

Original Article

Premastication: the second arm of infant and young child feeding for health and survival?

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Abstract

Premastication of foods for infants was a crucial behavioural adaptation to neoteny that ensured nutritional adequacy during the period of complementary feeding throughout the course of human evolution until recent times. While the paps and gruels of agricultural systems provided an alternative and modern food technology appears to make it unnecessary, we argue that, in addition to its role in nutrition, premastication also played a crucial role in supporting infant health. Its abandonment, particularly in poor communities, has placed children at increased risk of inadequate nutrition and decreased ability to confront infections associated with the introduction of complementary foods. We present two empirical studies. Section I is a cross-cultural study of the ethnographic literature in order to estimate prevalence in non-Western societies. One-third of ethnographies in the worldwide sample with data on infant feeding report premastication. Section II presents the results of a qualitative study in China, conducted in order to provide data on the likelihood that this percent is incorrect due to under-reporting. The finding that 63% of Chinese university students received premasticated food as infants, whereas none of eight ethnographic studies performed in Han China identified premastication in their reports, provides support for the conclusion that the cross-cultural study grossly underestimates its prevalence in non-Western societies. Section III is a discussion of potential benefits and risks of infant exposure to maternal saliva. We conclude with the argument for a concerted research effort to determine whether premastication can solve not only the 'weanling dilemma' in poor countries but also some of the health problems among the better-off.

Keywords: cross-cultural, complimentary feeding, infant immunology, infant feeding in China, human evolution, disease transmission, saliva.

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Introduction

As with all mammals, lactation provided a secure base for infant survival during the course of homo sapiens evolution. However, it did not solve the problem of what to do when breastmilk alone becomes inadequate to meet the growing infant's nutritional needs. This paper presents the argument for the second arm

of the solution to how humans, as a biological and culture-producing species, met the extraordinary challenge produced by selection pressures for neoteny beginning with our early homo sapiens ancestors. 'Neoteny' refers to the reduction in the rate of somatic development, relative to other species, which has permitted the evolution of critical human capacities, especially related to brain size and upright

posture (McNamara 2002). Humans develop more slowly, in utero and post-natally, and achieve the characteristics necessary to survive independently later than other mammalian species. This is particularly evident with respect to the dentition that is required to bite off and chew the foods of an omnivorous diet. As part of general neoteny, tooth eruption in humans is significantly delayed compared with other mammals, including other primates (Smith 1989).

Our closest primate relatives, who were not challenged to find an adaptation to the nutritional threat to infants created by late eruption of teeth, solve the problem of ensuring infant nutrition with two adaptations: (1) prolonged lactation and (2) early tooth eruption, which together provide offspring with the capacity to start consuming the adult diet while they are still consuming maternal milk (Sellen 2007). In humans, breastfeeding is not as prolonged as our life history parameters would predict (Sellen 2007) and becomes inadequate as the exclusive source of nutrition to the infant at about 6 months of age (WHO recommendation). Our teeth develop late, especially our molars, which only erupt at about 18–24 months and which are essential for consuming an adult diet. Thus, our evolving ancestors must have found another solution to making up for the shortfall in breastmilk.

The hypothesis of this paper is that a behavioural solution, premastication (pre-chewing) of adult diets by infants' caregivers provided the solution, a second arm following the first arm of breastfeeding. The idea of feeding infants premasticated foods seems as inappropriate today as breastfeeding seemed to many people only 40 years ago, yet without it, it is unlikely that our hunting-gathering ancestors would have survived to establish the agricultural revolution that

permitted the development of other modes of infant feeding. In fact, however, from the perspective of ensuring infant nutrition, plant domestication did not provide an adequate solution to the challenge of providing infants with nutritionally adequate diets before they were able to meet their nutritional requirements from the family diet. The paps and gruels of earlier farming cultures, like the unfortified complementary foods in use today, did not contain sufficient micronutrients to meet infants' biological requirements.

Even today and even in wealthy, industrialized countries, the micronutrient content of usual complementary foods is problematic. For example, with respect to iron, the PAHO/WHO document on Guiding Principles for Complementary Feeding of the Breastfed Child (2003), notes that the 'average intakes of breastfed infants in industrialized countries would fall short of the recommended intake of iron if iron-fortified products were not available' (p. 25). Moreover, as they are readily subject to inappropriate dilution, the paps and gruels made from the staples created by plant domestication set the stage for energy and protein undernutrition in infancy and early childhood. It is generally recognized that reliance on them as the primary or exclusive complement to breastmilk not only leads to kwashiorkor, but is implicated as a major cause of growth faltering and significant undernutrition in poor populations today. Moreover, malnutrition subsequent to the loss of hunting-gathering was exacerbated and rendered more fatal (Pelletier *et al.* 1993) by increased exposure to infectious disease (Cohen 1989) due to higher population densities that fostered not only the transmission of diseases, but also the development of new diseases.

Key messages

- With the discontinuation of premastication in infant feeding, we have lost a fundamental health practice.
- Premastication is a complementary health practice to breastfeeding.
- Premastication supports nutrition, resistance to infections in infancy and later life, and prevents immunological hypersensitivity (e.g. asthma).
- Premastication, historically and prehistorically, was practised in all continents and all types of societies. For example, premastication was a common infant feeding practice in China, although anthropological studies did not identify it.
- Multi-disciplinary research on premastication in infancy is essential.

The rationale for the pre-mastication hypothesis involves the following:

1. The need for energy, protein and micronutrients from non-breastmilk dietary sources occurs before dental development is sufficiently adequate to permit infants to consume family foods.
2. During our long evolution as a hunting-gathering species, foods were not easily processed into a form that children without a full set of teeth could consume.
3. Populations in which adults pre-chewed (pre-masticated) foods and fed them to infants had a strong survival advantage, to such an extent that this behavioural trait was sustained through selection.
4. In agriculture-based populations, the continuation of pre-mastication prevented malnutrition by providing protein and nutrient-dense foods to supplement carbohydrate-based paps and gruels. It also supported other aspects of infant health through maternal-infant saliva transfer.
5. The disappearance of pre-mastication as a usual practice is recent and has occurred in populations that either have access to modern food processing techniques or in which traditional practices have been lost as a consequence of culture change and economic impoverishment. The abandonment of pre-mastication is reinforced by modern, biomedical concepts of hygiene, which have labelled the practice as 'unhygienic' and 'dangerous.'

