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Immunoglobulin A deficiency and oral health status: a case–control study

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Abstract

Introduction: Immunoglobulin A (IgA) is important for mucosal health. Selective IgA deficiency (IgAD) is the most common primary immunodeficiency but its effect on oral health is unclear. The aim of this study was to investigate dental, periodontal and oral mucosal health in IgAD individuals.

Material and methods: In total, 32 adult IgAD subjects were compared with 63 randomly selected individuals. Participants answered questionnaires regarding general and oral health and underwent oral examination, including examination using the periodontal screening and recording (PSR) system and dental examination using the DMF system.

Results: The IgAD individuals had significantly more often undergone tonsillectomy (44% *versus* 24%, $p = 0.046$) and adenoidectomy (31% *versus* 8%, $p = 0.003$) compared with the controls. Furthermore, the IgAD subjects reported having pharyngitis, stomatitis and herpes labialis significantly more often. There was no significant difference in periodontal health (*mean PSR index*; 1.87 *versus* 1.77) or dental health (*mean DMFS*; 51.3 *versus* 53.7) between the two cohorts. A positive correlation between *Helicobacter pylori* infection and severity of periodontitis was found ($p = 0.036$).

Conclusion: IgAD predisposes to oral mucosal infections but does not influence periodontal or dental health. This is the first controlled study to include detailed clinical history and investigations, together with full oral and dental examination, in adults with IgAD.

Key words: autoimmunity; caries; *Helicobacter pylori*; IgAD; IgA deficiency; oral health; periodontitis; primary immunodeficiency

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Immunoglobulin A (IgA) is the predominant immunoglobulin secreted in oral mucosal sites. Thus, it is considered to be a major factor contributing to mucosal health and microbial defence. Secretory IgA (s-IgA) has a wide range of biological activities against pathogens and is believed to act as an immune barrier to prevent adherence and absorption of microbes and various other antigens to the mucosa. Furthermore, s-IgA can neutralize intracellular microbial pathogens within the epithelial cells and facilitate their exclusion into the lumen (Mazanec et al. 1993, 1996, Phalipon et al. 2002).

Chronic periodontitis is a disease resulting from inflammation within the supporting tissues of the teeth in response to the dental plaque biofilm. This can eventually lead to a progressive loss of attachment of the periodontal tissues and loss of the supporting alveolar bone. Periodontitis is characterized by pocket formation and/or gingival recession (Armitage 1999). It is generally accepted that the primary aetiological factor of periodontal disease is the dental plaque biofilm (Kinane 1999) but the host response is considered to be an important disease modifying factor (Page et al. 1997, Silva et al. 2008). Environmental and systemic risk factors such as smoking and diabetes, as well as some drug therapies, are also known to modulate periodontal progression and severity (Johnson et al. 1997, Albandar 2002, Mealey & Ocampo 2007).

The normal range of serum IgA is 4.96–0.78 g/l [clinical chemistry and immunology department, Landspitali-University Hospital, of Iceland, (LSH-CCID)]

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although it varies slightly between laboratories. Individuals with serum IgA between 0.77 and 0.07 g/l are considered to have ''low'' serum IgA. Selective IgA deficiency (IgAD) is defined as serum IgA levels <0.07 g/l, with normal levels of serum IgG and IgM (Conley et al. 1999). The prevalence of IgAD is approximately 1/600 in North-European populations, making it one of the most common primary immunodeficiencies (Koistinen 1975, Ulfarsson et al. 1982). Norhagen and colleagues evaluated immunoglobulin levels in saliva in individuals with IgAD, compared with healthy controls. Within the healthy control group, the normal range for salivary IgA (unstimulated) was found to be 70.3–329.4 mg/l but IgA could not be detected (<0.01 mg/l) in saliva from IgAD individuals (Norhagen et al. 1989). Individuals that lack serum IgA are therefore, also deficient in s-IgA. The clinical significance of IgAD ranges from relatively healthy individuals to various disease states such as recurrent infections especially of the upper respiratory tract, allergy, asthma and autoimmunity (Liblau & Bach 1992, Koskinen 1996, Jorgensen et al. 2009). Current knowledge on what predisposes IgAD individuals for a disease state or future complications is largely unknown.

