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Original Research Article

Explaining Sex Differences in Dental Caries Prevalence: Saliva, Hormones, and "Life-History" Etiologies

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ABSTRACT When dental caries rates are reported by sex, females are typically found to exhibit higher prevalence rates than males. This finding is generally true for diverse cultures with different subsistence systems and for a wide range of chronological periods. Exceptions exist, but are not common. In this paper, we present new data for sex differences in dental caries rates among the Guanches (Tenerife, Canary Islands), summarize results of meta-analyses of dental caries prevalence, and emphasize new research that stresses the critical role of female hormones and life-history events in the etiology of dental caries. Among the Guanches, corrected tooth-count caries rates for females (8.8%, 158/1,790) are approximately twice the frequency of caries among males (4.5%, 68/1,498). Higher caries prevalence among females is often explained by one of three factors: 1) earlier eruption of teeth in girls, hence longer exposure of girls' teeth to the cariogenic oral environment, 2) easier access to food supplies by women and frequent snacking during food preparation, and 3) pregnancy. Anthropologists tend to favor explanations involving behavior, including sexual division of labor and women's domestic role in food production. By contrast, the causal pathways through which pregnancy contributes to poorer oral health and higher caries rates are deemphasized or discounted. This paper presents recent research on physiological changes associated with fluctuating hormone levels during individual life histories, and the impact these changes have on the oral health of women. The biochemical composition of saliva and overall saliva flow rate are modified in several important ways by hormonal fluctuations during events such as puberty, menstruation, and pregnancy, making the oral environment significantly more cariogenic for women than for men. These results suggest that hormonal fluctuations can have a dramatic effect on the oral health of women, and constitute an important causal factor in explaining sex differences in caries rates. Am. J. Hum. Biol. 18:540–555, 2006.

The primary goal of this report is to call attention to the complex role of saliva, hormones, and pregnancy as critical etiological forces contributing to sex differences in dental caries rates. We begin by documenting the ubiquitous nature of sex dimorphism in dental caries prevalence by presenting results of several clinical meta-analytic studies of living populations, and by presenting a case study of caries prevalence among the Guanches, ancient inhabitants of the Canary Islands. Dental caries is defined as focal demineralization of dental tissue (commonly enamel) caused by acidogenic bacteria in plaque (Ten Cate, 1998; Featherstone, 2000). The prevalence of dental caries in a study group is typically reported by anthropologists as the percentage of individuals or teeth observed to be affected by dental caries (Lukacs, 1995). Clinical and epidemiological studies of oral health often utilize an index based on the number of decayed, missing, or filled teeth (DMFT; World Health

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Organization, 1997). Dental caries rates may be used to characterize an entire group, though dietary variation within groups by status, occupation, and sex often necessitates reporting caries rates by culturally meaningful subgroups.

Dental caries rates typically increase with the adoption and intensification of agriculture (Ettinger, 1999; Larsen, 1983; Larsen et al., 1991; Lukacs, 1992), though prehistoric rice agriculturalists are an exception (Domett et al., 2000; Tayles et al., 2000). The decline in oral health accompanying the transition to agriculture is marked by a differentially severe impact upon women (Larsen, 1998; Lukacs, 1996). Higher caries prevalence among females is often explained by one of three factors: 1) earlier eruption of teeth in girls, and longer exposure to the cariogenic oral environment; 2) proximity of women to food supplies and snacking during food preparation; and 3) pregnancy and hormonal influences. Anthropologists tend to favor explanations involving behavior, including sexual division of labor and women's domestic role in food production. By contrast, the causal pathways through which pregnancy and hormonal fluctuations contribute to poorer oral health and higher caries rates are perceived to be unclear or undocumented.

The heavy reliance by anthropologists on behavioral explanations for differences in caries rates is understandable, and appears to be widely and uncritically accepted as the exclusive reason for sex differences in caries prevalence (Cohen and Bennett, 1993; Walker and Hewlett, 1990). For example, among ancient Chileans, the tendency for females to experience more dental disease than males "is attributable to sexual division of labor with respect to food gathering and the females serving as principal food preparers, and the fact that dental eruption occurs earlier in females" (Kelley et al., 1991, p. 209). Basing his argument on ethnographic documentation of dietary practices and on archaeological evidence from prehistoric Georgia (Larsen, 1983), Larsen (1995, p. 189) stated that "the increase in dental caries with agriculture was greater in women than men in most regions, which indicates widespread gender-based differences in preparation and consumption of food. Some evidence indicates that a combined high-carbohydrate and low-protein diet in females may have predisposed their teeth to more decay than males." Finally, for prehistoric South Asia, a behavioral explanation relied on sexual division of labor and distinctive dietary behaviors to explain sex differences in dental caries among "Mesolithic" foragers of the Ganges Plains (Lukacs and Pal, 1993), Bronze Age agriculturalists from Harappa (Lukacs, 1992), and increasing sex differences through time (Lukacs, 1996).

Though pregnancy is occasionally advanced as a causal factor promoting higher caries rates among women, the mechanisms and etiological pathways that contribute to worse dental health are rarely specified in any detail, or are said to be unproven (Larsen, 1997). In a comprehensive review of factors potentially responsible for the higher caries prevalence among females, Larsen et al. (1991, p. 194) stated, "It has long been thought that pregnancy compromises dental health, and leads to an increase in periodontal disease and dental caries. Review of the dental literature, however, does not support this interpretation." This opinion on the role of pregnancy in contributing to worse dental health among women was recently restated, "There is a conventional belief that pregnancy compromises dental health provoking dental caries and tooth loss. However, such a relationship is not borne out by scientific evidence" (Larsen, 1998, p. 175). A growing body of clinical research, beginning in the 1990s, revealed that both physiological sex differences and pregnancy have an important though indirect impact on oral ecology and dental health. The biochemical composition of saliva and rate of flow vary significantly by sex, and play a prominent role in causing sex differences in oral health generally, and differences in dental caries rates in particular. Meta-analyses of caries prevalence and new dental caries data from the Canary Islands are presented to demonstrate the ubiquity of sex differences in caries rates. The functional role of saliva in oral health is discussed, with an emphasis on experimental and clinical evidence that demonstrates the influence that hormonal fluctuations and pregnancy have on the biochemistry of saliva and, ultimately, on oral health.