As there are no longer any groups of people who are living exclusively as hunter-gatherers, it is not possible to determine whether pre-mastication prevented malnutrition in such societies. However, it is possible to use ethnographic data to provide some insights into where and how it has been practised historically. Sections I and II present the results of two empirical studies we conducted to examine the hypothesis that pre-mastication was wide spread. The first study is a cross-cultural examination, using the Human Relations Area Files (HRAF) to obtain ethnographic data on the occurrence of pre-mastication in human societies. The second study is a qualitative survey of the infant feeding practices experienced two decades ago by students in an elite Chinese University, which was

undertaken to assess the potential for serious under-reporting of the practice in the HRAF files, and to describe specific features of it. Section III is a discussion of the potential risks and benefits of infant exposure to maternal saliva.

The cross-cultural study

The cross-cultural method, in which societies are treated as units of analysis, was initially developed by anthropologists in the first half of the 20th century. It has been used by social scientists to study the distribution of social and cultural traits and to test hypotheses descriptively through the examination of associations among traits. The method uses information from a large body of descriptive ethnographic research monographs, which are products of the primary research mode of cultural anthropologists from the inception of the discipline. Anthropologists set out to develop ethnographies that contained rich description of the culture, behaviours and lifeways of a geographically delimited social group. Typically, the description is produced as the result of long-term field research in a specific location in which the anthropologist obtains data through a combination of interviews and observations. Often, data collection is based on the method of 'participant-observation,' in which the ethnographer engages directly in daily or ritual behaviours in order to learn, first-hand, the complexities of cultural performance. Data are recorded in written form, on tape, on film, and in videos. From these sources the ethnography is written, typically organized in chapters that cover different aspects of social and cultural life.

Several databases have been constructed to facilitate cross-cultural research, of which the best known and most comprehensive is the HRAF. This ambitious endeavor '... currently contains over 800 000 pages of indexed information on over 370 different cultural, ethnic, religious, and national groups around the world. ... [It] ... contains mostly primary source materials – mainly published books and articles, but it also includes some unpublished manuscripts and dissertations. The files contain studies on cultures or societies in all of the regions in the world.' (Ember & Ember <http://www.yale.edu/hraf/basiccc.htm>) (Ember

& Ember 2007). Every page in each document is indexed and assigned subject category codes according to a classification scheme contained in the Outline of Cultural Materials (OCM) (Murdock 1961). One can search documents by subject codes, as well as by keywords and phrases.

A few investigators have used the cross-cultural method to address nutritional questions. For example, Sarah Nerlove (1974) studied the relationship between women's workload and infant feeding practices, and found that infants tend to begin receiving supplementary foods earlier in cultures in which women are more active in agricultural subsistence activities. Dan Sellen (Sellen 2001; Sellen & Smay 2001) applied the cross-cultural method to examine the ages when 'exclusive' breastfeeding ceased in order to compare cultural patterns with current feeding recommendations.

Methods

For this study, we used e-HRAF. This is an electronic version of the files that contains all of the documents (monographs, journal articles) for a subset of 155 cultures that were selected by the HRAF organization as a geographically representative sample, containing materials that conform to a pre-specified standard of methodological soundness. We began by identifying texts that included OCM numbers 853 ('infant feeding') and 862 ('weaning'). We also searched using different combinations of words related to premastication, such as 'chew,' 'chewing' and 'pre-chewing.' All texts that contained one or more of the relevant codes were read and coded for presence of premastication. In ethnographies in which a mention or description of premastication occurred, additional variables were coded to capture information on what foods were premasticated, when the practice was initiated and terminated, who chewed the foods, and the ethnographer's stated purpose for the practice. All relevant pages were also photocopied in order to ensure that original text was available for subsequent review.

Results

From the total of 155 cultures in the HRAF online database, the OCM codes for infant feeding and/or

Table 1. Occurrence of premastication in e-HRAF reports

Geographic area	Number of cultures with information under code '853' (infant feeding)	Number of cultures with mention or description of premastication
Africa	24	4
North and Middle America	37	9
South America	17	8
Asia	21	10
Europe and Middle East	11	2
Oceania	9	5
Total	119	38

HRAF, Human Relations Area Files.

weaning occurred in 119 (77%). The information ranged from a couple of lines to extensive discussion. Of the 119 cultures in which there was text to review, premastication was reported in 38; that is, nearly one-third of the cultures in which the ethnographer included some mention or discussion about feeding of infants includes a reference to premastication. Table 1 shows the geographic distribution by region of the world.

According to the ethnographers who reported the practice, the primary reason for engaging in premastication was to provide children with food, but occasionally other motivations (cultural and spiritual beliefs, and disease prevention and healing) were mentioned. In 31 out of 38 cultures, premastication is reported to be practised solely for the purpose of providing foods to babies. In four cultures, infants and young children were given specific premasticated foods to facilitate a beneficial outcome that originated in religious and cultural beliefs. In two cultures, premasticated herbs were used medicinally to cure disease, and in one to prevent disease. In one other cultures, the purposes were both to provide food and to induce a beneficial outcome related to a cultural belief.

Information about the ages at which the practice of premastication were initiated and terminated is sparse. For age at initiation, there are data for only 13 of the 38 cultures. These results, shown in Table 2, illustrate wide variability, with a median age of 6

Table 2. Age of introducing premasticated foods in e-HRAF reports

Age in months	Number of cultures
1–2	2
3–4	3
5–6	3
7–8	–
9–10	1
11–12	3
>12	1

HRAF, Human Relations Area Files.

months. It was impossible to estimate precisely the age at which premastication ended, but the descriptions suggest that it continued into the second year of life. When it had a spiritual dimension it may continue into adulthood, as in the following quotation from a Blackfoot: ‘. . . This would be some special old lady – one with a lot of power to doctor or put up Sun Dances. She would chew my meat and then give it to me to swallow. This was a blessing for me, just like getting part of her life. Whenever we had any spare change we were taught to give it to old people like that’ (Hungry Wolf 1980).

In 30 of the 38 cultures, we could ascertain the type of individual who pre-chewed the infant’s food. In the majority of cases it was only the mother (25 out of 30). In five cultures, other individuals – fathers, grandparents, siblings or a spiritually important person – also were reported to premasticate food for the child.

A wide variety of foods were reported to be premasticated. The level of detail varies considerably in the reports, but typically is quite general, with foods being reported in broad categories, such as ‘meat,’ ‘fish,’ ‘roots,’ etc. Table 3 summarizes the diverse list by plant and animal food groups. Below are two examples to illustrate how data on foods are reported in ethnographies:

The Kung San of the Kalahari (Africa):

‘The !Kung have no milk from cows or goats and no cereals to feed an infant, and they. . . [feed]. . . by chewing their tough meat, harsh roots, and nuts and feed the infant premasticated food from their own mouths’ (Marshall 1976)

The Garo (Asia):

Table 3. Premasticated foods reported in e-HRAF reports

Plant foods	Animal foods
Nuts	Game
Legumes	Domesticated meat
Maize	Fish
Rice	
Tubers	
Fruit	
Roots	

HRAF, Human Relations Area Files.