The clinical significance of IgAD for oral health has been rather contradictory with the earliest reports, more than 30 years old, demonstrating, in a few IgAD children, no predisposition to mucosal pathology, periodontal diseases or dental caries (Robertson & Cooper 1974, Robertson et al. 1978, 1980). A recent publication on oral and dental condition of children with IgAD in north-east Hungary showed significantly worse dental caries (higher DMFS and DMFT) in IgAD children compared with the control group, but this was only observed in their primary dentition. The short exposure time of secondary teeth of these IgAD children (the oldest being 15 years old) was suggested as a possible explanation for healthy secondary teeth. However, no difference in periodontal diseases was observed (Tar et al. 2008). Furthermore, in another study of IgAD children, a high occurrence of various oral disease manifestations including aphthous-like oral ulceration (61%), candidiasis (25%) and herpes labialis (25%) were observed. However, that cohort was possibly skewed towards a possible disease state and was without a control group (Porter & Scully 1993). In addition, in a Swedish adult IgAD cohort study focusing on mucosal and periodontal health, there was no difference in periodontal health but increased mucosal manifestations of lichenoid-type lesions were observed compared with the control group. No detailed dental examination was performed (Engström et al. 1992).

The objective of this study was to evaluate thoroughly not only the oral mucosa but also the periodontal and dental status of adult IgAD cohort in Iceland compared with a randomly selected adult control group. To our knowledge, this is the first study of its kind focusing on this important issue for oral health with the aid of various clinical parameters including a detailed questionnaire and oral examinations performed by a physician and a dentist specialized in periodontal diseases.

Material and Methods

Demography of the IgAD cohort

A total of 32 adult IgAD individuals were discovered by three different routes. Firstly, by screening for IgAD in 4004 blood donors at the Icelandic blood bank. In total, seven blood donors were found to be IgAD, and five of these further participated in this study. Secondly, by re-evaluating IgAD individuals from a previous IgAD study (1974–1979) in Iceland (Ulfarsson et al. 1982). Originally 24 IgAD individuals were found by a screening of more than 15,000 blood donors. Of those still alive and willing to participate, a total of 11 individuals still met the criteria for IgAD. Thirdly, by evaluating individuals who were found to have low IgA from 1992 to 2006 at the clinical chemistry and immunology department, LSH-CCID. In total, 16 adults were found to be IgAD. About 70% of the samples sent to LSH-CCID are from ambulatory- or general practice settings in Iceland, sent for various medical reasons (Jorgensen et al. 2009).

Demography of the control cohort

In the selection of a control group, a total of 96 individuals, age and gender matched, were randomly picked from the Icelandic National Registry (one IgAD: three control individuals). From those, eight individuals could not be contacted. Of the remaining 88 individuals, 63 (71.6%) participated in the study. As shown in Table 1, the demographics for the two cohorts were well matched in age, gender and smoking. There were no exclusion criteria for the control group.

The study was approved by the National Bioethics Committee of Iceland and the Data Protection Committee of Iceland. Informed consent was obtained from all participants in the study.

Clinical evaluation and analytical procedures on participants

This study is a part of a larger ongoing study and some parts of the clinical workup go beyond the focus of this article. All the participants answered a detailed questionnaire focusing on health in general, infections, asthma, allergy, socioeconomic status, smoking behaviour and quality of life. The questionnaire included questions on various

Table 1. Demography of the IgAD cohort

	IgAD	Controls	*p* value
Total number	32	63	
Gender			0.62
Male	19 (59%)	34 (54%)	
Female	13 (41%)	29 (46%)	
Age			
Mean years	48.1 ± 13.1*	50.5 ± 12.3	0.38
Age range	26–75	27–76	
Smokers			0.82
Never smoked	18/32 (56.3%)	32/63 (50.8%)	
Former smokers	6/32 (18.8%)	17/63 (27.0%)	
Active smokers	8/32 (25.0%)	14/63 (22.2%)	

Total of 32 IgAD individuals were compared with 63 randomly selected controls that were well comparable with regard to gender, age and history of smoking.
*Number after ± represents standard deviation (SD). The two cohorts were compared using two-tailed *t*-test (for age) and Mann–Whitney *U*-test.
IgAD, immunoglobulin A deficiency.

symptoms focusing on oral health, such as oral ulcers, gingivitis, pharyngitis, history of tonsillectomy, stomatitis, dryness in mouth, herpes labialis and gastric acid reflux.