EPIDEMIOLOGICAL AND CLINICAL META-ANALYSES OF CARIES PREVALENCE

The nearly universal pattern of sex differences in dental caries prevalence is more widely appreciated by epidemiological and clinical investigators of oral health than by anthropologists. The National Research Council (1952) surveyed 24 research articles on dental caries prevalence, and found that 21 of these reported caries as more prevalent in females than males. Two studies found no sex difference in caries prevalence, and one found caries to be more frequent in males than in females. A subsequent analysis of a large sample of 7–12-year-old Edinburgh schoolchildren reported that at each age, girls showed a higher prevalence of caries than boys (Mansbridge, 1959). The gender difference in dental caries is sufficiently well-established in the health sciences that it comprises a central component of some research designs. For example, the gender difference in decayed, missing and filled index (DMF) was used in a meta-analysis to assess the role of fluoride in the caries decline in industrialized nations (Haugejorden, 1996). This study was based on nine reports of caries prevalence among 12–17-year-olds from the prefluoride era (1946–1959) and 10 studies of the same age group in the fluoride era (1983–1993). The hypothesis was that more frequent use of fluoride toothpastes among females would decease the "gender gap" in dental caries prevalence. Girls displayed significantly higher caries prevalence than males in all 19 study samples, however the hypothesis was unsupported. The gender difference in fluoride exposure was too small to matter, or the role of fluoride toothpastes as a causal factor in caries decline was overrated (Haugejorden, 1996). An extensive meta-analysis of a global sample of more than 50 epidemiological and clinical reports and 50 paleopathological studies of dental caries prevalence is in progress, and preliminary findings strongly support the female gender bias in caries prevalence (Lukacs and Thompson, 2006).

SEX DIFFERENCES IN DENTAL CARIES PREVALENCE AMONG THE GUANCHES

Guanche origins and culture

Hypotheses regarding the origin of the Guanches, prehistoric inhabitants of Tenerife, are based on data derived from osteological, genetic, linguistic, and ethnographic research. In the 18th century, Blumenbach (1808) recognized perceptible differences in facial and mandibular anatomy between Guanches and ancient Egyptians. However, von Humboldt and Bonpland (1819) maintained that the origins of the Guanches could only be inferred from linguistic evidence. They observed that several Guanche words have common roots with Berber dialects of northwest Africa, and thought that although these similarities may not constitute a proof of common origin, they suggest the existence of ancient connections between the Guanches and Berbers. This idea is supported by recent analyses of Guanche dental morphology. Several studies, based on large samples and multivariate statistical methods, revealed close physical similarities to the Berbers of northwest Africa (Bermudez de Castro, 1985; Guatelli-Steinberg et al., 1997, 2001; Irish, 1993; Irish and Hemphill, 1997).

The study of molecular genetic diversity recently confirmed insights from dental morphology, while also yielding more precisely the source populations and their relative contribution to the modern Canarian gene pool. Questions regarding the origin of the aboriginal inhabitants of the Canary Islands were initially approached using genetic markers in the 1950s (Flores et al., 2003). More recently, a molecular genetic perspective on Guanche origins commenced in the 1990s, based on uniparental (mitochondrial DNA (mtDNA) and Y-chromosome) and biparental (*Alu* insertion) polymorphisms. Analysis of these polymorphisms revealed three sources for the modern Canary Islander gene pool: a major Iberian contribution (62–78%); a substantial northwest African component (23–38%); and a minor sub-Saharan African component (3%; Maca-Meyer et al., 2004a). Importantly, the aboriginal genetic contribution to the modern Canarian gene pool exhibits a strong sexual bias. Evidence based on Y-chromosome data indicates a low (10%) contribution from males, while aboriginal mtDNA lineages are substantially more common (45%; Flores et al., 2001). Y-chromosome haplogroup types and diversity indicate that paternal lineages are overwhelmingly of European origin, and imply a highly asymmetric mating pattern after European occupation (Flores et al., 2003).

Ancient mtDNA was recently analyzed from 131 Guanche teeth from 14 archaeological sites on four islands (La Gomera, 7; Gran Canaria, 1; El Hierro, 1; and Tenerife, 5). This study yielded the first admixture estimates for modern Canarians based on genetic diversity in the aboriginal parent population (Maca-Meyer et al., 2004b). High genetic diversity of ancient mtDNA and four "founder haplotypes" were documented. They are interpreted as evidence against strong founder effects, and are congruent with a high level of diversity among immigrants or multiple waves of genetically different founding populations (Maca-Meyer et al., 2004b). Collectively, the results of molecular genetic studies suggest a greater time depth (ca. 2500 BP) and diversity of source populations than previously believed (Mercer, 1980).

Although questions regarding the number of founding events, colonization models, and exact sources of early migrations remain to be fully answered, the genetic perspective on the biological composition of Canary Islanders is regarded as consistent with archaeological, osteological, and linguistic data, and leads to some reasonable conclusions. A colonization scenario with three primary components can be derived: 1) northwest Africans settled the islands from east to west, following a stepping-stone model; 2) this aboriginal population was subsequently augmented by slave-trade immigration from sub-Saharan and northwest Africa; and 3) in the 15th century, the islands experienced extensive European immigration associated with the Norman conquest and Iberian colonization (Rando et al., 1999; Flores et al., 2001). That the genetic composition of modern Canarians varies from island to island is due to the differential impact of European colonization and extent of the slave trade.