‘. . . with a banana leaf beside her containing food which she chews mouthful by mouthful, before spitting it into her hand and placing it in the baby’s mouth. . . Gradually she tries feeding the baby meat, dried fish, and all the other Garo foods’ (Burling 1963)

Discussion

The data in the ethnographies provide evidence that premastication has been practised on all continents and in every type of subsistence system, from hunter-gatherers, through horticultural societies to complex societies based on intensive agricultural. Although it is difficult to determine with precision, it appears that the types of foods that are prechewed for infants by their caregivers reflect the household diets consumed by other family members. They include animal-source foods, fruits, vegetables and nuts, as well as the staples of agricultural societies.

Can we conclude that, leaving aside the 25% of societies for which we have no information, one-third of the societies in this representative sample of human groups practised premastication? On one hand, this is an impressive finding. It provides evidence that it was commonly practised in different types of societies and environments. Its occurrence in widely different cultural traditions and environments indicates that it was not a unique invention of a particular cultural group, which then spread to neighboring societies. One-third is also significant in that it indicates that a substantial portion of humanity experienced this practice over the course of human history.

On the other hand, one-third is far from universal. Is this proportion actually correct? The cross-cultural method has several problems that affect the ability of researchers to investigate hypotheses (Bernard 2006). A major weakness in using the HRAF files to address a nutritional question is the problem of missing information. Ethnographers focus on describing social and cultural features in human societies, and nutrition has not been highly salient for most of them. It is surprising, therefore, to find that the majority of ethnographies actually have an entry for the OCM code for infant feeding. However, on closer inspection, one finds that the level of detail is so poor that it is difficult to come to any conclusions about nutritionally relevant questions (Pelto *et al.* 2003). Ethnographers are not trained in nutrition, and what they observe and report reflects the common wisdom and perceptions about what was important to note about food and nutrition issues that was extant at the time of their work.

Given the lack of attention to the details of infant feeding practice in most ethnographies, it is probable that premastication is under-reported in the ethnographic literature. To test this hypothesis, we turned to a specific culture area for more in-depth investigation of the magnitude of a potential reporting problem. We began by conducting a study of all the ethnographies of Han societies in mainland China in the full HRAF files, as contrasted with the reduced numbers in the electronic version. There are a total of eight Han societies in the files, representing groups in North China, Northwest China, Central China, East China, Southwest China, South China and Inner Mongolia. Seven of these eight contain information under the OCM subject code 853 ('infant feeding'). Not a single description of premastication is found in the texts on any of these eight societies.

If we conclude that premastication is not under-reported in the ethnographic reports, we would also have to conclude that the practice is a very recent cultural introduction in Mainland China because we know from personal observation that it is currently practised there. In fact, one of us (Zhang) has not only seen it, but personally experienced it, having received premasticated foods from her medically trained, cardiologist mother and her grandmother.

A qualitative survey of infant feeding among students in an elite Chinese university

To provide some indication of the degree of under-reporting in the HRAF files, we undertook a study to examine premastication in Han cultures in China. A review of the non-ethnographic nutrition literature on infant feeding in China provided no insights about feeding behaviours. Studies reported information about nutrient intake but not about how the foods containing the nutrients were fed. As a large field study was not feasible, we decided to conduct a qualitative survey to determine whether our (Zhang's) experience was aberrant or whether premastication was widespread in the student population. We reasoned that if it was widespread, such a finding would indicate that premastication is under-reported in the ethnographic literature.

Methods

Students were recruited from the biological sciences, agronomy and biotechnology in a large, elite university in Beijing. The student interviewers were initially recruited from friends who were part of Zhang's personal network and then by snowball sampling. The students came from all parts of China. Clearly a volunteer sample of university students is not a random sample, but if premastication was reported at all in this group, it is probably practised by other social groups in China as well, especially as most of the students came from well-educated families whose feeding practices 20 years ago would represent acceptable 'modern' practices.

We asked the students to interview their parents and/or grandparents, with the focus on how they (the interviewers) were fed as infants. We gave them an interview schedule to follow in conducting the interview. The interview schedule was pilot tested with Chinese students studying at Cornell, and, by telephone, with their mothers in China. Decisions about face and content validity were based on feedback from the pilot process.

The interviews were conducted by telephone (in most cases) because students came from all over the

country and usually return home only for holidays. If a student returned home during the period of data collection, the interview was conducted face-to-face. As pre-mastication is generally discouraged by physicians and nurses, we felt it was necessary to embed questions about this practice within a larger set of questions about infant feeding. The study design and the interview protocol were approved by the Cornell University Human Subjects Committee. Procedures to ensure anonymity were carefully followed, and in accord with the assurance of privacy, we do not disclose the name of the university from which the student investigators and their respondent caregivers were recruited.

Results

One hundred twenty copies of the interview schedule were distributed, and 104 were returned and used for this analysis. The interviewers ranged in age from 20 to 24 year of age, of which 54 were female and 50 were male. The university recruits students from all over the country, and the 104 child/parent pairs of respondents represented 27 out of 34 provinces, autonomous regions and municipalities.

The parent respondents were 90 female and 14 males, of which 89 were mothers of the interviewers, 14 were fathers and 1 was a grandmother. The median age of the parent respondents was 48 years old. As expected, the education levels of respondents were high, far beyond the average of their age group in China. Only 4 out of 104 caregiver respondents had not received any formal education. Nearly 32% had received a college level education or above, another 38% had received a high school level education. At the time of the child's birth, 23 mothers had no outside job, while 79 were employed full time outside the home; 52 out of 77 (68%) of the working mothers had a maternal leave equal to or less than 3 months, 17 mothers (24%) had a maternal leave of 4–6 months, and only 7 (9%) mothers had a maternal leave of 6–12 months.

Virtually all of the students were breastfed: 102 of the 104. The two mothers who did not breastfeed said that this was due to lack of breastmilk. Seventy-two percent of the mothers started breastfeeding within

Table 4. Age of introduction of complementary foods by pre-mastication status in Chinese student study

Age of introduction of complementary food in months	Premastication reported		
	Yes	No	Total
1–2	6	2	8
3–4	19	11	30
5–6	11	12	23
7–8	9	3	12
9–10	2	1	3
11–12	5	4	9
>12	6	4	10
Missing information	7	2	9
Total respondents	65	39	104

the first day of their children's birth. The median duration of breastfeeding was 12 months, with a minimum of 1 month and a maximum of 48 months.

Premastication was a common practice. Only 37% of respondents (39 of 104) reported that they never gave pre-masticated food to the infant. Of the 65 families who reported practising pre-mastication, 22% said they used this practice 'often' or 'very often' (the two highest categories of a five-point Likert scale ranging from 'Never' to 'Very Often').