The clinical evaluation of all the participants was carried out by a physician. A detailed medical history was taken, followed by physical and oral examination. Various tests were performed on all participants including: *urea breath test*; to detect active *Helicobacter pylori* infection in the gastric mucosa and the *Schirmer test* to measure tear flow. Blood samples were also evaluated for immunoglobulin status, including IgA for confirmation of IgAD status.

The above clinical evaluation was followed by a detailed oral examination by a dentist who was blinded as to whether or not participants belonged to the IgAD or the control cohort. Oral investigation included registration of all mucous membrane lesions, number of teeth (excluding third molars) and periodontal status. The periodontal screening and recording (PSR) system introduced in 1992 was used to assess periodontal status. PSR is endorsed by the American Dental Association and the American Academy of Periodontology for the detection of periodontal disease (Piazzini 1994). Caries data were expressed according to the DMF system (Baume 1961, WHO 1997). The DMFT/DMFS caries index is a score of the cumulative caries prevalence composed from the sum of decayed (D), missing (M) and filled (F) teeth (T) or tooth surfaces (S).

Laboratory measurements

Serum IgA, IgG and IgM measurements were carried out using Beckman Array 360 System Rate Nephelometer (Beckman Coulter Inc., Brea, CA, USA). IgAD was defined as serum IgA levels < 0.07 g/l, with normal levels of serum IgG and IgM.

Statistical analysis

In addition to the descriptive statistics, the groups were compared by the two-tailed *t*-test or the Mann–Whitney *U*-test in case of continuous variables and by the χ^2-test or Fisher's exact test, in case of categorical data. Association between variables was evaluated by Kendall's and Pearson correlation coefficients or by partial correlation when adjusting for other variables (using log transformation where appropriate). The level of significance was set at 0.05 and the program package SPSS 11.0 was used for processing the data.