Ethnohistorical insight into the first contact between Europeans and Canarians is poorly chronicled, yet informative (Gaspar and Vallejo, 1992). Several early sources provide valuable descriptions of Guanche culture at the time of European contact (Glas and Abreu de Galindo, 1764; de Espinosa and Markham, 1907). Significant interisland variation existed in language, dwellings, religion, and behavior, and were due to differences in environment, ecology, and history of colonization. Each island had its own unique features within the broader Guanche culture. Natural and manmade caves were used for human habitation, storage, and burials. Habitation caves were modified by leveling floors and constructing front walls of stone and timber. Some were occupied by chiefs; others served as convents. The symbolism of space in Guanche-culture cave sites contradicts earlier ideas on status and habitation sites (Eddy, 1997). On Gran Canaria, grain was stored in specially sealed and marked rock-cut pits, whereas on Tenerife, food was kept in ceramic urns in grain-storage caves known as *auchones*. Burial rites were remarkably complex and involved washing the corpse in the sea, sun-drying after the removal of internal organs, and wrapping in basketry or a leather shroud. Mummies were then either placed on stone platforms or strapped to wooden planks, and stood upright against the wall of burial caves. Burial caves contained as many as 300 individuals at the time of contact: some mummified, and others skeletonized. No complete mummies exits today. During the Middle Ages, most Guanche mummies were shipped to Europe for use by apothecaries in preparing medicinals.

Politically, Tenerife was subdivided into nine chiefdoms or *menceyes*. The title (*mencey*) was hereditary, yet required confirmation by a council of elders (Eddy, 1989, 1995). Land disputes and civil disagreements often led to a duel, which was resolved through a form of ritual combat that involved stone-throwing, stick fighting, and fisticuffs (Lukacs, 2006; http://ejmas.com/jwma/articles/2000/jwmaart_wolf_0500.html).

Women played a key role in making pottery and basketry, and in organizing and conducting religious practices. On Tenerife, men engaged in hunting, fishing, and plowing, but women sowed, tended, collected, and stored the harvest. Near shore, fish, wild cat, wild pig, partridge, and quail were preferred species, and were high-status items in the diet. Commoners relied heavily on shellfish, and shell middens are abundant throughout the islands. The Guanches of Tenerife subsisted on a diet that included dogs, goats, and goat milk, and a bread made of toasted barley flour and goat milk (*gofio*). Goats were the main source of meat, but pigs and sheep were also tended. Other dietary items included local fruits, berries, and roots.

Methods

During an analysis of the dental anthropology of the Guanches in 1991, the presence and size of dental caries were systematically recorded. Guidelines and recommendations for recognizing, scoring, and reporting dental caries in archaeologically derived skeletal collections were followed (Metress and Conway, 1975; Lukacs, 1989; referencess in Hillson, 2001). Different methods of reporting dental caries rates were described and critically reviewed by several investigators (Lukacs, 1995; Hillson, 2001; Duyar and Erdal, 2003). Standardized methods were employed in sex determination, with priority given to the most accurate and reliable skeletal elements available for examination (Ferembach et al., 1980; Krogman and İşcan, 1986). Sex assessment of crania and mandibles relied on traditional sex-dimorphic variations in morphology (Bass, 1987; references in Buikstra and Ubelaker, 1994). Statistical comparison of caries rates by

TABLE 1. Observed and corrected dental caries rates among Guanches by sex and region (Tenerife, Canary Islands)[1]

	Male				Female				Sexes pooled			
	Observed		Corrected		Observed		Corrected		Observed		Corrected	
	%	+/n	%	$+_e/n_e$	%	+/n	%	$+_e/n_e$	%	+/n	%	$+_e/n_e$
Maxillary												
North	7.5	11/146	3.9	11/279	10.9	25/229	7.8	27/347	9.6	36/375	6.1	38/626
South	0.3	1/333	0.2	1/414	7.2	29/404	5.5	29/532	4.1	30/737	3.2	30/946
N and S	2.5	12/479	1.7	12/693	8.5	54/633	6.4	56/879	5.9	66/1,112	4.3	68/1,572
Mandibular												
North	6.5	23/352	5.2	23/416	15.6	60/384	11.2	60/476	11.3	83/736	9.3	83/892
South	10.4	33/318	7.8	33/389	12.1	42/348	8.8	42/435	11.3	75/666	9.1	75/824
N and S	8.4	56/670	7.0	56/805	13.9	102/732	11.2	102/911	11.3	158/1,402	9.2	158/1,716
Mx and Md	5.9	68/1,149	4.5	68/1,498	11.4	156/1,365	8.8	158/1,790	8.9	224/2,514	6.9	226/3,288

[1]Observed and corrected caries rates calculated according to procedures described in Lukacs (1995). N, North; S, South; Mx, Maxillary; Md, Mandibular; +, number of teeth observed with dental caries; n, total number of teeth observed; $+_e$, estimated number of teeth afflicted with caries; n_e, estimated number of teeth prior to tooth loss.

region and sex employed chi-square tests of data arranged in contingency tables (Zar, 1999).

The frequency of pathological dental lesions among the Guanches of Tenerife was initially analyzed to determine if skeletal samples from distinctive regional geoclimatic zones on the island expressed different patterns of dental health (Vallianatos and Lukacs, 1997; Lukacs and Vallianatos, 2006). A secondary objective was to assess the presence and level of sex dimorphism in dental health. Both regional and sex differences in dental health were found in this study. Northern groups expressed a higher prevalence of caries, attrition, attrition-induced pulp exposure, and antemortem tooth loss, while females were found to have higher caries rate and males to have more calculus, antemortem tooth loss, and linear enamel hypoplasia.