The start of pre-mastication ranged from 1 month to 24 months with a median of 8 months. The range in reported cessation was from 5 months to 48 months with a median of 24 months (Table 4). Parents with less education were more likely to give pre-masticated foods ($P < 0.001$). There was no difference in reporting the practice in nuclear compared with extended families, but infants had a higher likelihood of receiving pre-masticated food if someone other than the parents was involved in their feeding ($P < 0.002$).

The most frequently pre-masticated food was meat, followed by rice, other grains, other 'tough foods' and nuts. Table 5 lists all the items reported by parent respondents as foods they pre-masticated before giving it to their infants.

Discussion

The findings provide confirmation that pre-mastication was undoubtedly seriously under-reported in the ethnographies on Chinese societies in the HRAF files.

Table 5. Premasticated foods reported by parents of students in an elite university in China

Animal foods	Fresh fruits and vegetables
Meat	Apple
Dried meat	Orange
Fish	Tomato
Dried fish	Tangerine
Eggs	
Staples	Nuts
Rice	Walnuts
Millet	Peanuts
Porridge	
Noodles	Other
Potato	Dumplings
Corn bread	Cookies
Steamed buns	

None of the ethnographies mentioned this practice, but we found that it was practised by a majority of families in a sample that would be least likely to give premasticated food to their babies. It is unlikely that the discrepancy for China is unique to that country, particularly in view of the fact that nearly all of the China cultures (7 of 8) reported data under the 'infant feeding' OCM numbers and none identified premastication.

In addition to providing support for the hypothesis that premastication is significantly under-reported in ethnographic accounts, the study in China also provided some information about the nature of premastication within the context of infant feeding practices in generally well-educated Chinese families two decades ago. These include:

1. Premastication happened in all parts of China, in large cities and provincial areas.
2. It was practised in both nuclear and extended families, so it was not limited to older generation grandparents.
3. Parents with more education were less likely to premasticate foods for their babies, as would be expected because they are more likely to have been exposed to the counsel of pediatricians.

Saliva: non-nutritional benefits and risks of premastication

An evaluation of the role of premastication as a behavioural adaptation to ensure infant nutrition

must also examine the practice in relation to other aspects of health. There are no systematic reviews relating premastication to the benefits and risks of transferring saliva from mother to infant. However, the results of our initial exploration were surprising to us, as they will probably be for many readers. Transferring saliva to the infant may not only have immediate digestive, immunological and other protective benefits, but also long-term immunocompetence and immunotolerance benefits. These potential benefits raise interesting issues that need further attention, as do potential disadvantages. In this section, we sketch out some of the issues that warrant further examination.

In their thorough review of the literature, Humphrey & Williamson (2001) enumerate the composition and describe the functions of saliva, primarily in relation to oral health. Saliva contains electrolytes, immunoglobulins, proteins, enzymes, mucins and nitrogenous products that are important in the promotion of oral health, mastication, swallowing and pre-gastric digestion. Apart from its well-recognized functions in oral health, of particular interest with respect to premastication are its potential digestive health promoting properties, which need to be weighed against its potential to transmit diseases.

With respect to digestion, Humphrey and Williamson note the role of saliva in early stages of digestion, particularly of starches (Mandel 1987) and fats (Valdez & Fox 1991). The ability to digest complex carbohydrates develops slowly in infants. At birth, there is a physiologic deficiency of pancreatic amylase. It is not until 9 months of age that adult values are reached (Lebenthal & Lee 1980; Zheng *et al.* 1996). The degree to which saliva actually improves digestion needs to be examined in relation to specific food systems, including present-day and future complementary feeding practices, as well as those of the past.

Saliva also contains multiple growth factors that can enhance the body's repair mechanisms after tissue injury and may also have protective functions (Kongara & Soffer 1999). Table 6 presents a list of the many health-promoting substances that are found in both breastmilk and saliva. There are some substances in breastmilk that have not been reported for saliva, including bifidus factor, α_1 -antichymotrypsin,

Table 6. Health-promoting factors in breastmilk and saliva*

Antimicrobial factors	Cytokines and anti-inflammatory factors
secretory IgA, IgM, IgG (Norhagen <i>et al.</i> 1989)	tumour necrosis factor (Pezelj-Ribaric <i>et al.</i> 2004)
lactoferrin (Tenovuo 1989)	interleukins (Dugue <i>et al.</i> 1996)
lysozyme (Tenovuo 1989)	interferon-g (Sfriso <i>et al.</i> 2003)
complement components (Andoh <i>et al.</i> 1997)	prostaglandins (Kasinathan <i>et al.</i> 1995)
leucocytes (Wright 1959)	platelet-activating factor: acetyl hydrolase (Ribaldi <i>et al.</i> 1998)
lipids and fatty acids (Tenovuo 1989)	
antiviral mucins, GAGs (Shugars 1999)	
oligosaccharides (Rosenblum <i>et al.</i> 1988)	
thiocyanate (breastmilk: Kirk <i>et al.</i> 2007; saliva: Schultz <i>et al.</i> 1996)	
Hormones	Growth factors
insulin (Marchetti <i>et al.</i> 1986)	epidermal (EGF) (Kagami <i>et al.</i> 2000)
prolactin (Vining & McGinley 1986)	nerve (NGF) (Kagami <i>et al.</i> 2000)
thyroid hormones (Vining & McGinley 1986)	insulin-like (IGF) (Kagami <i>et al.</i> 2000)
corticosteroids: ACTH (Lowe & Dixon 1983)	transforming (TGF) (Kagami <i>et al.</i> 2000)
oxytocin (Carter <i>et al.</i> 2007)	taurine (Soderling <i>et al.</i> 2002)
	polyamines (Venza <i>et al.</i> 2001)
Digestive enzymes	Transporters
amylase (Tenovuo 1989)	lactoferrin (Fe) (Komine <i>et al.</i> 2007)
esterase (Tenovuo 1989)	folate binder (Verma & Antony 1992)
lipases (Tenovuo 1989) [†]	cobalamin binder (Hippe 1972)
	corticosteroid binder (Gröschl <i>et al.</i> 2008)

*Breastmilk factors, except for thiocyanate, are from major review by Prentice (1996). All other references in parentheses, are references for presence of these factors in saliva; [†]Lipase may have a different form of aggregation in breastmilk and saliva (Larsson *et al.* 1996) but whether this results in different functions has not been established.

a₁-antitrypsin, calcitonin parathyroid hormone, erythropoietin, IgF binder, thyroxine binder. Similarly, some substances found in saliva have not been reported as present in breastmilk, including gonadotrophins, basic fibroblast growth factor (bFGF), peroxidase, proteases and peptidases, salivary acid phosphatase A, salivary acid phosphatase

B, N acetylmuramyl-alanine, amidase NAD(P)H dehydrogenase-quinone, and Glucose-6-phosphate isomerase. However, the striking feature of Table 6 is how many substances the two body fluids – breastmilk and saliva – have in common. In short, the substances in maternal saliva, like the substances in breastmilk, have many potential beneficial roles for infant health.

