

Saliva contact during infancy and allergy development in school-age children



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Background: Parent-child saliva contact during infancy might stimulate the child's immune system for effective allergy prevention. However, few studies have investigated its relation to allergy development in school-age children.

Objective: We sought to investigate the relationship between parent-child saliva contact during infancy and allergy development at school age.

Methods: We performed a large multicenter cross-sectional study involving Japanese school children and their parents. The self-administered questionnaires including questions from the International Study of Asthma and Allergies in Childhood were distributed to 3570 elementary and junior high school children in 2 local cities. Data were analyzed for the relationship between saliva contact during infancy (age <12 months) and the risk of allergy development, specifically eczema, allergic rhinitis, and asthma. For detailed Methods, please see the Methods section in this article's Online Repository at www.jacionline.org.

Results: The valid response rate was 94.7%. The mean and median age of children was 10.8 ± 2.7 and 11 (interquartile range, 9-13) years, respectively. Saliva contact via sharing eating utensils during infancy was significantly associated with a lower risk of eczema (odds ratio, 0.53; 95% CI, 0.34-0.83) at school age. Saliva contact via parental sucking of pacifiers was significantly associated with a lower risk of eczema (odds ratio, 0.24; 95% CI, 0.10-0.60) and allergic rhinitis (odds ratio, 0.33;

95% CI, 0.15-0.73), and had a borderline association with the risk of asthma in school-age children.

Conclusions: Saliva contact during infancy may reduce the risk of developing eczema and allergic rhinitis in school-age children. (J Allergy Clin Immunol Global 2023;2:100108.)

Key words: Allergy, eczema, allergic rhinitis, saliva contact, eating utensils, pacifier, oral microbes, infancy, school age

INTRODUCTION

The prevalence of allergic diseases such as eczema, allergic rhinitis, food allergy, and asthma has been increasing worldwide, particularly in industrialized countries.¹ Allergic diseases have a major effect on the quality of life, imposing a substantial burden on the society.² The hygiene hypothesis suggests that the incidence of allergic diseases has been increasing owing to a decrease in the incidence of infectious disease in the Western society's cleaner environment.³ This hypothesis has been expanded to correlate commensal and symbiotic microbes (intestinal microbiota) with immune development.⁴ The development of allergen tolerance may depend on several factors, including microbial colonization, immune stimulation during infancy, and microbe acquisition from the mother at birth.⁵ Insufficient microbial stimulation during infancy may lead to the hypersensitivity of barrier tissues and an increase in type 2 immune responses (allergic disease).⁵

Animal and human studies suggest that oral microbes translocate to the gut, altering gut microbiota and possibly immune defenses.⁶ In humans, the oral cavity has the second richest microflora after the gastrointestinal tract.⁷ Saliva plays an essential role in the formation and maintenance of the ecological equilibrium of the oral commensal flora.⁸ Early changes in the composition of the oral microbiota influence immune maturation and allergy development.⁹ In Sweden, parental sucking of infants' pacifiers reportedly reduced the risk of developing allergies (eczema and asthma) at age 18 months and eczema at age 36 months, possibly owing to immune stimulation by the oral microbes transferred from parental saliva to the infant.¹⁰ Our previous study showed that premastication (ie, chewing the child's food to soften it before feeding) during infancy may reduce the risk of allergy development, especially eczema, at school age, possibly because of the transmission of oral microbes from caregivers to infants.¹¹

Therefore, we hypothesized that saliva contact during infancy (age <12 months) would reduce the risk of developing allergies in Japanese children. To test this hypothesis, we performed a multicenter study by conducting a survey in Japanese school-age children and their parents using a cross-sectional design in 2 local cities using 91 self-administered questions including

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This work was supported by Grants-in-Aid for Scientific Research of Japan Society for the Promotion of Science (Tokyo, Japan; grant no. 17K09124) and the Joint Research Fund of the Japanese Society for Cutaneous Immunology and Allergy (Tokyo, Japan). The funders had no role in designing the study; in the collection, analysis, and interpretation of data; in writing the report; and in the decision to submit the article for publication.

Disclosure of potential conflict of interest: The authors declare no conflicts of interest associated with this study.