Results: Guanche caries prevalence

In Table 1, we present new data for observed and corrected caries rates among the Guanches of Tenerfie, the largest island in the Canary archipelago. Caries rates are presented by geoclimatic region (north and south), by jaw (maxilla and mandible), and by reporting method (observed and corrected). In addition, rates are presented for composite samples, including northern and southern samples combined, and maxillary and mandibular samples combined. The aggregate sample reveals a corrected caries rate of 6.9%; 226 of 3,288 teeth displayed dental caries (jaws, sexes, and regions pooled). When data for jaws are pooled, the corrected caries rate for females (8.8%) is nearly twice the male caries rate (4.5%) (bottom line of Table 1). This is a highly significant difference statistically. Results of all chi-square tests of sex differences in caries rates are presented in Table 2, and reveal that corrected caries rates are highly significantly different, with females displaying higher caries rates in all comparisons except for mandibular teeth in the southern region. These results are graphically presented, separately by region and for regions combined, in Figure 1. The traditional anthropological explanation for sex differences in caries rates typically involves sexual division of labor: differences in access to food stores, time devoted to food preparation, and tasting of dishes during the process of preparation. In explaining sex differences in dental caries prevalence, we contend that anthropologists have not given adequate consideration to the crucial etiological influence that saliva, hormones, and pregnancy have on cariogenesis. A reinterpretation of sex differences in Guanche caries prevalence is presented in the Discussion below.

THE ROLE OF SALIVA IN PROMOTING ORAL HEALTH

Saliva is a complex fluid that coats the inner surface of the oral cavity, including the outer enamel surface of teeth (Ten Cate, 1998). Humans have three major and a multitude of minor salivary glands. The three major salivary glands include the parotid, the submandibular, and the sublingual. Secretions from each of the three paired major salivary glands

TABLE 2. Chi-square test results for sex differences in corrected caries rates by jaw and by region[1]

	Maxilla		Mandible		Maxilla and Mandible	
	χ^2	P	χ^2	P	χ^2	P
North						
Obs	1.176	0.276	15.170	<0.001	14.235	<0.001
Corr	13.418	<0.001	13.172	<0.001	16.566	<0.001
South						
Obs	22.114	<0.001	0.476	0.490	8.969	<0.001
Corr	20.577	<0.001	0.341	0.559	7.595	0.006
North and South						
Obs	17.732	<0.001	10.878	<0.001	23.340	<0.001
Corr	20.152	<0.001	9.190	0.002	23.419	<0.001

[1]Obs, observed; Corr, corrected.

vary in composition, and become mixed in the oral cavity. The major functions of saliva are directly related to the composition and quantity of saliva produced by the three major salivary glands (Scott and Symons, 1982). The parotid gland weighs 14–28 g and produces a "watery" serous saliva (99% water) high in amylase (carbohydrate-splitting enzymes), the submandibular gland (10–15 g) secretes a mucinous saliva, and the sublingual gland is the smallest (2 g), and produces a viscous saliva (Brand and Isselhard, 1990). The composition of mixed saliva is not equal to the sum of these three secretions, because some salivary proteins adhere to enamel surfaces, while others affix to the oral mucosa. Collectively, mixed saliva produces 3 buffering agents, 5 antibacterial agents, and 5 factors affecting mineralization (Dowd, 1999) which perform many diverse functions (Tables 3 and 4), including protection, buffering, digestion, taste, antimicrobial action, and tooth integrity (Ten Cate, 1998). Recent attention to human variation in the composition of saliva and salivary gland size documented significant differences between the sexes and between ethnic groups in climatically distinct geographic regions (Lukacs and Martin, 2002; Shields, 1998). A complex model of balancing selection was proposed to explain this variability in saliva composition and gland size, but further data are required to fully test the natural-selection hypothesis (Shields and Mann, 1996).

Saliva has a significant and direct impact on the health status of the oral cavity, but since skeletal biologists and human osteologists primarily study dry, archaeologically derived skeletons, the multifunctional role of saliva on oral health and on dental caries susceptibility is often neglected or ignored.

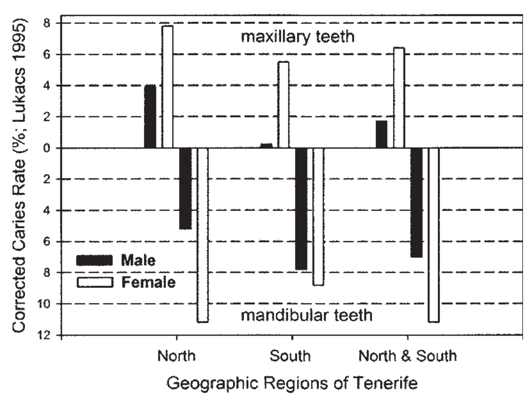

Fig. 1. Dental caries prevalence among Guanches of Tenerife, by sex, jaw, and region (percent, tooth count, corrected).

For example, the text *Dental Anthropology* contains just two passing references to the functional role of saliva in maintaining the health status of the oral cavity (Hillson, 1996). A brief review of the functions of saliva, and of how mixed saliva impacts dental health, is followed by a discussion of experimental and clinical evidence for sex differences in the composition and flow of saliva.

There are seven primary functions of saliva:

1. Protection: The fluid portion of saliva provides lubrication of the oral cavity and a mechanical washing action that flushes away cellular debris and sugars from the oral cavity, thus reducing their availability to acidogenic bacteria that cause demineralization of enamel. Calcium-binding proteins in saliva help form the salivary pellicle, a protective membrane-like coating that protects the outer enamel surface.

TABLE 3. *Factors and effects of salivary components (including aggregation and adherence)*[1]

Salivary factors	Effects and functions
On buffering	
HCO_3^- (bicarbonate)	Main buffer in saliva
Urea	Releases NH_3 (ammonia)
Arginine-rich proteins	Releases NH_3
On mineralization	
Histatins	Binds to hydroxyapatite, aids in supersaturation of saliva
Proline-rich proteins	
Cystatins	
Statherin	
Mucin	Provides physical and chemical barrier in enamel pellicle
On bacteria	
Lactoferrin	Binds to iron
Lysozyme	Hydrolizes wall polysaccharides, may promote clearance by aggregation
Peroxidase	Produces $OSCN^-$ (hypothiocynate), inhibits glycolysis
Secretory lgA	Neutralizes toxins and enzymes, binds to bacterial surface, prevents adherence
α-amylase	Produces maltose and glucose, indirectly produces glucans
Histatins	Inhibition of *Streptococcus mutans*
Mucins	Aggregation and clearance of oral bacteria

[1]Modified from Dowd (1999).