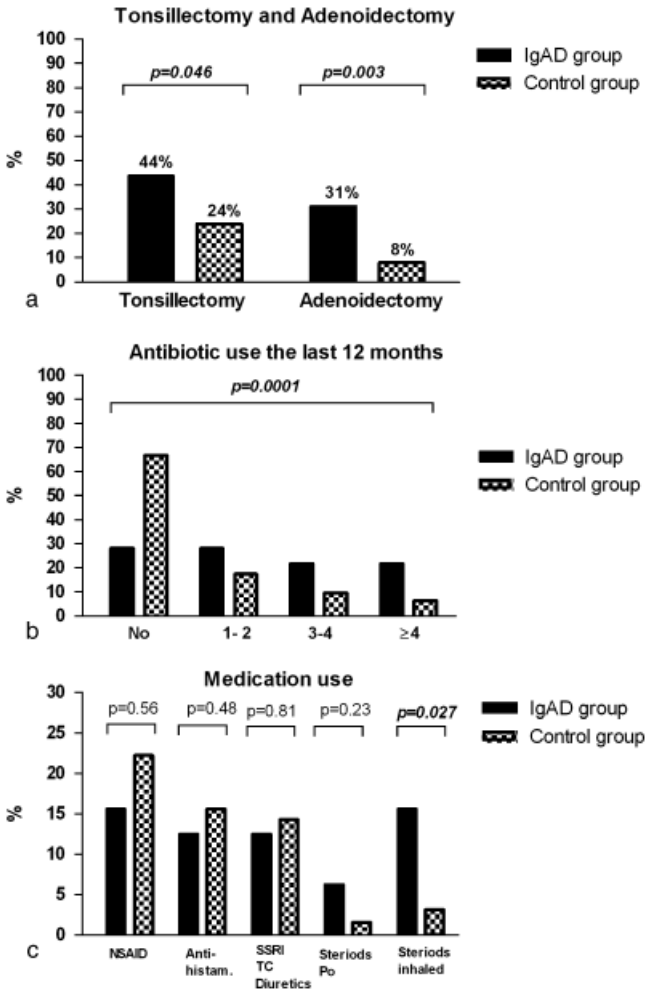

Fig. 1. Increased oral surgical intervention and antibiotic use among the immunoglobulin A deficiency (IgAD) individuals. (a) Demonstrates the lifetime prevalence of tonsillectomy and adenoidectomy within the IgAD group, compared with the control group. (b) Demonstrates a 12 months use of antibiotics, in the IgAD group compared with the control group. The *X*-axis represents the number of systemic antibiotic treatments. (c) Demonstrates the daily or regular use of medications, potentially affecting dental or periodontal health. There was a significant increase in the use of oral inhaled steroids among the IgAD group but it did not correlate with dental or periodontal health, and neither did any of the other medication. Furthermore there was no difference in the use of drugs that possibly cause dry mouth such as SSRI, TC and diuretics. A detailed history of medication use was obtained by a physician. NSAID, non-steroidal anti-inflammatory drugs; SSRI, serotonin-specific reuptake inhibitors; TC, tricyclic anti-depressants.

Results

Subjective oral mucosal findings

As shown in Fig. 1a, the IgAD cohort had significantly more often undergone tonsillectomy (IgAD 44% *versus* control 24%, $p = 0.046$) and adenoidectomy (IgAD 31% *versus* control 8%, $p = 0.003$), probably indicating higher occurrence of upper respiratory tract infections during childhood in the IgAD cohort. Furthermore, as shown in Table 2, the IgAD cohort also reported a higher incidence of pharyngitis and stomatitis. However, there was no statistical difference in the self-reported occurrence of gingivitis between the cohorts. The IgAD cohort also reported higher 12-month incidence (IgAD 59.4% *versus* controls 33.3%), and recurrence of herpes labialis ($\geqslant 3$ herpes labialis infections: IgAD 18.8% *versus* controls 7.9%), $p = 0.012$. There was no difference between the two cohorts in the incidence of $\geqslant 1$ oral ulcers reported (IgAD 28.1% *versus* controls 22.2%, the last 12 months, $p = 0.53$). Furthermore, there was no

Table 2. Subjective oral mucosal symptoms, retrospective analysis

	5 years	2 years			
	never	never	1–4 times	⩾5 times	*p* value
Pharyngitis					
IgAD	1/32 (3.3%)	5/32 (15.6%)	19/32 (59.4%)	8/32 (25.0%)	5y* ***0.0001***
Controls	17/63 (27.0%)	24/63 (38.1%)	36/63 (57.1%)	3/63 (4.8%)	2y† ***0.005***
Stomatitis					
IgAD	11/32 (34.4%)	11/32 (34.4%)	17/32 (53.1%)	4/32 (12.5%)	5y ***0.009***
Controls	44/63 (69.8%)	47/63 (74.6%)	12/63 (19.0%)	4/63 (6.3%)	2y ***0.015***
Gingivitis					
IgAD	21/32 (65.6%)	24/32 (75%)	7/32 (21.9%)	1/32 (3.1%)	5y 0.67
Controls	45/63 (71.4%)	51/63 (81.0%)	12/63 (19.0%)	0%	2y 0.54

Comparison of the IgAD group and the control group, using retrospective data analysis obtained from a self-reported questioner on oral mucosal symptoms. The two groups were compared using Mann–Whitney *U*-test and *p* values given for both.
*5 years (5y) comparison.
†2 years (2y) comparison.
Bold and italic numerals signifies $p<0.05$.
IgAD, immunoglobulin A deficiency.

Table 3. Oral mucosal disorders noted in clinical examination in the IgAD cohort compared with the controls

	IgAD ($n=32$)	Controls ($n=63$)
Inflamed or infected tonsils	3/32 (9.4%)	2/63 (3.2%)
White tongue (thrush)	2/32 (6.3%)	2/63 (3.2%)
Minor aphthous-like ulcer <10 mm	2/32 (6.3%)	1/63 (1.6%)
Lichenoid type lesions	2/32 (6.3%)	0
White plaque lesion (leukoplakia)	0	1/63 (1.6%)
Buccal hyperkeratosis	0	1/63 (1.6%)
Condyloma ''wart-like lesion on uvula''	0	1/63 (1.6%)
Total	7/32 (21.9%)	8/63 (12.7%)

All the participants had an oral examination by a physician but two in each group did not finish the oral examination by a dentist. Despite higher prevalence of oral mucosal disorders within the IgAD cohort (21.9% *versus*. 12.7%), the increase was not significant ($p=0.37$).
IgAD, immunoglobulin A deficiency.

difference in self-reported dry mouth between the cohorts (dry mouth every day; IgAD 9.3% *versus* controls 6.3%, $p=0.25$). In addition, there was no correlation between reporting dry mouth and using medication with a potential side effect of causing drying of the mouth (Fig. 1c).