However, there is also the potential for harm from ingestion of saliva. A number of pathogens that have been isolated from maternal saliva are thought to be transmitted to their children. These include *H. pylori* (Bassily *et al.* 1999), Hepatitis B (Armstrong *et al.* 2001), Human herpes virus 6 (HHV-6) (Yamanishi 2000) and human herpes virus 8 (HHV-8) (Brayfield *et al.* 2003).

Saliva has also been linked to the contamination of pre-masticated foods. Imong *et al.* (1995) examined the bacterial contamination of infant weaning foods in a study in Thailand and found that in households who reported practising pre-mastication, the weaning food samples were significantly higher in bacterial content than households who did not pre-masticate foods. The authors speculate that the diseases that could be introduced through pre-mastication could include, among others, leprosy and tubercle mycobacterium, hemolytic streptococci, and respiratory tract viruses. However, a finding of increased bacterial count without further specification of which bacteria were involved does not tell us whether there is a greater risk of infection. Moreover, the authors present no rationale for their list of specific diseases or any evidence that these were present in their samples.

The presence of pathogens in saliva does not necessarily mean that they are infectious, especially because saliva contains IgG, IgM and especially secretory IgA, which contain antibodies to viruses and bacterial antigens, and inhibit bacterial attachment to host tissues, thus controlling bacterial, fungal and viral colonization. A case in point is human immunodeficiency virus (HIV), which can be isolated in saliva. A substantial body of research has shown that there are mechanisms which reduce the infectivity of HIV in saliva (Baron *et al.* 1999) thus making the the risk of transmission low (Campo *et al.* 2006), lower than in breast milk. A recent meta-analysis of oro-genital transmission confirms that genital exposure to saliva

of HIV positive partners is associated with low risk (Baggaley *et al.* 2008). The potential importance of premastication as a risk factor for HIV in infants and young children appears to be likely to be negligible.

There is better evidence to suggest that saliva transfer between mothers and their children is a cause of child infections with *H. pylori* (Taylor & Blaser 1991; Sinha *et al.* 2001). The evidence for maternal transmission of *Streptococcus mutans* and *Streptococcus sobrinus*, the primary microorganisms associated with dental caries, is well established and it seems likely that transmission occurs through saliva (Berkowitz *et al.* 1981).

As part of an assessment of the risks and benefits of premastication from the perspective of disease transmission, it is useful to compare saliva to breastmilk. To date, many more pathogens have been identified in breastmilk than in saliva, but this reflects the greater attention that has been given to breastmilk as a potential source of disease transmission to infants. The fact that pathogens can be identified in both breastmilk and saliva raises two important points: (1) Virtually all biological adaptations have downsides, and to put these into perspective requires a risk/benefit analysis; (2) Research on breastfeeding demonstrated that the risks of disease transmission were so small relative to the advantages that nobody would recommend curtailing breastfeeding except in very unusual and specific situations (e.g. HIV in wealthy populations). Similar results may pertain for premastication in view of the fact that, in addition to its nutritional benefits, premastication may play other positive roles in infant health. The extent to which maternal to infant transfer of saliva conveys specific antibody protection and promotes immunological health needs to be studied.

The potential for pathogen transmission leads to another question: Is transmission of disease agents from mother to child through saliva (or breastmilk) unequivocally bad? This question deserves careful consideration. When diseases are widespread and kill early, they prevent reproduction; therefore mechanisms that promote acquired immunity in childhood that either prevent or attenuate severity of disease in reproductively active adults would be advantageous. This has indeed occurred for many widespread patho-

gens, including rubeola (measles), varicella-zoster (chicken pox), paramyxovirus (mumps) and poliovirus (poliomyelitis), in which the diseases are significantly more serious when they occur in adulthood. The potential role of late exposure to Epstein-Barr (HHV-4) in the genesis of several cancers is currently attracting research attention (Stoppler 2008) and, with the development of further knowledge, may join the list of pathogens for which early exposure reduces adult health risks.

Apart from infectious disease, there is increasing evidence that early exposure to modern sanitary environments markedly increases the risk of atopic diseases, including asthma (Eder *et al.* 2006). In other words, early exposure to a rich microbial environment is important in priming the immune system. In a similar vein, early exposure to potential food allergens in premasticated foods, particularly when the infant is still breastfeeding, may also have a role in reducing allergic responses to foods.

In summary, the argument for potential benefits from saliva exposure through premastication is strong. If the positive characteristics of saliva are sustained through infancy, then, apart from its nutritional aspects, it may be an important mechanism for supporting child, and even adult, health. At present, there is simply insufficient information to permit an estimate of the trade-offs between the potentially positive and negative features.

Conclusions

In a seminal paper on the evolution of infant and young child feeding, Sellen (2007) lays out two related paradoxes in the relationship of lactation and the role of foods in complementing and/or replacing breastmilk in human societies. These are: (1) although humans have the longest period of dependence on others for subsistence compared with other mammals, they generally do not maximize the period of exclusive breastfeeding, and (2) they wean their infants sooner than other apes do. He also highlights 'The most remarkable change [in the evolution of human infant feeding compared to other animals] is the human use of complementary foods, which is unique among mammals . . . and results in a pattern of tran-

sitional feeding that appears to be fundamentally different from that of other primates.' (p. 130).

To find an explanation for the apparent paradoxes in human management of infant feeding, Sellen examines the energetic costs of lactation in relation to other critical features of reproductive success using a comparative life history analysis of humans and other apes. He points out that 'Lactation, nutritional intake, energy expenditure, and net energy balance are the key influences on fecundity among humans' (p. 133). Focusing on the physiologic costs of lactation in relation to other aspects of reproduction, and the potential to share child complementary feeding with other caregivers, Sellen concludes that 'Flexibility in weaning age reflects an evolved maternal capacity to vary reproduction in relation to ecology . . . the availability of alternate caregivers and other environmental and social factors affecting the costs and benefits of weaning to mothers and infants.' (p. 135). In other words, the paradoxes are, ultimately, explained by the energetic costs of reproduction in relation to the alternative behavioural solutions that humans were able to evolve.

Sellen ends the article with a set of issues about our understanding of the evolution of infant and child feeding that have not yet been resolved. Among these he identifies: 'How humans evolved to meet the complex challenge of introducing appropriate complementary foods in a timely manner while satisfying other demands on caregivers' (p. 136). We believe that the key to this understanding lies in pre-mastication.