TABLE 4. *Multiple functions of saliva*[1]

Function	Effect	Active component
Protection	Lubrication	Glycoprotein
	Waterproofing	
	Lavage	Water
	Pellicle formation	
Buffering	Maintains Ph, unsuitable for bacterial colonization	Phosphate and bicarbonate
	Neutralizes acid	
Digestion	Bolus formation	Water
	Neutralizes esophageal contents	Phosphate and bicarbonate
	Digests starch	Amylase
Taste	Solution of molecules	Water
	Taste-bud growth and maturation	Gustin
Antimicrobial action	Barrier	Glycoproteins
	Antibodies	Immunoglobulin A
	Hostile environment	Lysozyme
		Lactoferrin
Tooth integrity	Enamel maturation	Calcium and phosphate
	Repair	

[1]Modified from Ten Cate (1998, p. 326).

2. Buffering: The buffering function of saliva promotes oral health in two ways: a) by denying bacteria an optimal environmental pH, it prevents potential pathogens from colonizing the oral cavity; and b) by neutralizing acids produced by bacterial microorganisms in plaque, it prevents the demineralization and cavitation of enamel (Dowd, 1999). For example, the salivary peptide *sialin* helps raise the pH of dental plaque following exposure to fermentable carbohydrates.
3. Antimicrobial action: Saliva contains a wide array of proteins with antimicrobial action. These proteins have a dramatic influence on the ecology of the oral cavity, and impact the many microorganisms that attempt to colonize it. *Lysozyme* can break down the cell walls of some bacteria, while *lactoferrin* binds free iron and thereby withholds this essential element from bacteria (Marsh, 1999; Percival et al., 1994).
4. Tooth integrity: Though teeth are morphologically completely formed at eruption, they are crystallographically immature. The calcium and phosphate ions in saliva assist in posteruptive maturation of enamel by diffusing essential ions into the surface apatitie of hydroxyapatite crystals. This increases the hardness and decreases the permeability of the outer enamel surface, promoting caries resistance.

5. Digestion: Saliva has several important roles in the digestive process. It facilitates taste acuity, promotes formation of the food bolus, and initiates the breakdown of starch.
6. Taste: Saliva is essential to dissolve substances so that they can be tasted, and to carry substances to the taste buds. Taste serves the protective function of recognizing and rejecting noxious and toxic substances. The salivary protein *gustin* is thought to be partly responsible for the growth and maturation of taste buds.
7. Tissue repair: Oral tissues appear to heal faster than other tissues. The shorter bleeding time of oral tissues may be influenced by as-yet unidentified clotting factors contained in human saliva. Epidermal growth factor produced by the submandibular salivary gland in mice enhances the rate of wound reduction (Ten Cate, 1998).

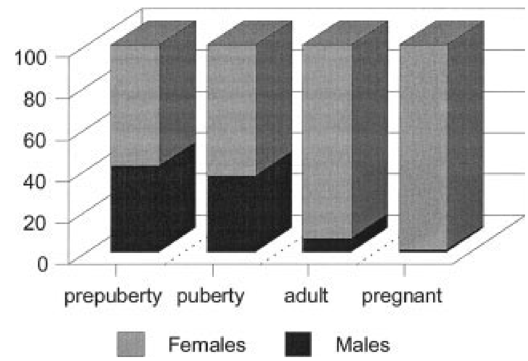

Fig. 2. Estrone levels of males and females throughout life cycle. Pregnant female levels are compared to nonpregnant adult male levels. Adapted using data from Angsusingha et al. (1974), Liu and Lin (1973), Mikhail et al. (1970), Muhler and Shafer (1955), Ngai and Longcope (1971), Shafer and Muhler (1954), Wright, et al. (1973), and Wu and Lundy (1971).

HORMONAL FLUCTUATION AND ORAL HEALTH

Throughout the life history of an individual, hormone levels fluctuate on a daily basis. Hormones are messenger chemicals produced by endocrine glands (Jagiello and Vogel, 1981). When hormones enter the bloodstream, they target certain organs and tissues, coordinating and controlling the way tissues and organs function. Gonadal steroid hormones primarily target male and female reproductive systems (Burrows, 1945; Nelson, 1995). Males and females both have different levels of two key groups of gonadal steroid hormones: estrogens and androgens (Vines, 1993). Estrogen is the group name of a class of steroid hormones which includes estradiol, estrone, and estriol. Estrogens are responsible for the development of female sexual characteristics, and are found in higher levels in females (Fig. 2). Androgens, which include testosterone and dihydrotestosterone, are found in higher levels in males, and are responsible for the development of male sexual characteristics (Nelson, 1995).

Many major differences in the physiology of men and women result from the activity of gonadal steroid hormones. Prior to and up through puberty, androgen and estrogen levels go through a series of peaks to stimulate the growth of secondary sexual characteristics such as pubic hair, breasts, and the onset of menstruation (Burrows, 1945; Nelson, 1995). Estrogen levels peak in women monthly in response to the menstrual cycle, and during certain life-history events such as puberty and pregnancy (Jagiello and Vogel, 1981). While males have small amounts of estrogen, research confirms that estrogen levels are higher in females throughout the life cycle, and that estrogen levels are significantly higher during puberty, pregnancy, and menstruation (Angsusingha et al., 1974; Niswender et al., 1976; Worthman, 1995).