We investigated if other systemic factors were possibly contributing to oral pathosis in the cohorts. Thus, a significantly higher proportion of IgAD had symptoms suggestive for acid reflux (acid regurgitation) than the control cohort (IgAD 28.1% *versus* control 11.1%, $p=0.036$). In addition, as shown in Fig. 1b, there was a significant difference regarding the use of antibiotics between the two cohorts, with the IgAD group using antibiotics two to three times more frequently. However, regarding acid reflux, it did not have any effect on periodontal health or tooth decay, whereas correlation analyses demonstrated that antibiotics had a significant positive correlation with acid reflux (CC 0.259, $p=0.012$).

Oral examination

As shown in Table 3, mucosal disorders seemed to occur more often among the IgAD cohort. In total, 22% of the IgAD cohort had some form of mucosal disorders, compared with 13% in the control cohort. However, probably due to the low numbers of study participants, the difference was not statistically significant ($p=0.37$).

Periodontal and dental examination

Mean PSR scores were similar for the IgAD cohort and the control cohorts, 1.87 and 1.77, respectively ($p=0.55$). Interestingly, no subject was found to have completely healthy periodontal tissues, according to the PSR scoring system. As shown in Table 4, there were no statistically significant differences between the cohorts with respect to the frequency of persons having gingivitis (PSR = 1 or 2), shallow (PSR = 3) or deep periodontal pockets (PSR = 4). In order to evaluate if IgAD could affect the periodontal tissue differently with respect to oral location, PSR scores for each sextant (I–VI) were compared separately with matching sextants within the control cohort. There was no difference between any of the six sextants (I, $p=0.66$), (II, $p=0.56$), (III, $p=0.62$), (IV, $p=0.44$), (V, $p=0.95$) and (VI, $p=0.09$). No significant differences were found between the mean DMFT and DMFS indices or the number of teeth present.

Other variables correlating with periodontal disease

Smoking is a known risk factor for periodontal diseases. Thus, when both cohorts were combined, smoking correlated significantly with the severity of periodontitis. Those who smoked were significantly less likely to have healthy sextants (sextants scoring 0) (CC -0.23, $p=0.015$) and more likely to have the worst score (sextants scoring 4) (CC 0.37, $p<0.0001$), compared with non- smoking participants. However, because of the small number of participants, the data did not have enough statistical power to determine if smoking predisposed those with IgAD more to periodontal disease than controls. Smoking history did not influence the selection of the control group but, as shown in Table 1, the two cohorts were not different in smoking behaviour.

The prevalence of active gastro-duodenal infection with *H. pylori* (defined by a positive urea breath test) was similar for both cohorts [IgAD 12/32 (37.5%) *versus* 21/63 (33.3%) in the control group, $p=0.82$]. Moreover, in relation to periodontal health, the *H. pylori* infection had a positive correlation with the severity of periodontitis (CC 0.188, $p=0.036$), when both cohorts were combined and after correcting for age.

The use of antibiotics and anti-histamines (both having been suggested as known preventive factors for periodontal disease) correlated positively with periodontal health. However, no such correlation existed after correcting the variables for age (data not shown). In addition, the use of NSAID or the use of steroids did not correlate with the severity of periodontitis (see Fig. 1c, for

Table 4. Dental and periodontal status in the IgAD cohort compared with the controls

