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SMOKELESS TOBACCO AND BLOOD PRESSURE

To the Editor: On January 22, 1985, the Federal Trade Commission asked the Surgeon General, Everett Koop, to undertake a comprehensive investigation on the health dangers of smokeless tobacco, similar to the investigation that led to the 1964 Surgeon General's Report on Smoking and Health. We support this decision, particularly in the light of the latest published literature and our recent findings on the relation between "smokeless tobacco" and blood pressure.

An increase in consumption of smokeless tobacco is apparent among children and adolescents. One report indicated that 18 per cent of sixth and ninth graders dipped snuff.[1] Other reports indicated that 7.1 per cent of youths in grades 7 through 12 chewed tobacco, and 11 per cent of school children aged 13 to 14 used snuff. Increasing trends in the use of smokeless tobacco have been noted among high-school and college students.[2] These statistics suggest that the use of smokeless tobacco indeed represents a health concern of growing magnitude for children and adolescents. As a consequence of its addictive qualities, the consumption of smokeless tobacco often becomes a lifelong habit with cumulative and deleterious effects on health. Specifically, these effects include halitosis, discoloration of teeth and fillings, destruction of periodontal bone and soft tissue, slower healing of cuts and sores in the mouth, tooth abrasion, gum recession, leukoplakia, and oral cancer, particularly verrucous carcinoma.[2-4] There is also a large body of medical literature that deals with the hemodynamic effects of smoked tobacco and intravenously administered nicotine. Smokeless tobacco can also produce changes in the cardiovascular system in dogs and human beings,[5] but for the most part, the acute hemodynamic responses and chronic effects of oral smokeless tobacco have been neglected as a topic for investigation, especially with regard to hypertension in children and adolescents.

Our findings indicate a direct and positive relation between smokeless-tobacco use and higher blood-pressure readings, particularly among young men aged 18 to 25. These findings are based on screening for oral cancer and blood pressure in users of various categories of tobacco among 1663 volunteers. Our sample consisted of 710 male subjects and 923 female subjects, 18 years of age and older. Sixty-nine of the male subjects (9.7 per cent) were self-reported smokeless-tobacco users, and 35 (4.9 per cent) were previous smokeless-tobacco users. Less than 1 per cent of the female subjects had used smokeless tobacco. The mean blood pressure of the 19 current male smokeless-tobacco users aged 18 to 25 was 143.7/80.7 mm Hg, and that of the 23 male cigarette smokers in this age group was 127.7/70.0. Among nonusers of tobacco in this age group, the mean blood pressure was 131.6/72.8. The mean difference in diastolic pressure between tobacco users and nonusers was 7.9 mm Hg ($P \leq 0.01$). The average duration of smokeless-tobacco use in this age category was 5.5 years (range, 2 to 10). Thus, along with the addictive characteristics of nicotine and its etiologic role in cancer, smokeless-tobacco use appears to be associated with higher blood-pressure levels in young adults. This may hold true in the preadolescent and adolescent populations, in which its use is of growing magnitude.

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SMOKELESS IS NOT SALTLESS

To the Editor: Great attention is paid to the sodium consumption of patients with a wide variety of disease processes. Items not considered foodstuffs are often ignored by physicians, and among these items are the various forms of smokeless or chewing tobacco (moist snuff, loose leaf, and plug). Because of the booming popularity of smokeless tobacco in the United States,[1] 16 retail brands were analyzed for sodium content (Table 1).

These samples contained large amounts of sodium (mean, 1.76 per cent by weight), comparable in magnitude to such foods as dill pickles (1.43 per cent sodium) and cured, fried bacon (1.09 per cent sodium),[2] which are traditionally considered extremely high in sodium. Considering that users of these products have been re-

Table 1. Sodium Content of Smokeless Tobaccos.

Brand	Container Size	% Sodium	Sodium/ Container
	g		*mg*
Snuff			
Copenhagen	34.02	3.17	1078
Gold River	34.02	0.61	207
Happy Days Mint	34.02	3.53	1201
Hawken	34.02	0.92	313
Kodiak	34.02	3.33	1126
Skoal	34.02	3.38	1150
Loose leaf			
Beech-Nut	85.05	0.97	829
Beech-Nut Wintergreen	85.05	0.97	822
Big Red	85.05	0.88	748
Red Man	85.05	0.79	673
WB Cut	34.02	3.07	1044
Plug			
Apple Sun Cured	45.62	1.19	545
Bloodhound	44.93	1.77	795
Brown's Mule	44.26	1.20	533
Days-O-Work	69.78	1.46	1020
Red Man Plug In A Pouch	57.27	0.85	488

ported to chew as much as 8 to 12 pouches of loose-leaf tobacco daily,[3] each pouch containing 85 g of tobacco, the potential for substantial sodium ingestion from these products becomes apparent.

The proportion of sodium absorbed by the smokeless-tobacco user has yet to be determined. It may depend on whether the tobacco juice is swallowed or expectorated, as was the case with one diabetic chewer whose blood sugar came under control only after he was convinced to stop swallowing the juice from the sweetened tobacco.[4] Like sugar,[5] sodium is added for flavor during the manufacturing of these products.