A growing body of research, performed on laboratory animals, reveals that caries rates increase proportionally with increasing estrogen levels, whereas increasing androgen levels have no effect. For example, Muhler and Shafer (1954) put male and female rats on a cariogenic diet and gave them various levels of androgens and estrogens, to assess the effects of these sex steroids on caries rates. They found that androgens had no effect on caries rates, while estrogens significantly increased the caries rate. The effect of estrogens on the rate of caries was further increased when androgens were removed from the blood circulation entirely by removal of the gonads, the glands responsible for androgen production. Several researchers replicated this study, and their research confirmed that estrogen levels are positively correlated with caries rates, and that androgens have no effect (Delman, 1955; Laine et al., 1988; Liu and Lin, 1973; Legler and Menaker, 1980).

Animal research was also used to elucidate the mechanism by which increased estrogen levels lead to increased caries rates. Several animal studies conducted in the 1950s found a connection between increased thyroid levels in the blood, and a decrease in caries rate (Muhler and Shafer, 1955; Ryan and Kirkwood, 1955). Early animal research also revealed that fluctuations in the level of estrogens influenced thyroid activity, and led to a reduction in the saliva flow rate, and an increase in caries rate (Delman, 1955; Muhler and Shafer, 1955). An increase in caries rates was reported among patients with hypothyroidism, i.e., deficient activity of the thyroid gland (Persson et al., 1998).

SEX DIFFERENCES IN COMPOSITION AND FLOW RATE OF HUMAN SALIVA

Animal research and clinical studies in humans revealed sex differences in both the composition and flow rate of saliva. These two key aspects of saliva, the composition (quality) and flow rate (quantity), interact synergistically and impact oral health. The quality of saliva is determined by the level of minerals, amount of antimicrobial constituents, and buffer capacity, while the quantity is a reflection of average flow rate. The quantity and quality of saliva do not have an equal influence on oral health. Since saliva flow is the medium that brings protective agents into the oral cavity, qualitative factors are dependent on quantitative factors. If saliva quality is high, but saliva flow rate is low, oral health can still be negatively impacted. In fact, anything that compromises saliva flow is expected to have a negative impact on oral health (Bardow et al., 2001; Tenovuo, 1997, 1998). Saliva quality and quantity differ on an individual basis, and may be influenced by factors such as malnutrition (Lingström and Moynihan, 2003). However, the quality and quantity of saliva vary even more dramatically between males and females, and in response to certain life-history events.

Research on the salivary flow rate of individuals of various ages revealed a significant sex difference (Dodds et al., 2005). Percival et al. (1994) found that females had a significantly lower mean saliva flow rate than men, for both unstimulated whole saliva and stimulated parotid saliva. These researchers stated that the differential flow rates were attributed to smaller salivary glands in women; however, they contended that the degree of difference is such that gland size alone cannot fully account for the difference. The role of female sex hormones (specifically estrogen) in the suppression of saliva flow was put forth as the causative factor. Several studies found significant sex differences in saliva flow rates, with female flow rates significantly lower than male (Bergdahl, 2000; Dodds et al., 2005; Dowd, 1999). Other researchers reported a reduced salivary flow rate in postmenopausal women, and discussed the implications for increased caries rates later in life (Friedlander, 2002; Streckfus et al., 1998). One possible mechanism underlying these relationships is suggested by the presence of estrogen-receptor mRNA and immunoreactive estrogen-receptor protein in the salivary glands and oral mucosa, implicating the influence of estrogens on oral health (Leimola-Vitranen et al., 2000).

The composition and flow rate of human saliva can be indirectly affected by factors including disease, medical procedures, and medications, through their effects on the endocrine system (Dowd, 1999; Papas et al., 1993). An extensive literature documents the effects of hormone replacement therapy and birth-control pills on salivary composition and flow rate (Laine and Leimola-Virtanen, 1996; Leimola-Virtanen et al., 1997; Sewón et al., 2000). Xerostomia, a term describing dryness resulting from low salivary flow, is positively correlated with increased caries rates in the elderly and those who suffer from a variety of ailments, including arthritis, diabetes, and hypertension (Papas et al., 1993; Garg and Malo, 1997; Persson et al., 1998). Radiation therapy which targets the head and neck may result in xerostomia (Daniels and Fox, 1992). In fact, the increase in caries rate is positively correlated with the radiation dosage and frequency of treatment (Valdez et al., 1993). Severe xerostomia is associated with Sjögren's syndrome, in which decreased saliva flow from major saliva glands results in elevated caries rates (Dowd, 1999).

Current clinical research clearly illustrates the detrimental effects of estrogen fluctuation, and associated changes in the composition and flow rate of saliva, on the oral health of women (Streckfus et al., 1998). Clinical studies document the strong inverse correlation of salivary flow rate and dental caries rate (Bergdahl, 2000; Dowd, 1999; Valdez et al., 1993). However, one life-history event—pregnancy—presents an extreme case of hormonal fluctuation, and further illustrates the causal link between estrogen and caries rate (Delman, 1955; Laine et al., 1988; Legler and Menaker, 1980; Liu and Lin, 1973; Muhler and Shafer, 1955; Orosz et al., 1975; Vadiakas and Lianos, 1988).

THE COMPOUNDING EFFECTS OF PREGNANCY

During pregnancy, estrogen levels reach a peak which is higher than at any other time in the life history of a female (Fig. 2). Clinical studies showed that caries rates also increase among pregnant women as compared to women who are not pregnant, and that each pregnancy compounds the effect (Orosz et al., 1975; Vadiakas and Lianos, 1988).

The effect of pregnancy on caries rates has moved with a great deal of fluidity from the realm of folk knowledge, to the realm of science, and back again. The saying "for every child a tooth is lost" used to be considered a truism of pregnancy (Cassorla and Román, 1999; Christiensen et al., 1998; US Department of Health, Education and Welfare, 1972, p. 22). This saying was based on the so-called "maternal depletion syndrome," a belief that pregnancy caused nutrients, especially calcium, to leech from the teeth and bones, and that a large number of births, or births spaced closely together, increased this effect (Winikoff and Castle, 1987). By the late 1930s and early 1940s, research had illustrated that the "maternal depletion syndrome" was not the cause of an increased caries rate in pregnant women (Lynch et al., 1939). At this time in the history of caries research, there was no consensus on the etiology of dental caries.