If pre-mastication poses significant dangers from the perspective of disease transmission, it is unlikely that it would have been sustained through the course of cultural evolution. Although there are examples of negative practices that become deeply embedded in cultural repertoires, these are not usually widely dispersed across all regions of the world. In addition to the empirical evidence, cultural-ecological theory would also predict that the behaviour could not have been sustained.

If pre-mastication was an integral part of the evolutionary process associated with selection for neoteny, one would expect to find bio-behavioural traits in adults and infants that reinforced it. We believe there

are such traits, which are still observable today. When infants of complementary feeding age are face-to-face with adults, they often reach for the adult's mouth, in preference to other parts of the face, pulling on his/her lips and sticking their fingers into the adult's mouth. The typical response of the adult is to suck playfully on the tiny fingers, often pretending to chew them lightly. The response, in turn, provokes laughter and smiles from both infant and adult. Another common adult behaviour that might be related to reinforcement of pre-mastication is the tendency for adults to nuzzle their head and mouth into or close to the lower part of a baby's face or neck.

It is also the case, as was apparent in the comments from Hungry Wolf quoted previously, that pre-mastication can be viewed as a form of expressing affection. In informal interviews with mothers of young children, we have encountered women who describe or justify pre-mastication as a way of showing affection and reinforcing the special bond they have with their infants. As one young mother recently put it 'I know I probably shouldn't because of germs and all, but it's a way of sharing my love with my baby.'

If both nutrition and immunological health are involved in the evolutionary benefits of pre-mastication, it is probable that it also has implications with respect to the synergistic relationship of nutrition and disease on child mortality (Pelletier *et al.* 1993). A behaviour that simultaneously supports better nutrition and better immunological status would be expected to reduce the risk of mortality during the period when infants and young children are at high risk of dying. Until recently, diarrhea was been the primary killer of children throughout the developing world, and it still remains a major cause of mortality (Boschi-Pinto *et al.* 2007). The incidence of diarrhea in young children peaks during the period of complementary feeding when infants are exposed to contaminated foods. Thus, the sharp rise in diarrhea that occurs when complementary foods are added can be seen as due to a trade-off between meeting nutritional needs and increasing the risk of life-threatening illness through ingestion of contaminated foods. This trade-off is called the 'the weanling's dilemma' (Gordon *et al.* 1963; Rowland 1986). If it is correct that pre-mastication neutralizes contamination, it may

be that the 'weanling dilemma' is a consequence of lack of premastication. Worldwide, half of deaths from infectious diseases today, including diarrhea (Caulfield *et al.* 2004), occur because children are malnourished. This is compounded by the fact that diarrhea exacerbates malnutrition (Lutter *et al.* 1989). Thus, there is promise that premastication could reduce, or even eliminate, the 'weanling dilemma' by both improving nutrition and reducing infection.

In summary, did premastication protect children from the devastating consequences of diarrhea associated with the introduction of complementary foods by improving their nutritional status? Did the additional immunological substances transferred through saliva improve their ability to prevent and fight infections? Are the present high rates of diarrheal disease-related mortality the results of wide-spread loss of premastication as a basic childcare practice?

Issues for further investigation

Current understanding of the biology and biochemistry involved in premastication promises a potential for improving infant feeding in poor populations. However, to assess this potential requires a concerted research effort. At the level of understanding evolutionary processes, the loss of adaptive behaviours that conferred survival advantage for our ancestors and shaped our evolution as a biological and social species continues to be a subject of considerable scholarly concern. Modern humans' departure from the dietary patterns of our predecessors has been linked to the development of diet-related chronic disease and obesity (cf. Cohen 1989; Eaton *et al.* 1989). Continued research in this area will contribute to understanding the place of premastication.

Of critical importance to assessing the public health implications is an examination of the nutritional benefits of premastication founded on empirical clinical and epidemiological research. In view of the ubiquitous prevalence of iron deficiency in infancy (Beard & Stoltzfus 2001), and the fact that humans have evolved with greater iron requirements than can be met from breastmilk alone (PAHO/WHO 2003), as well as the fact that infants experience declining iron stores before they are physically capable of consuming heme

iron from external sources, an area of special interest is the role of premastication in preventing iron deficiency in infants and young children. Iron is just one of several nutrients whose adequacy in infancy may have relied on premastication. In practice, it is likely that the potential nutritional benefits are going to be related to the diet of the adult who is feeding the child, and this raises the issues of the best foods for premastication feeding and their accessibility.

The subject of early immunological health and its relationship to health outcomes of older children and reproductively active adults is becoming increasingly better understood (Barrett *et al.* 1998; Von Hertzen 2000). What is required is evidence for the role of premastication specifically for present and future health.

Another research issue of central importance is a systematic examination of the health and other benefits and risks to infants of receiving premasticated foods from their mothers. An early probe of the issue would be to undertake, for premastication, the kind of survey and analysis that demonstrated that breastfeeding saved lives (Habicht *et al.* 1986), and had high enough plausibility that intervention trials were warranted.

When one considers the reasons for contemporary departures from evolution-shaped practices, it is readily apparent that they are extremely complex and restoring or sustaining them in the contemporary world presents major, some would argue, insurmountable, challenges. However, at least with respect to infant feeding, the resurgence of breastfeeding in populations where there were severe declines in the prevalence of this essential health practice, provides clear evidence that human societies are capable of re-institutionalizing adaptive practices.

The aversion with which many people today regard the very thought of premastication is similar to the negative views of breastfeeding that characterized many people's view of breastfeeding until recently. Fortunately, as research has demonstrated the benefits of breastfeeding, and as these benefits have become widely understood and accepted, negative attitudes about breastfeeding has largely disappeared. Whether or not premastication should be considered as part of a larger strategy to improve infant

feeding and health, the second arm, requires, as a first step, a research investment similar to the investments in breastfeeding, which have so richly paid off in supporting improvements in infant survival and health.

Acknowledgements

We would like to acknowledge Penny Van Esterik for her close reading of the manuscript and her valuable insights and suggestions.

Source of Funding

None.

Conflicts of Interest

None declared.