In 1980, an estimated 22 million Americans used chewing tobacco or snuff. Tobacco-industry analysts estimate that this number could double during the current decade.[6] This growing popularity necessitates that physicians and the public understand the potentially harmful effects of smokeless tobacco. Physicians should be aware that in addition to the other risks associated with these products,[7] they may pose a potential threat to patients who must restrict their sodium intake.

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PREMENSTRUAL SYNDROME

To the Editor: The article by Muse et al. in the November 22 issue* is a welcome addition to a growing body of literature on the premenstrual syndrome. The authors are to be congratulated for their willingness to investigate a syndrome that defies precise definition and for which there are no universally accepted diagnostic criteria. Their use of prospective data to establish a premenstrual pattern of symptoms and their careful attempts to eliminate other psychiatric conditions that may mimic the premenstrual syndrome distinguish this study from most others.

One methodologic point requires clarification, however. The authors state: "The possibility of coexisting psychiatric illness was evaluated . . . with the use of the Minnesota Multiphasic Personality Inventory [MMPI]. . . ." They do not state, however, when in the menstrual cycle the MMPI was administered. We have been using this test for three years as one part of the evaluation of women with premenstrual symptoms. Our experience with the MMPI in women with premenstrual symptoms demonstrates that conclusions based on the MMPI or clinical interviews performed randomly and only once during the menstrual cycle can be misleading and inaccurate.

We administered the MMPI to 111 women with a premenstrual pattern of physical and emotional symptoms as determined by the history and prospective charting. The MMPIs were highly valid in both menstrual phases. As shown in Table 1, mean scores on MMPI scales 1, 2, 3, 4, 6, 7, 8, 0, and A were significantly higher ($P<0.001$) in the luteal than in the follicular phase of the menstrual cycle. Scores on the ego-strength scale were significantly lower ($P<0.001$) in the luteal phase.

*Muse KN, Cetel NS, Futterman LA, Yen SSC. The premenstrual syndrome: effects of "medical ovariectomy." N Engl J Med 1984; 311:1345-9.

Thus, if a woman with severe premenstrual syndrome was tested in the luteal phase alone, she may have been inappropriately excluded from the study on the basis of an abnormal result on the MMPI, when in fact the abnormal profile was related to her premenstrual syndrome. Our results suggest that women undergoing psychiatric evaluation should be questioned about the relation between their symptoms or abnormal behavior and their menstrual cycle. When an association between psychiatric symptoms and the menstrual cycle is established, an accurate assessment may be obtained only if the patient is tested and evaluated in both the luteal and follicular phases.

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To the Editor: Muse et al. investigate a potentially valuable new therapeutic maneuver aimed at treating a disabling disorder. The authors present evidence suggesting that daily subcutaneous injections of gonadotropin-releasing hormone (GnRH) reduce the symptoms of the premenstrual syndrome as well as induce a medical ovariectomy. However, they do not demonstrate, as their paper title and discussion imply, that medical ovariectomy itself reduces these symptoms. The authors neither eliminate nor consider alternatives to their supposition that functional ovariectomy is essential to therapy. They favor their stated hypothesis because ovarian hormones are known to influence brain function and behavior. However, GnRH has also been shown to influence brain function and behavior directly.[1,2] Thus, one must entertain the hypothesis that the alteration of plasma levels of GnRH (resulting from the daily injections of that hormone) could itself be responsible for reducing the symptoms of the premenstrual syndrome, irrespective of changes in the plasma levels of the sex steroids. One must also consider other explanatory hypotheses that take into account the complex alterations in the hypothalamic–pituitary–gonadal axis and associated target organs occurring as a result of the daily injections of GnRH. For example, one might hypothesize that the recorded alterations in plasma levels of follicle-stimulating hormone and luteinizing hormone (resulting from the GnRH injections) could be responsible for relieving the symptoms, again irrespective of resultant changes in plasma levels of other hormones.

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REDUCTION OF BIOAVAILABILITY OF VERAPAMIL BY RIFAMPIN

To the Editor: In the December 27 issue Engelhard et al.[1] reported a clinically important pharmacokinetic drug interaction between rifampin and ketoconazole. We recently observed a similar interaction between rifampin and the calcium-entry blocker verapamil.

A hypertensive patient was treated with oral doses of verapamil. At the same time he received a combination of rifampin, isoniazid,

Table 1. Mean Scores on the Minnesota Multiphasic Personality Inventory among 111 Women.

CYCLE	MEAN RAW SCORE											
Scale * →	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*0*	*A*	*Es*
Follicular	18.6	26.6	27.8	24.5	40.3	12.4	32.6	30.5	18.4	30.8	16.7	39.3
Luteal	21.2	34.3	31.9	28.3	40.8	14.8	38.4	37.4	18.7	39.3	25.4	33.1

*Scale A refers to conscious anxiety, and Es ego strength.