Received for publication May 23, 2022; revised February 3, 2023; accepted for publication March 21, 2023.

Available online April 11, 2023.

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2772-8293

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<https://doi.org/10.1016/j.jacig.2023.100108>

Abbreviation used

OR: Odds ratio

questions from the International Study of Asthma and Allergies in Childhood.

RESULTS AND DISCUSSION

The valid response rate was 94.7%, and the data of 3380 children were analyzed. The mean and median age of the children was 10.8 ± 2.7 and 11 (interquartile range, 9-13) years, respectively. Our study population was almost evenly distributed between the sexes and among grades of elementary and junior high schools (see [Table E1](#) in this article's Online Repository at www.jacionline.org). Regarding saliva contact, 9.9% ($n = 336$) of the children were fed using shared eating utensils during infancy and 39.6% used a pacifier, which was cleaned by parental sucking in 2.2% ($n = 76$) of the infants (see [Table E2](#) in this article's Online Repository at www.jacionline.org). The incidence of eczema, allergic rhinitis, and asthma symptoms was 18.3%, 59.2%, and 27.1%, respectively.

Sharing eating utensils was more frequent ($P < .05$) among mothers smoking during pregnancy, children having siblings, and parents without knowledge of oral infections ([Table I](#)). Mothers without a history of allergy, fathers without a history of allergy, mothers who smoked during pregnancy, parents having a cat or dog at home during infancy of their child, and parents without knowledge of oral infections had a tendency ($P < .05$) to clean their child's pacifier by sucking.

Current or previous eczema symptoms in children correlated ($P < .05$) with mothers with a history of allergy, fathers with a history of allergy, and the child being exclusively breast-fed for the first 6 months ([Table II](#)). Current or previous allergic rhinitis symptoms also correlated ($P < .05$) with mothers with a history of allergy, fathers with a history of allergy, parents having knowledge of oral infections, sharing eating utensils, and cleaning pacifiers by parental sucking. Finally, there was a relationship ($P < .05$) between current or previous asthma symptoms and mothers with a history of allergy, fathers with a history of allergy, and smoking during pregnancy.

Children who shared eating utensils were significantly less likely to have eczema currently (odds ratio [OR], 0.53; 95% CI, 0.34-0.83) ([Table III](#)). After adjusting for possible confounding factors (mothers with a history of allergy, mothers who smoked during pregnancy, and parents with knowledge of oral infection), the association was still significant (adjusted OR, 0.52; 95% CI, 0.32-0.84). Current allergic rhinitis and asthma symptoms were not significantly associated with sharing of eating utensils. Children whose parents sucked their pacifier for cleaning were significantly less likely to have eczema currently (OR, 0.24; 95% CI, 0.10-0.60) and the association was still significant (adjusted OR, 0.35; 95% CI, 0.13-0.91) after adjustment. Similarly, children whose parents sucked their pacifier for cleaning were significantly less likely to have allergic rhinitis currently (OR, 0.33; 95% CI, 0.15-0.73) and this association was also significant (adjusted OR, 0.32; 95% CI, 0.14-0.72) after adjustment. The estimate for pacifier cleaning by parental sucking and current

asthma suggested a strong inverse relationship and borderline significance (adjusted OR, 0.17; 95% CI, 0.02-1.31).

Although the epidemiology of allergic and immunologic diseases in Asia is not well understood,¹² we revealed that the risk of eczema and allergic rhinitis at school age was lower in Japanese children who have parental saliva contact during infancy. The oral cavity is the site of the first encounter between many foreign antigens and the immune system,⁹ and it is suggested that oral microbes translocate to the gut, altering its microbiota and possibly altering immune defenses.⁶ Furthermore, early changes in oral microbial composition may affect immune maturation and allergy development.⁹ Hesselmar et al¹⁰ reported that the use of pacifiers cleaned by parental sucking significantly reduces the risk of eczema and asthma at age 18 months and eczema at age 36 months in Swedish children, possibly owing to immune stimulation by oral microbes transferred from parents to the infants.¹⁰ The present study showed that using pacifiers cleaned by parental sucking may reduce the risk of eczema and allergic rhinitis development in children at school age (aged 6-15 years) in Japan. Regarding the use of pacifiers cleaned by parental sucking and the risk of asthma, there is a strong inverse relationship and borderline significance. Furthermore, our study showed that saliva contact by sharing eating utensils during infancy was significantly associated with the reduced risk of current eczema. However, the risk of current allergic rhinitis and asthma development was not significantly associated with sharing eating utensils. Earlier saliva contact might be associated with a lower risk of allergies, because parental sucking of pacifiers typically precedes the use of eating utensils. It has been reported that the practice of parental sucking of pacifiers allows parents and children to have a close oral contact at an early stage, before the children start using eating utensils, and will facilitate the transfer of oral microbes.¹⁰ Microbial colonization in the early postnatal period may be important in guiding the maturation of the immune system and controlling the development of childhood allergies, and the oral microbiota may play an important role in the development of allergy.¹³