	IgAD ($n = 30$)	Controls ($n = 61$)	p values
Tendal status			
Edentulous*	2	2	
Number of individuals with no missing teeth	10/28 (35.7%)	20/59 (33.9%)	1
Number of teeth	23.57 ± 1.00†	24.17 ± 0.75	0.51
Mandible	12.14 ± 0.37	12.29 ± 0.31	0.54
Maxillary	11.43 ± 0.72	11.88 ± 0.50	0.34
Mean DMFT‡	15.89 ± 1.15	16.90 ± 0.75	0.48
Mean DMFS‡	51.32 ± 5.33	53.68 ± 3.57	0.81
Periodontal status			
Number of individuals affected by highest PSR score			0.86
0. Healthy periodontal tissues	0	0	
1. Bleeding	2/28 (7.1%)	3/59 (5.1%)	
2. Calculus	10/28 (35.7%)	26/59 (44.1%)	
3. Shallow pockets (4 or 5 mm)	10/28 (35.7%)	16/59 (27.1%)	
4. Deep pockets (⩾6 mm)	6/28 (21.4%)	14/59 (23.7%)	
Missing sextants;			
⩾1 missing sextant	5/28 (17.9%)	7/59 (11.9%)	0.51
Mean PSR index§	1.87 ± 0.18	1.77 ± 0.12	0.55

*Edentulous refers to participants having no teeth and are therefore not included in the DMFT/S or the periodontal screening and recording score (PSR).

†All numbers after ±, indicate standard error of mean (SEM). p values were calculated by using Mann–Whitney U-test (and Fisher's exact test for comparison of numbers of individuals with no missing teeth). Two subjects from each group did not finish the examination by a dentist and are therefore not included in the table.

‡The DMFT/DMFS represent cumulative prevalence indices composed from the sum of decayed (D), missing (M), filled (F), teeth (T) or (FS) filled surfaces. DMFT score ranges 0–28, DMFS score ranges 0–128, with higher scores representing worse condition.

§The PSR index divides the mouth into six segments (sextants) and the greatest probe depth in each sextant of the mouth is determined and recorded. By combining the scores from each sextant and dividing by the number of sextants, the PSR index for each individual is obtained. The table compares mean PSR indices between the two cohorts.

IgAD, immunoglobulin A deficiency.

comparison of medication use between cohorts).

The prevalence of autoimmunity was high within the IgAD cohort compared with the control cohort [IgAD cohort 8/32 (25%) *versus* 3/63 (4.8%)] $p = 0.004$ (for details on types of autoimmunity, see reference Jorgensen et al. 2009). However, autoimmunity had no correlation with periodontal or dental health (data not shown).

Finally, the use of NSAID, systemic intake or orally inhaled steroids or the diagnosis of autoimmunity did not correlate with the severity of periodontitis.

Discussion

This study is the first to include a detailed history of physical conditions, oral/dental status and clinical investigations, together with a full-oral and dental examination, in adults with IgAD, compared with a randomly selected control cohort. The results demonstrated that IgAD individuals are not at an increased risk for periodontal diseases or dental decay. However, infection-related disorders such as herpes labialis, pharyngitis and stomatitis were reported significantly more often in the IgAD cohort.

Our results are in agreement with a Swedish case–control study on adult IgAD individuals, which showed that IgAD does not seem to predispose to periodontal diseases (Engström et al. 1992). The present study includes, additionally, a detailed examination on dental decay and the subjects' general clinical history. Furthermore, the present study addresses a recent question raised in a publication on the oral and dental condition of children with IgAD in north-east Hungary (Tar et al. 2008). In that study, significantly higher dental caries scores were found in IgAD children, compared with controls, but only in the primary dentition. The possibility of a too-short exposure time of the secondary teeth of these IgAD children was mentioned and the authors concluded that these children would possibly develop worse dental health later on. Our results show that this is probably not the case for the adult Icelandic IgAD cohort. Thus, the higher dental caries scores found in the Hungarian IgAD children may have had other causes than IgAD. For example, the increased caries could possibly be explained by the numerous upper respiratory infections that would probably have been associated with periods of worse dental hygiene and, particularly, by the of use antibiotic mixtures, containing sugar. Sugar-containing antibiotic mixtures are known to be a significant factor in causing higher caries scores in young Icelandic subjects (Holbrook et al. 1989, Holbrook 1993). Antibiotics may also directly influence dental health (Hong et al. 2004). Furthermore upper respiratory tract infections in infancy are associated with enamel hypoplasia, in the form of white spots particularly in the permanent dentition, as has been reported in Icelandic children (Árnadóttir et al. 2005). It is not unreasonable to expect more upper respiratory tract infections in children with IgAD, as was indeed found in the present study.

