summary, it is not the pH of smokeless tobacco, but a variety of other chemical, biological and behavioral factors that are responsible for the degree of absorption of nicotine from smokeless tobacco."

I was incredulous and perhaps a bit naïve. How could a major corporation flat-out lie to a U.S. federal agency when the evidence that contradicted the company's claims was publicly available? If pH was not a significant factor in nicotine bioavailability, why was information on product pH so secret that tobacco company attorneys were fighting its reporting? In response to this episode, we published a peer-reviewed journal article on pH and nicotine absorption (Tomar and Henningfield, 1997). CDC ultimately prevailed, and as of June 30, 1999 the smokeless tobacco manufactures were required to follow the published ``Protocol for Analysis of Nicotine, Total Moisture, and pH in Smokeless Tobacco Products'' and report their data to CDC annually (Centers for Disease Control and Prevention, 1999).

Smokeless Tobacco and "Tobacco Harm Reduction"

Despite evidence that smokeless tobacco products are carcinogenic, are associated with other adverse health effects, and almost entirely taken up by adolescent and young adult males, in the 1990s several proponents began touting the use of these products as part of a "tobacco harm reduction" strategy. The theory behind this strategy is that smokers who are unable or unwilling to quit all tobacco could switch to a less harmful form (Stratton *et al*., 2001). Advocacy of smokeless tobacco as a harm reduction approach was heavily driven by the experience in Sweden, where tobacco-related mortality rates had dropped significantly, due to a declining prevalence of cigarette smoking. That drop in smoking was attributed by some to greater use of snus (oral snuff) among the male tobacco users (Ramstrom, 2000; Henningfield & Fagerstrom, 2001; Foulds *et al.*, 2003). Others questioned whether snus really was the primary driver of reduced smoking in Sweden: nearly all growth in snus use occurred among adolescent and young adult males, nearly all smoking cessation occurred among middle age adults who did not use snus, and smoking was declining at the same rate among females as it was among males despite nearly no female snus consumption (Tomar *et al*., 2003).

While some tobacco control advocates sincerely believed that moist snuff or snus could play a role in tobacco harm reduction, including in populations with little history of using oral tobacco, it is clear that transnational tobacco companies were major drivers of the debate. Tobacco corporations were assisted in their marketing efforts by willing researchers, including some from the oral health community. One of the earliest and most vocal proponents of the tobacco harm reduction theory in the United States was Dr. Brad Rodu, an oral pathologist (Rodu, 1995). Dr. Rodu currently holds the position of Endowed Chair in Tobacco Harm Reduction Research at the University of Louisville, a position created by major donations from US Smokeless Tobacco Company, now part of Altria, and Swedish Match, Europe's largest smokeless tobacco company. Although Rodu's disclosures in a letter to the editor he recently co-authored (Hughes *et al*., 2019) and his curriculum vitae (Rodu, 2018) note that his only source of extramural research support since 1999 has been "unrestricted grants" from Swedish Match, Altria Client Services, British American Tobacco and Reynolds American Inc., internal tobacco industry documents and communications suggest a much more active involvement in helping the industry with marketing, media, and regulatory challenges (Rodu 2000; Smith 2000; Rodu 2009).

Swedish Match has played a major role in funding many Swedish studies on the health effects of snus. Both Swedish case-control studies cited as evidence that snus does not cause oral cancer (Schildt *et al*., 1998; Lewin *et al*., 1998) were supported by research funds largely controlled by Swedish Match. Drs. Freddi Lewin and Lars Rutqvist, who co-authored one of those studies, subsequently left the Karolinska Institute to join Swedish Match (Swedish Match, 2006). Those case-control studies, whose findings have been misinterpreted and suggest serious methodological concerns, helped the company promote its products as part of a tobacco harm reduction strategy. The emboldened company pressed the Swedish government to seek removal of the ban on moist snuff in the rest of the European Union (Swedish Match, 2008), a move recently rejected by the European Court of Justice (Reuters, 2018).

As has been shown in a previous study of internal tobacco company documents, the transnational tobacco companies' adoption of the term "harm reduction" occurred in direct response to the public health agenda and The Institute of Medicine's 'Clearing the Smoke' study (Peeters and Gilmore, 2015). That study concluded that harm reduction serves the interests of transnational tobacco companies in two main ways. First, those companies use harm reduction to facilitate access to, and dialogue with scientists, public health experts and policy makers, presenting themselves as 'partners, rather than adversaries' who share a common goal. Second, harm reduction helped the tobacco industry rehabilitate its image, and provided it with the facade of being a socially responsible business while it still heavily markets its deadliest products throughout the world. The focus of tobacco harm reduction efforts has largely shifted from smokeless tobacco to e-cigarettes and other electronic nicotine delivery devices, or ENDS (Drope *et al*., 2017). The multi-billion dollar market of a class of products that first emerged just over a decade ago continues to grow, despite the near-absence of data on their long-term oral or overall health effects. We are witnessing an epidemic of e-cigarette use among young people (Drope *et al*., 2017; Glantz and Bareham, 2018; NHS Digital, 2018), and nicotine exposure during adolescent is associated with cognitive and behavioural impairments and lifelong structural and functional changes in the brain (England *et al*., 2015). These products also may represent new threats to oral health (Tomar *et al*., 2015), with emerging *in vitro* evidence of adverse effects on periodontal tissues (Sultan *et al*., 2018), cytotoxicity (Behar *et al*., 2016), and impaired immune function (Clapp *et al*., 2017). Like many chapters in the history of the transnational tobacco industry, tobacco harm reduction is much more about corporate profit than about concern for public health.

Discussion

The transnational tobacco industry has a long history of deception, corruption, and devastation, as has been well documented in the literature (Kessler, 2001; Brandt, 2012). The evidence of the industry's pattern of pernicious behaviour was so overwhelming that, in 2006, U.S. District Judge Gladys Kessler found the major U.S. tobacco companies had violated the Racketeer Influenced and Corrupt Organizations (RICO) Act and engaged in a decades-long conspiracy to deceive the American public about the health effects of smoking and their marketing to children (U.S. District Court for the District of Columbia, 2006).

Analysis of internal tobacco industry documents and recent events suggests that oral health effects are among the many diseases and conditions subject to denial and obfuscation by transnational tobacco corporations. There is also evidence that organized dentistry partnered with the tobacco industry for many years, including a decade after authorities in Europe and the United States had definitively concluded that cigarettes cause cancer and premature death. The ADA itself passed a resolution calling for dentists to inform their patients of the health hazards of tobacco use (American Dental Association, 1964). It is not possible to quantify the effects of that relationship, but there is some evidence that the tobacco industry was able to gain early access to emerging research findings on oral health effects and help spin the news shared with the public.

In the current era of "tobacco harm reduction", we are witnessing an increasing partnership between the transnational tobacco corporations and the research community, including some oral health researchers. Sales of electronic nicotine delivery devices are exploding although, as happened with earlier generations of novel tobacco products, the market is heavily driven by teenage consumers (Glantz and Bareham, 2018). Meanwhile, transnational tobacco companies continue to market conventional cigarettes heavily, their most profitable and lethal product, killing more than 7 million people worldwide in 2016 alone (Drope *et al*., 2018). Oral health receives little or no attention in the discussions of tobacco product development or regulation. We urgently need research on the health effects of these new products to catch up with their sales, while remembering that their manufacturing and marketing are increasingly controlled by the same vectors of disease as other tobacco products: the transnational tobacco corporations (Glantz and Bareham, 2018).

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