This study has some potential limitations of self-report and recall bias. We used the internationally validated International Study of Asthma and Allergies in Childhood questions to ensure that the participants responded as accurately as possible. Recall bias should be noted for children of all grades. However, in Japan, a maternal and child's health handbook is officially provided for all parents to record the child's growth from pregnancy until school age, which helps parents remember past events. Furthermore, because of the rapid decline in saliva contact between children and their parents in Japan due to increased oral hygiene awareness, we decided to survey a wide range of grades; however, comparisons by grade could not be performed owing to the small number of respondents to saliva contact.

In summary, for the first time in Asia, we performed a large multicenter study involving Japanese school-age children and their parents and obtained evidence that parent-child saliva contact—whether through sharing of eating utensils during infancy or parental sucking of the infant's pacifier—may reduce the risk of eczema and allergic rhinitis. Both practices lead to the transmission of oral microbes from the parents to the child, which provides a biologically plausible explanation for the finding. The findings support those of Hesselmar et al¹⁰ in Swedish children at least for the risk of eczema. We found that parent-child saliva contact during infancy was borderline associated

TABLE I. Analysis of factors associated with sharing eating utensils and cleaning pacifiers by parental sucking

Factor	Factor present	Sharing eating utensils, n (%)			Cleaning pacifiers by parental sucking, n (%)		
		Yes	No	P value	Yes	No	P value
Mother with a history of allergy	Yes	154 (9.4)	1485 (90.6)	.503	27 (4.7)	546 (95.3)	.007
	No	173 (10.1)	1543 (89.9)		49 (8.7)	513 (91.3)	
Father with a history of allergy	Yes	122 (9.3)	1191 (90.7)	.498	17 (3.8)	429 (96.2)	.002
	No	201 (10.0)	1808 (90.0)		57 (8.6)	609 (91.4)	
Mother smoking during pregnancy	Yes	59 (15.3)	327 (84.7)	<.001	24 (13.6)	152 (86.4)	<.001
	No	267 (9.0)	2690 (91.0)		49 (5.1)	906 (94.9)	
Having siblings	Yes	307 (10.4)	2646 (89.6)	.001	69 (7.0)	914 (93.0)	.239
	No	21 (5.1)	392 (94.9)		7 (4.5)	149 (95.5)	
Delivered by cesarean section	Yes	56 (8.7)	586 (91.3)	.354	18 (7.6)	219 (92.4)	.528
	No	270 (9.9)	2450 (90.1)		58 (6.4)	842 (93.6)	
Exclusively breast-fed for 6 mo	Yes	106 (9.1)	1061 (90.9)	.535	13 (6.3)	193 (93.7)	.818
	No	173 (10.1)	1545 (89.9)		55 (7.5)	676 (92.5)	
Cat or dog at home during infancy	Yes	81 (11.0)	654 (89.0)	.132	26 (9.0)	263 (91.0)	.048
	No	240 (9.2)	2377 (90.8)		48 (5.7)	798 (94.3)	
Having oral infection knowledge	Yes	309 (9.5)	2937 (90.5)	.003	63 (5.8)	1021 (94.2)	<.001
	No	20 (18.0)	91 (82.0)		12 (22.6)	41 (77.4)	

P values were calculated using Pearson χ^2 test.