One of the most difficult factors common to many previous studies focusing on the oral health of subjects with IgAD is the selection bias of the study cohort. Very few studies have had their IgAD study cohort composed of two different study groups, i.e. one from the screening for IgAD among predominantly healthy males (blood donors) and the other found at the clinical chemistry and immunology department, initially showing signs or symptoms that gave reason to immunoglobulin measurements. Interestingly, for none of the oral-related variables presented in this study was there a difference between the two IgAD cohorts, not even pharyngitis or tonsillectomy. There are some possible explanations for this. Bad oral health is to our knowledge never an exclusion criterion for donating blood. Furthermore, 11 of 16 IgAD subjects found by blood bank screening were discovered decades ago and in that time, their clinical picture might have changed. Finally, concerning periodontal diseases and tooth decay, there was no statistical difference between the two IgAD cohorts or between the total IgAD cohorts and controls, thus, indicating that IgA plays only a minor role, if any, in periodontal and dental protection, with the possible exception of children.

Another possible bias, well known in retrospective studies, is the recollection bias. As part of the questionnaires answered by participants is reliant on the memory of health-related events, such as number of infections per year, the possibility of recollection error exists. We expected the recollection error to be similar within the study group and the control group, without ever knowing if that was true. This limitation of accuracy must be kept in mind with regard to the results presented here, as it is for all retrospective studies.

We observed an increased prevalence of mucosal disorders of infectious origin within the IgAD cohort, such as pharyngitis, stomatitis and herpes infection. In addition, there was an increased prevalence of surgical interventions, tonsillectomy and adenoidectomy, that often are regarded as a consequence of recurrent upper respiratory infections. This supports the apparently important role of the s-IgA in inhibiting mucosal colonization and invasion of pathogens, and inactivating these pathogens and enhancing the clearance of pathogens, such as viruses and bacteria (Porter & Linggood 1983, Mazanec et al. 1993, Bomsel et al. 1998, Renegar et al. 1998, Phalipon et al. 2002, Brandtzaeg 2003). With particular regard to the IgAD individuals reporting more herpes infections, it has been demonstrated that in patients with relapsing herpes virus infection, those with infrequent relapses had significantly higher s-IgA levels in comparison with those with frequent relapses, during the herpes infection (Briazzhikova & Iurlova 2005). Furthermore, because of its structural stability, s-IgA can retain its antibody activity for prolonged periods in a hostile environment, such as the oral cavity (Ma et al. 1998).

Characterization of the salivary IgA response to organisms known to cause dental plaque has been thought by some investigators to be interesting in the context of the possible production of an active caries vaccine (Russell & Mestecky 1986, Michalek et al. 2001, Russell et al. 2004, Brandtzaeg 2007a, b). Somewhat contradictory, in our study, we found no increase in dental decay among individuals who totally lack serum and salivary IgA, when compared with randomly selected controls with total IgA within normal limits. This indicates that either the immune system is able to compensate for the lack of IgA or possibly, that the protective role of salivary IgA against dental decay is only a minor one. In fact, the protective role of salivary IgA against dental diseases has for long been a matter of dispute (Russell & Mestecky 1986). While some reports have found an inverse relationship between caries susceptibility and the output of salivary IgA, others have not (Taubman & Smith 1993). Additionally, studies correlating salivary antibody levels with counts of *Streptococcus mutans* and caries score are, when taken together, inconclusive (Taubman & Smith 1993). Furthermore, the activity of salivary IgA against *S. mutans* has been considered critical in modulating the onset of caries (Nogueira et al. 2005) and, therefore, as dental caries is primarily a childhood disease, this might possibly explain the difference found in children with IgAD (Tar et al. 2008) and our adult IgAD cohort. IgA has been postulated to have a protective role in the pathogenesis of periodontal disease, although the precise mechanism is not known. In this context, it has been suggested, that the humoral response in periodontal disease may involve features of both the mucosal and systemic immune systems, depending on whether this occurs in the marginal gingiva or the deeper granulomatous tissue of periodontal lesions (Takahashi et al. 1997, Kinane et al. 1999). The interaction of salivary IgA with putative periodontal pathogens could inhibit their adherence, decrease their colonization and, consequently, possibly affect the development of periodontitis. As with dental caries, the data on the protective role of salivary IgA in periodontitis are similarly controversial (Taubman & Smith 1993, Hägewald et al. 2000, 2003). Dental caries and periodontal diseases are caused by the accumulation of largely commensalistic bacteria on the non-shedding surfaces of teeth where they form biofilms, which can be retained for a long time. Thus, there may exist different mechanisms of disease initiation in the dento-periodontal environment when compared with disease on the shedding mucosal surfaces of other areas of the oral cavity. Indeed, the oral cavity is particularly resistant to infection, considering its frequent exposure to potential pathogens. This is probably due to a combination of defence mechanisms including the regular shedding of mucosal cells, protection by the commensal flora against potential exogenous pathogens and the physical, chemical and antibody-related protective mechanisms of saliva. This present study found that the loss of one of these protective mechanisms, s-IgA, did not result in any increase in periodontitis among the IgAD individuals and this is a finding that confirms other controlled studies on the effect of IgAD on periodontitis (Engström et al. 1992, Tar et al. 2008).