References

- Andoh A., Fujiyama Y., Kimura T., Uchihara H., Sakumoto H., Okabe H. *et al.* (1997) Molecular characterization of complement components (C3, C4, and factor B) in human saliva. *Journal of Clinical Immunology* **17**, 404–407.
- Armstrong G.L., Mast E.E., Wojczynski M. & Margolis H.S. (2001) Childhood hepatitis B virus infection in the United States before hepatitis B immunization. *Journal of Pediatrics* **108**, 1124–1128.
- Baggaley R.F., White R.G. & Boily M.-C. (2008) Systematic review of orogenital HIV-1 transmission probabilities. *International Journal of Epidemiology* **37**, 1255–1265.
- Baron S., Poast J. & Cloyd M.W. (1999) Why is HIV rarely transmitted by oral secretions? Saliva can disrupt orally shed, infected leukocytes. *Archives of International Medicine* **159**, 303–310.
- Barrett R., Kuzawa C., McDade T. & Armelagos G.J. (1998) Emerging and re-emerging infectious diseases: the third epidemiologic transition. *Annual Review of Anthropology* **27**, 247–271.
- Bassily S., Frenck R.W., Mohareb E.W., Wierzba T., Savarino S. & Hall E. *et al.* (1999) Seroprevalence of *Helicobacter pylori* among Egyptian newborns and their mothers: a preliminary report. *The American Journal of Tropical Medicine and Hygiene* **61**, 37–40.
- Beard J. & Stoltzfus R. (2001) Iron-deficiency anemia: reexamining the nature and magnitude of the public health problem. Proceedings of the Belmont Conference. *Journal of Nutrition* **131** (Suppl.), 563S.
- Berkowitz R.J., Turner J. & Green P. (1981) Maternal salivary levels of *Streptococcus mutans* and primary oral infection of infants. *Archives of Oral Biology* **26**, 147–149.
- Bernard H.R. (2006) *Research Methods in Anthropology. Qualitative and Quantitative Approaches*. Alta Mira Press: New York.
- Boschi-Pinto C., Velebit L. & Shibuya K. (2007) Estimating child mortality due to diarrhoea in developing countries. *WHO Bulletin* **86**, 50–54.
- Brayfield B.P., Phiri S., Kankasa C., Muyanga J., Mantina H., Kwenda G. *et al.* (2003) Postnatal human herpesvirus 8 and human immunodeficiency virus type 1 infection in mothers and infants from Zambia. *Journal of Infectious Disease* **187**, 559–568.
- Burling R. (1963) *Rengsangri: Family and Kinship in a Garo Village*. University of Pennsylvania Press: Philadelphia, PA.
- Campo J., Perea M.A., del Romero J., Cano J., Hernando V. & Bascones A. (2006) Oral transmission of HIV, reality or fiction? An update. *Oral Disease* **12**, 219–228.
- Carter C.S., Pournajali-Nazarloo H., Kramer K.M., Ziegler T.E., White-Traut R., Bello D. *et al.* (2007) Oxytocin: behavioral associations and potential as a salivary biomarker. *Annals of the New York Academy of Sciences* **1098**, 312–322.
- Caulfield L.E., de Onis M., Blössner M. & Black R.E. (2004) Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. *American Journal of Clinical Nutrition* **80**, 193–198.
- Cohen M.N. (1989) *Health and the Rise of Civilization*. Yale University Press: New Haven, CT.
- Dugue B., Ilardo C., Aimone-Gastin I., Gueant J.L., Mouze-Amady M., Cnockaert J.C. *et al.* (1996) Cytokines in saliva. Basal concentrations and the effect of high ambient heat (sauna). *Stress Medicine* **12**, 193–197.
- Eaton S.B., Shostak M. & Konner M. (1989) *The Paleolithic Prescription: A Program for Diet and Exercise and a Design for Living*. Harper Collins: New York.
- Eder W., Ege M.J. & von Mutius E. (2006) The asthma epidemic. *New England Journal of Medicine* **355**, 2226–2235.
- Ember C.R., Ember M. (2007) *User's Guide: HRAF Collection of Ethnography*. Available at: <http://www.yale.edu/hraf/basiccc.htm>
- Gordon J.E., Chitkara I.D. & Wyon J.E. (1963) Weanling diarrhea. *American Journal of the Medical Sciences* **246**, 245–251.
- Gröschl M., Köhler H., Topfa H.-G., Rupprecht T. & Rauha M. (2008) Evaluation of saliva collection devices for the analysis of steroids, peptides and therapeutic drugs. *Journal of Pharmaceutical and Biomedical Analysis* **47**, 478–486.