TABLE II. Analysis of factors associated with current or previous eczema, allergic rhinitis, and asthma symptoms in school-age children

Factor	Eczema symptom, n (%)			Allergic rhinitis symptom, n (%)			Asthma symptom, n (%)		
	Yes	No	P value	Yes	No	P value	Yes	No	P value
Mother with a history of allergy									
	Yes	384 (23.5)	1250 (76.5)	<.001	1138 (69.7)	494 (30.3)	<.001	548 (33.6)	1084 (66.4)
	No	229 (13.4)	1478 (86.6)		850 (49.8)	857 (50.2)		358 (21.0)	1348 (79.0)
Father with a history of allergy	Yes	304 (23.2)	1007 (76.8)	<.001	891 (67.9)	421 (32.1)	<.001	439 (33.5)	870 (66.5)
	No	306 (15.3)	1689 (84.7)		1075 (53.9)	918 (46.1)		458 (23.0)	1537 (77.0)
Mother smoking during pregnancy	Yes	70 (18.2)	314 (81.8)	.875	224 (58.3)	160 (41.7)	.546	125 (32.5)	260 (67.5)
	No	547 (18.6)	2400 (81.4)		1764 (59.9)	1179 (40.1)		779 (26.5)	2161 (73.5)
Having siblings	Yes	550 (18.7)	2392 (81.3)	.302	1745 (59.4)	1194 (40.6)	.549	798 (27.2)	2139 (72.8)
	No	68 (16.6)	342 (83.4)		251 (60.9)	161 (39.1)		114 (27.7)	298 (72.3)
Delivered by cesarean section	Yes	110 (17.2)	529 (82.8)	.390	393 (61.6)	245 (38.4)	.258	192 (30.0)	447 (70.0)
	No	506 (18.7)	2203 (81.3)		1602 (59.2)	1106 (40.8)		719 (26.6)	1987 (73.4)
Exclusively breast-fed for 6 mo	Yes	240 (20.6)	925 (79.4)	.017	683 (58.9)	477 (41.1)	.550	298 (25.7)	860 (74.3)
	No	375 (17.2)	1799 (82.8)		1305 (59.9)	872 (40.1)		614 (28.2)	1564 (71.8)
Cat or dog in home during infancy	Yes	129 (17.7)	601 (82.3)	.537	433 (59.4)	296 (40.6)	.947	207 (28.3)	524 (71.7)
	No	487 (18.7)	2121 (81.3)		1552 (59.5)	1055 (40.5)		701 (26.9)	1903 (73.1)
Having oral infection knowledge	Yes	604 (18.7)	2628 (81.3)	.168	1938 (60.0)	1292 (40.0)	.027	878 (27.2)	2350 (72.8)
	No	15 (13.5)	96 (86.5)		55 (49.5)	56 (50.5)		30 (27.0)	81 (73.0)
Sharing eating utensils	Yes	55 (16.7)	275 (83.3)	.391	175 (52.7)	157 (47.3)	.007	90 (27.0)	243 (73.0)
	No	564 (18.6)	2469 (81.4)		1827 (60.3)	1202 (39.7)		826 (27.3)	2202 (72.7)
Cleaning pacifier by parental sucking	Yes	12 (16.0)	63 (84.0)	.482	36 (47.4)	40 (52.6)	.007	23 (30.3)	53 (69.7)
	No	205 (19.3)	857 (80.7)		666 (62.9)	392 (37.1)		307 (29.0)	753 (71.0)

P values were calculated using Pearson χ^2 test.

with asthma. Further research is needed to identify the mechanism of the apparent risk reduction and ways to apply these findings to prevent childhood eczema and allergic rhinitis development.