In this study, no difference was observed in the prevalence of active gastro-duodenal infection by *H. pylori* between the two cohorts, as judged by a positive urea breath test [IgAD (37.5%) *versus* (33.3%) in the control group $p = 0.82$]. This is the first time that active *H. pylori* infection in an IgAD cohort has been evaluated and the results indicate that IgA does not play a critical role in the host defense against the organism. However, it was observed that active gastro-duodenal infection with *H. pylori* correlated positively with the severity of periodontitis (CC 0.188, $p = 0.036$). There was, however, no correlation between *H. pylori* infection and DMFT/S status or other oral-related variables in the study and this included reports of oral ulcers or gingivitis. The role of *H. pylori* in the aetiology of gastric diseases is now undisputed (Suerbaum & Michetti 2002), but its potential role in the pathogenesis of periodontitis remains unclear. In contrast, *H. pylori* has been detected in supragingival and subgingival plaques (Song et al. 2000, Allaker et al. 2002), saliva (Bürgers et al. 2008), oral lesions and on oral mucosa (Mravak-Stipeti et al. 1998), but it is difficult to compare prevalence rates between these sites due to variations in detection methodology (Dowsett & Kowolik 2003). Most attempts to culture *H. pylori* from oral samples have failed but recent studies using polymerase chain reaction techniques have shown high discrepancy in the prevalence of *H. pylori* in the oral environment, ranging from 0 to 100% (Song et al. 2000, Dowsett & Kowolik 2003). As haematogenic spread of *H. pylori* infection is highly improbable, it is clear that this bacterium must reach the stomach via the oral cavity, but whether the oral cavity serves solely as a route of passage or as a reservoir for the gastric *H. pylori* infection, is still not clear. Thus while gastric infection could be responsible for the occurrence of *H. pylori* in the oral cavity by oesophageal reflux, a recent study has also demonstrated that *H. pylori* can become established in the

oral cavity independent of stomach colonization (Bürgers et al. 2008).

As the antibiotics commonly used for the treatment of *H. pylori* infections are also frequently used in the treatment for respiratory infections, it was perplexing that antibiotics usage had a positive correlation with acid reflux in our study. However, it is very unlikely that a single drug therapy is enough for *H. pylori* eradication. There is a scarce amount of information on this subject in the literature although, antibiotics such as doxycyclin (commonly used for i.e. acne and respiratory tract infections) are known to be able to cause oesophagitis (Boyce 1998).

We conclude that while IgAD does indeed predispose to infection-related oral mucosal disorders, it does not seem to play a major role in the pathogenesis of periodontal disease or dental caries in adult subjects.

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Clinical Relevance

Scientific rationale for study: IgA is believed to contribute to good oral health. However, oral and dental health and its association with active *H. pylori* infection, has never been thoroughly investigated in adults with IgAD.

Principal findings: IgAD predisposes adults to infectious-related oral mucosal disorders but not to worse dental or periodontal health, when compared with a randomly selected control group. *H. pylori* infection had a positive correlation with the severity of periodontitis, regardless of subjects IgA status.

Practical implications: These findings suggest that special periodontal and dental monitoring might not be necessary for adults with IgAD.