While calcium-leeching was discounted as the cause of an increased rate of caries, many physicians continued to contend that "some women do suffer markedly from dental decay during pregnancy" (Eastman, 1942, p. 68). In the 1980s, physicians continued to state that pregnant women were at risk for dental disease, although few offered a physiological or biochemical mechanism to explain this observed phenomenon. For example, a very popular book for expectant mothers, entitled *What to Expect When You Are Expecting*, states that "gums swell as a result of increased hormone production ... Gums may become inflamed and bleed ... and teeth too, occasionally may fall victim to the maternal condition" (Eisenberg et al., 1984). The effect of hormones on gingival health during pregnancy is supported by extensive research (Laine et al., 1988; Muramatsu and Takaesu, 1994). Many studies reported increases in gingival edema lesions in pregnant women which often become infected and lead to gingivitis (Brambilla et al., 1998).

When calcium depletion and the "maternal depletion syndrome" were refuted as factors contributing to increased caries rates in pregnant women, many scholars turned to a dietary explanation. However, some scholars still contended that diet alone could not explain differences in caries rates between various populations. Orland (1955) examined two factors which produce caries in the oral cavities of rats: food substrates and microorganisms. Of three study groups, one was fed cariogenic foods through the oral cavity and had microorganisms present, one group was freed of microorganisms and was fed cariogenic foods, and the final group had cariogenic foods piped directly to the stomach. The researchers found that caries only developed in the rats that had microorganisms present, indicating that both cariogenic food debris and microorganisms must co-occur for caries to develop.

More recently, increased caries prevalence among pregnant women received additional support (Laine et al., 1988), and the search for a biochemical and biophysiological basis for the observed phenomenon has yielded positive results. For example, research shows that pregnancy modifies the biochemical composition of saliva (Salvolini et al., 1998), reducing the buffer capacity and promoting bacterial growth, factors that play a pivotal role in cariogenesis. In a study of 504 pregnant women, a correlation between pregnancy and caries rates was established. In fact, there was a positive correlation between the number of children a woman had and the total incidence of caries (Orosz et al., 1975). Vadiakas and Lianos (1988) also examined the correlation between dental caries and pregnancy, and noted that four factors appeared highly significant during pregnancy: changes in mouth flora and saliva, vomiting, neglected oral hygiene, and nutritional changes. Although neglected oral hygiene and nutritional patterns have been favored explanations through time, these authors contended that all four factors may be involved, and none can be discounted with certainty.

Villagran et al. (1999) studied changes in mouth flora during pregnancy, and examined the correlation with caries rates. They measured *Streptococcus mutans* levels in pregnant and nonpregnant women, to establish baseline bacterial levels prior to, during, and after pregnancy. Salivary *Streptococcus mutans* is considered a primary microbiological risk factor in the development of caries (Edwardsson, 1984). Villagran et al. (1999) analyzed *Streptococcus mutans* levels of 174 pregnant women during pregnancy. Women who had delivered in the months prior to the study were used as the control group. While no significant difference was observed in *Streptococcus* levels of women in various stages of pregnancy, a significant difference was found in bacterial levels between the pregnant study group and nonpregnant control group. The pregnant women had higher streptococci levels and a lower salivary buffer capacity than controls; both factors contributed to increases caries rates (Kedjarune et al., 1997; Muracciole, 1955; Sewón et al., 1998).

DISCUSSION: INTERPRETING CARIES RATES AMONG THE GUANCHES OF TENERIFE

This survey of clinical research on sex differences in the quantity and quality of saliva associated with hormonal fluctuations in women throughout the life span has direct implications for interpreting sex differences in caries rates in prehistoric and aboriginal populations such as the Guanches. Given the findings summarized above, anthropologists are encouraged to adopt a broader perspective in interpreting sex differences in dental caries prevalence. Increased attention must be focused on the role of women's reproductive history in the etiology of dental caries. The role of hormonal fluctuation must be considered in conjunction with traditional explanations of sex differences in caries such as precocious dental emergence, and sex differences in diet and division of labor. Interpreting caries rates should routinely entail an assessment of population demography, including relevant components of women's life histories. The ability to estimate variables such as fertility rates, duration of women's childbearing years (age at first menses and menopause), variation in women's relative parity, and length of interbirth intervals would help gauge the potential impact of hormonal fluctuation on caries rates.

Preindustrial societies, like the Guanches, practice a subsistence system based on agriculture augmented by coastal foraging and fishing, domesticated goats and pigs, and some hunting. Comparative meta-analyses of subsistence and fertility suggest that agriculturalists have higher fertility than societies with nonagricultural subsistence systems (Bentley et al., 1993a,b; Handwerker, 1983). Evidence from demography and reproductive ecology combines to reinforce the interpretation that horticulturalists and foragers have lower fertility, intensive agriculturalists have the potential for high fertility, and many agricultural societies realize high total fertility rates (Bentley et al., 2001). The causal factors responsible for higher fertility among agriculturalists remain controversial (Kramer and Boone, 2002). If Guanche demography was consistent with a primary reliance on agriculture, and secondary utilization of coastal resources (as believed), then Guanche women may well have had high fertility. In preindustrial societies, where women are valued for their reproductive and child-rearing potential as well as for their contributions to subsistence and ritual aspects of culture (Sellen and Smay, 2001), both diet and hormonal fluctuations associated with eventful reproductive histories may combine to impact dental caries rates. The anthropological and clinical literature presented above suggests that women's oral health is directly and indirectly impacted by female reproductive hormones, especially during pregnancy. In societies with preindustrial intensive agricultural subsistence economies and high birth rates, the negative impact on women's oral health and dental caries rates will be greater than among hunter and foragers or horticulturalists with low birth rates and less cariogenic diets.