We thank all those who participated in and cooperated with this study: Yutaro Okuno, Principal; Tomoko Nakata, City Board Education Assistant Chief; and school principals, teachers, children, and parents in Kaga and Tochigi cities. We also acknowledge the support of Toshio Shimokawa, Yumi

TABLE III. Effects of sharing eating utensils and pacifier cleaning by parental sucking on 3 types of current allergy symptoms in children at school-age

Allergic symptom*	Factor during infancy†	Before adjustment		After adjustment‡	
		OR (95% CI)	P value	OR (95% CI)	P value
Eczema	Sharing of eating utensils	0.53 (0.34-0.83)	.006	0.52 (0.32-0.84)	.007
	Pacifier cleaning by parental sucking	0.24 (0.10-0.60)	.002	0.35 (0.13-0.91)	.032
Allergic rhinitis	Sharing of eating utensils	0.72 (0.46-1.14)	.166	0.69 (0.43-1.09)	.110
	Pacifier cleaning by parental sucking	0.33 (0.15-0.73)	.006	0.33 (0.14-0.73)	.007
Asthma	Sharing of eating utensils	0.93 (0.56-1.56)	.786	0.89 (0.52-1.50)	.652
	Pacifier cleaning by parental sucking	0.19 (0.03-1.38)	.100	0.17 (0.02-1.31)	.089

*Allergic symptoms in the last 12 mo (current) before the questionnaire survey.

†During infancy, which was defined as <12 mo from birth.

‡Adjusted for possible confounding factors (mother with a history of allergy, mother smoking during pregnancy, and parents with the knowledge of oral infection).

Nakatani, Kaori Kaji, Tokumi Takahashi, Shintaro Okada, Kazumi Maio, and Takayoshi Sano. We are grateful to Dr Walter C. Willett, Dr Carlos A. Camargo Jr, and Janice A. Espinola.

Clinical implications: Saliva contact via shared eating utensils or parental sucking of pacifiers during infancy may reduce the risk of allergy development, especially eczema and allergic rhinitis, in school-age children.

REFERENCES

1. Renz H, Skevaki C. Early life microbial exposures and allergy risks: opportunities for prevention. *Nat Rev Immunol* 2021;21:177-91.
2. Dierick BJH, van der Molen T, Flokstra-de Blok BMJ, Muraro A, Postma MJ, Kocks JWH, et al. Burden and socioeconomics of asthma, allergic rhinitis, atopic dermatitis and food allergy. *Expert Rev Pharmacoecon Outcomes Res* 2020;20:437-53.
3. Perkin MR, Strachan DP. The hygiene hypothesis for allergy - conception and evolution. *Front Allergy* 2022;3:1051368.
4. Alexandre-Silva GM, Brito-Souza PA, Oliveira ACS, Cerni FA, Zottich U, Pucca MB. The hygiene hypothesis at a glance: early exposures, immune mechanism and novel therapies. *Acta Trop* 2018;188:16-26.
5. Haspeslagh E, Heyndrickx I, Hammad H, Lambrecht BN. The hygiene hypothesis: immunological mechanisms of airway tolerance. *Curr Opin Immunol* 2018;54:102-8.
6. Olsen I, Yamazaki K. Can oral bacteria affect the microbiome of the gut? *J Oral Microbiol* 2019;11:1586422.
7. Verma D, Garg PK, Dubey AK. Insights into the human oral microbiome. *Arch Microbiol* 2018;200:525-40.
8. Lyng Pedersen AM, Belstrøm D. The role of natural salivary defences in maintaining a healthy oral microbiota. *J Dent* 2019;80:S3-12.
9. Dzidic M, Abrahamsson TR, Artacho A, Collado MC, Mira A, Jenmalm MC. Oral microbiota maturation during the first 7 years of life in relation to allergy development. *Allergy* 2018;73:2000-11.
10. Hesselmar B, Sjöberg F, Saalman R, Aberg N, Adlerberth I, Wold AE. Pacifier cleaning practices and risk of allergy development. *Pediatrics* 2013;131:e1829-37.
11. Kubo Y, Yoshizawa K. The negative association of pediatric allergy risk and pre-mastication in infancy: a cross-sectional study [in Japanese]. *J Prevent Med* 2015;10:19-24.
12. Yamamoto-Hanada K, Pak K, Saito-Abe M, Yang L, Sato M, Irahara M, et al. Allergy and immunology in young children of Japan: the JECS cohort. *World Allergy Organ J* 2020;13:100479.
13. Cai Y, Zhao Y, Kang Y, Yang Y. Future prospect of oral microbiota influencing allergy/asthma development. *Front Microbiol* 2022;13:875664.