- Habicht J-P, DaVanzo J. & Butz, W.P. (1986) Does breast-feeding really save lives, or are apparent benefits due to biases? *American Journal of Epidemiology* **123**, 279–290.
- Hippe E. (1972) Studies on the cobalamin-binding protein of human saliva. *Scandinavian Journal of Clinical and Laboratory Investigation* **29**, 59–68.
- Humphrey S.P. & Williamson R.T. (2001) A review of saliva: normal composition, flow, and function. *Journal of Prosthetic Dentistry* **85**, 162–169.
- Hungry Wolf (1980) *The Ways of My Grandmothers*. William Morrow: New York.
- Imong S.M., Jackson D.A., Rungruenthanakit K., Wongsawasdi L., Amatayakul K., Drewett R.F. *et al.* (1995) Maternal behaviour and socio-economic influences on the bacterial content of infant weaning foods in rural northern Thailand. *Journal of Tropical Pediatrics* **41**, 234–240.
- Kagami H., Hiramatsu Y., Hishida S., Okazaki Y., Horie K., Oda Y. *et al.* (2000) Salivary growth factors in health and disease. *Advances in Dental Research* **14**, 99–102.
- Kasinathan C., Sundaram R. & William S. (1995) Effects of prostaglandins on tyrosylprotein sulfotransferase activity in rat submandibular salivary glands. *General Pharmacology* **26**, 577–580.
- Kirk A.B., Dyke J.V., Martin C.F. & Dasgupta P.K. (2007) Temporal patterns in perchlorate, thiocyanate, and iodide excretion in human milk. *Environmental Health Perspectives* **115**, 182–186.
- Komine K., Kuroishi T., Ozawa A., Komine Y., Minami T., Shimauchi H. *et al.* (2007) Cleaved inflammatory lactoferrin peptides in parotid saliva of periodontitis patients. *Molecular Immunology* **44**, 1498–1508.
- Kongara K.R. & Soffer E.E. (1999) Saliva and esophageal protection. *American Journal of Gastroenterology* **94**, 1446–1452.
- Larsson B., Olivecrona G. & Ericson T. (1996) Lipid in human saliva. *Archives of Oral Biology* **41**, 105–110.
- Lebenthal E. & Lee P.C. (1980) Development of functional responses in human exocrine pancreas. *Pediatrics* **66**, 556–560.
- Lowe J.R. & Dixon J.S. (1983) Salivary kinetics of prednisolone in man. *Journal of Pharmacy and Pharmacology* **35**, 390–391.
- Lutter C.K., Mora J.O., Habicht J-P, Rasmussen K.M., Robson D.S., Sellers S.G. *et al.* (1989) Nutritional supplementation: effects on child stunting because of diarrhea. *American Journal of Clinical Nutrition* **50**, 1–8.
- Mandel I.D. (1987) The function of saliva. *Journal of Dental Research* **66**, 623–627.
- Marchetti P., Benzi L., Masoni A., Cecchetti P., Giannarelli R., Di Cianni G. *et al.* (1986) Salivary insulin concentrations in type 2 (non-insulin-dependent) diabetic patients and obese non-diabetic subjects: relationship to changes in plasma insulin levels after an oral glucose load. *Diabetologia* **29**, 695–698.
- Marshall L. (1976) *The !Kung of Nyae Nyae*. Harvard University Press: Cambridge, MA.
- McNamara K.J. (2002) Sequential hypermorphosis: stretching ontogeny to the limit. In: *Human Evolution through Development Change* (eds N. Minugh-Purvis & K. McNamara), pp. 102–121. JHU Press: Baltimore, MD.
- Murdock G.P. (1961) *Outline of Culture Materials*, 5th edn. Toplinger Publishing: New York.
- Nerlove S.B. (1974) Women's workload and infant feeding practices: a relationship with demographic implications. *Ethnology* **13**, 207–214.
- Norhagen G.E., Engström P.E., Hammarström L., Söder P.O. & Smith C.I.E. (1989) Immunoglobulin levels in saliva in individuals with selective IgA deficiency: compensatory IgM secretion and its correlation with HLA and susceptibility to infections. *Journal of Clinical Immunology* **9**, 279–286.
- Pan American Health Organization & World Health Organization (2003) *Guiding Principles for Complementary Feeding of the Breastfed Child*. Pan American Health Organization and World Health Organization: Washington, DC and Geneva.
- Pelletier D.L., Frongillo E.A. & Habicht J-P. (1993) Epidemiologic evidence for a potentiating effect of malnutrition on child mortality. *American Journal of Public Health* **83**, 1130–1133.
- Pelto G.H., Levitt E. & Thairu L. (2003) Improving feeding practices: current patterns, common constraints and the design of interventions. *Food and Nutrition Bulletin* **24**, 45–82.
- Pezelj-Ribaric S., Brekalo Prso I., Abram M., Glazar I., Brumini G. & Simunovic-Soskic M. (2004) Salivary levels of tumor necrosis factor-alpha in oral lichen planus. *Mediators of Inflammation* **13**, 131–133.
- Prentice A. (1996) Constituents of human milk. *Food and Nutrition Bulletin* **17**, 305–312.
- Ribaldi E., Guerra M., Mezzasoma A., Staffolani N., Goracci G. & Gresele P. (1998) PAF levels in saliva are regulated by inflammatory cells. *Journal of Periodontal Research* **33**, 237–241.
- Rosenblum J.L., Irwin C.L. & Alper D.H. (1988) Starch and glucose oligosaccharides protect salivary-type amylase activity at acid pH. *American Journal of Physiology Gastrointestinal and Liver Physiology* **254**, G775–G780.
- Rowland M.G. (1986) The weanling's dilemma: are we making progress? *Acta Paediatrica Scandinavica* **323**, 33–42.
- Schultz C., Ahmed K., Dawes C. & Mantsch H. (1996) Thiocyanate levels in human saliva: quantitation by Fourier transform infrared spectroscopy. *Analytical Biochemistry* **240**, 7–12.

- Sellen D.W. (2001) Comparison of infant feeding patterns reported for non-industrial populations with current recommendations. *Journal of Nutrition* **131**, 2707–2715.
- Sellen D.W. (2007) Evolution of infant and young child feeding: implications for contemporary public health. *Annual Review of Nutrition* **27**, 123–148.
- Sellen D.W. & Smay D.B. (2001) Relationship between subsistence and age at weaning in 'pre-industrial societies'. *Human Nature* **12**, 47–87.
- Sfriso P., Ostuni P., Botsios C., Andretta M., Oliviero F., Punzi L. *et al.* (2003) Serum and salivary neopterin and interferon- γ in primary Sjögren's syndrome: correlation with clinical, laboratory and histopathologic features. *Scandinavian Journal of Rheumatology* **32**, 74–78.
- Shugars D.C. (1999) Endogenous mucosal antiviral factors of the oral cavity. *Journal of Infectious Diseases* **179**, S431–S435.
- Sinha S.K., Martine B., Gold B.D., Nyren Q. & Granstrom M. (2001) *Helicobacter pylori* infection in Swedish school children lack of evidence of child-to-child transmission outside the family. *Gastroenterology* **121**, 310–316.
- Smith B.H. (1989) Dental development as a measure of life history in primates. *Evolution* **43**, 683–688.
- Soderling E., Parto K. & Simell O. (2002) Saliva flow rate and composition in lysinuric protein intolerance. *Brazilian Journal of Oral Science* **1**, 40–44.
- Stoppler M.C. (2008) *The Broad Spectrum of EBV Disease*. Available at: <http://www.medicinenet.com/script/main/hp.asp?articlekey:89105>
- Taylor D.N. & Blaser M.J. (1991) The epidemiology of *Helicobacter pylori* infection. *Epidemiologic Review* **13**, 42–59.
- Tenovuo J.O. (1989) *Human Saliva: Clinical Chemistry and Microbiology*, Vol. 1. CRC Press: New York.
- Valdez I.H. & Fox P.C. (1991) Interactions of the salivary and gastrointestinal systems: I. The role of saliva in digestion. *Digestive Diseases and Sciences* **9**, 125–132.
- Venza M., Visalli M., Cicciu D. & Teti D. (2001) Determination of polyamines in human saliva by high-performance liquid chromatography with fluorescence detection. *Journal of Chromatography B: Biomedical Sciences and Applications* **757**, 111–117.
- Verma R.S. & Antony A.C. (1992) Immunoreactive folate-binding proteins from human saliva. Isolation and comparison of two distinct species. *Biochemistry Journal* **286**, 707–715.
- Vining R.F. & McGinley R.A. (1986) Hormones in saliva. *Critical Reviews in Clinical Laboratory Sciences* **23**, 95–146.
- Von Hertzen L.C. (2000) Puzzling associations between childhood infections and the latter occurrence of asthma and atopy. *Annals of Medicine* **32**, 397–400.
- Wright D.E. (1959) A note on leucocytes in saliva. *Journal of Microsc Society* **77**, 139–141.
- Yamanishi K. (2000) Human herpesvirus 6: an evolving story. *Herpes* **7**, 70–75.
- Zheng B., Khin-Maung-U, Lu R., Hill I.D. & Lebenthal E. (1996) Age-related changes in exocrine pancreatic function in infants and children. *International Pediatrics* **11**, 23–26.