A recent study of dental caries rates among the precontact inhabitants of Gran Canaria permits a comparative assessment of sex differences in dental caries rates among the Guanches of Tenerife (Delgado-Darias et al., 2005). This analysis of dental caries was conducted to gain knowledge of dietary patterns, as well as to determine if caries rates differ between burial types (status) and through time. Though caries frequency in the Gran Canaria sample (16.4%, n = 5,629) is nearly twice the caries rate among the Guanches (6.9%, n = 3,288), data from Table 7 in Delgado-Darias et al. (2005) reveal that in the composite Gran Canaria sample, females (19.8%, n = 1,786) have significantly higher tooth-count caries rates than males (14.8%, n = 3,843; $\chi^2 = 22.87$, df = 1, $P < 0.001$). This observation agrees with the general pattern for sex differences in caries rates globally, and with the findings reported here for the Guanches of Tenerife. The Gran Canaria data are of broader interest for two reasons. First, sex differences appear to covary with burial type. In the sample of skeletons derived from

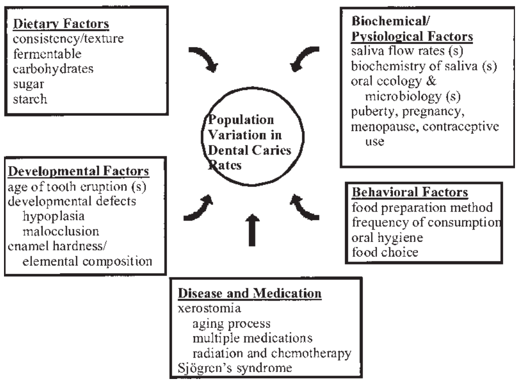

Fig. 3. Physiological, environmental, and behavioral factors which influence dental caries rates in a population.

high-status tumuli, females (13.0%) have more than double the male caries rate (5.6%). By contrast, the skeletal sample derived from "commoner" cave contexts exhibits less distinct sex differences (male, 13.6%; female, 16.7%). Variations in dietary patterns are thought to be partly responsible for the higher caries rates among cave-dwellers, and for the greater difference between the sexes in the tumuli sample. The second noteworthy feature of the study by Delgado-Darias et al. (2005) is that references are made to the functional role of saliva and pregnancy in relation to cariogenesis. In the introduction, passing reference is made to the impact of saliva composition on caries etiology, and the concluding sentence mentions the recently documented increase in cariogenic microbes in saliva during pregnancy (Laine, 2002). These investigators implied that sex differences in diet, in concert with salivary microbes during pregnancy, are collectively responsible for the higher caries rates in female skeletons from tumuli.

CONCLUSIONS

Higher caries rates among women are well-documented in dental studies of contemporary human populations (Beck and Ludwig, 1966; Beck et al., 1964; Carr, 1957; Chawla and Chaudhry, 1957; Legler and Menaker, 1980; Mao, 1950; Massler and Chand, 1950). However, in parallel with the prehistoric evidence, this pattern is ubiquitous, yet not universal. Some studies found no difference in caries rate between the sexes (Walker et al., 1998), while others reported that males will occasionally have a higher rate of caries than females (Holst et al., 1999). These findings reveal the complex and dynamic influences of physiological, behavioral, and environmental factors and their synergistic influence on caries rates (Fig. 3). Caries rates in human populations are influenced by a variety of behavioral, environmental, and physiological factors. A greater understanding of sex differences in caries prevalence can be obtained by considering each of these influences, the relative impact of which will vary by cultural affiliation, environment, and genetic constitution.

A call for life-span perspectives in anthropological research is designed to probe key linkages between human biology and society (Oudshoorn, 1994; Panter-Brick and Worthman, 1999; Vines, 1993). A greater understanding of the underlying causes of sex differences in caries rates is possible through the adoption of a life-span perspective that considers singular and recurring life events such as puberty, menses, pregnancy, and menopause. An evolutionary life-span perspective reveals underlying interactions and tensions in human biology. The negative impact of estrogen fluctuation on oral health is tied to estrogen's role in heightening immune responses during critical points in the life span, such as pregnancy. Clinical research shows that estrogen peaks correspond with a heightened immunological response, thus affording women further protection from pathogens during life-history events such as puberty, menses, and pregnancy (Nicol et al., 1964; Paavonen, 1994; Sbarra et al., 1970).

The anthropological literature on dental pathology oversimplifies the causal factors involved in cariogenesis. Evidence from ethnographic and epidemiological studies of dental caries in living human populations, as well as documentation from prehistoric human skeletal populations, shows that females usually, but not always, suffer from a higher prevalence of dental caries. New data regarding sex differences in dental caries rates among the Guanches of Tenerife (Canary Islands, Spain) are presented as evidence of the generalized pattern of sex differences in caries rates. Anthropologists, not surprisingly, emphasize the behavioral component in cariogenesis, stressing sex differences in diet and frequency of food consumption that typically accompany sexual division of labor. By contrast, most anthropologists have either neglected, downplayed, deemphasized, or "disproved" the role that hormonal fluctuations and pregnancy play in caries etiology.

Our survey of recent clinical and experimental caries research confirms the impact of hormonal fluctuations and pregnancy on the quantity and quality of saliva, and thereby on oral ecology. The physiological mechanisms by which life-history events have a more direct and significant influence on poorer dental health in women than in men is becoming clearer. While we agree with Larsen (1997, p. 76) that "variation in caries prevalence in females and males is behaviorally mediated," the evidence presented here strongly suggests that sex differences in estrogen levels also play an important role in the complex process of cariogenesis. The relative contributions of culture and biology in explaining the human condition are the source of discussion and debate among anthropologists (Worthman, 1995). This analysis demonstrates the mechanisms by which hormone levels and pregnancy influence oral ecology and consequently predispose women to higher rates of dental caries than men. This literature is recent, at the cutting edge of oral epidemiology and caries research, and has profound implications for the anthropological understanding of human behavior.

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