

RELATIONSHIP BETWEEN TOOTH AND PALATAL RUGA ANOMALIES IN RHESUS MONKEYS PRENATALLY AND LACTATIONALLY EXPOSED TO TCDD

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Abstract

In rodents, variant patterns of palatal rugae are known to be warning signs of developmental toxicity of chemicals. We examined teeth and palatal rugae in rhesus monkeys exposed to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) prenatally and lactationally to analyze relationship between tooth and ruga anomalies. Pregnant rhesus monkeys were given TCDD subcutaneously on day 20 of gestation at an initial dose level of 30 or 300 ng/kg. Controls received the vehicle. For maintenance of a certain body burden, 5% of the initial dose was given to dams every 30 days during pregnancy and lactation until 90 days after delivery. The numbers of observed specimens were 3, 5, and 6 stillborn fetuses and neonatally died offspring, and 13, 13, and 11 surviving offspring in the control, 30 ng/kg, and 300 ng/kg groups, respectively. Tooth anomalies such as precocious eruption, dysplasia, missing, cone-shaped, and maldirected were detected only in the 300 ng/kg group. Various variant patterns of palatal rugae were found in all three groups. General hyperplasia of rugae seemed to be associated with tooth anomalies. Further studies are needed to establish frequencies of variant patterns of palatal rugae in control populations of rhesus monkeys.

Introduction

In rodents, variant patterns of palatal rugae are known to be warning signs of developmental toxicity of chemicals.¹ We reported that prenatal exposure to TCDD affected palatal ruga development in mice.² Developmental dental toxicity of dioxin and related compounds has been well documented,³ and we detected various tooth anomalies in rhesus monkeys prenatally and lactationally exposed to TCDD.⁴ This study aimed at evaluation of abnormal patterns of palatal rugae in non-human primates for detection of developmental toxicants by analyzing relationship between tooth and ruga anomalies.

Materials and Methods

Details of the experimental procedure were previously described.⁴ Briefly, pregnant rhesus monkeys were given TCDD subcutaneously on day 20 of gestation at an initial dose level of 30 or 300 ng/kg. Controls received the vehicle. For maintenance of a certain body burden, 5% of the initial dose was given to dams every 30 days during pregnancy and lactation until 90 days after delivery. At intervals conventional intraoral radiographs were taken using a portable X-ray apparatus. Stillborn fetuses and offspring postnatally died were necropsied and the jaws were observed under a dissecting microscope. Surviving offspring were lightly anesthetized and photographs were taken using an intraoral digital camera. Variant patterns of palatal rugae were classified following previous descriptions in rodents.^{1,5,6} The numbers of observed stillborn fetuses and postnatally died young in the control, 30 ng/kg, and 300 ng/kg groups were 3, 5, and 6, respectively, and those of surviving young were 13, 13, and 11, respectively.

Results and Discussion

The number and types of teeth of the rhesus monkey are similar to those of humans (Figure 1). Palatal rugae are much more distinct in monkeys than humans. An adult rhesus palate usually has 9 pairs of rugae (Figure 1). Tooth anomalies such as precocious eruption, dysplasia, missing, cone-shaped, and maldirected were detected only in the 300 ng/kg group. Various variant patterns of palatal rugae as schematically shown in Figure 2 were found in all the control and TCDD treated groups. Only the hyperplasia of rostrally located rugae was frequently observed in the 300 ng/kg, especially in stillborns and early postnatal deaths (Figures 3 and 4). Types of tooth anomalies and presence or absence of ruga hyperplasia in the 300 ng/kg group are tabulated in Table 1 for stillbirths and early postnatal deaths, and in Table 2 for surviving offspring.

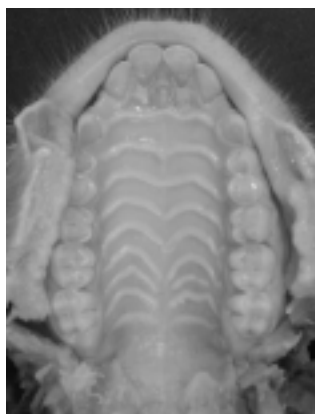


Figure 1. Teeth and palatal rugae in an untreated adult rhesus monkey

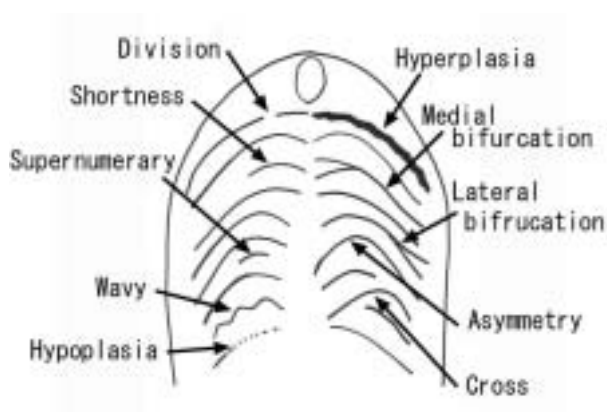
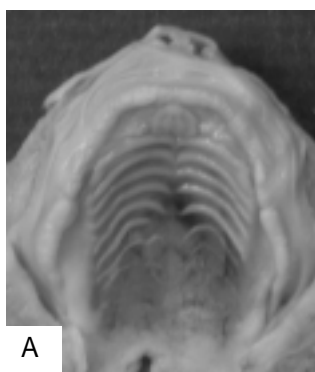


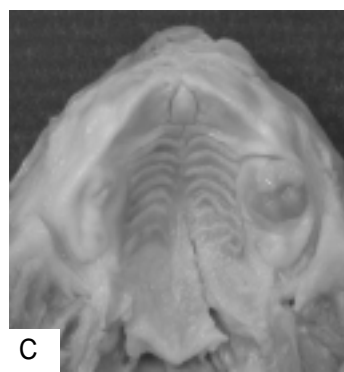
Figure 2. Schematic line drawing of variant patterns of rugae



A

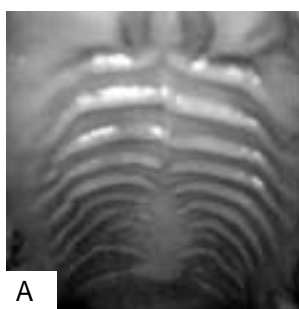


B

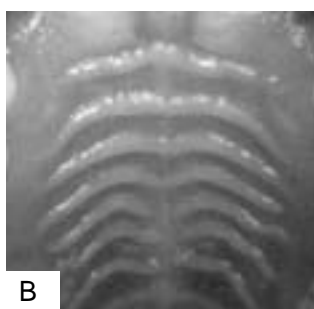


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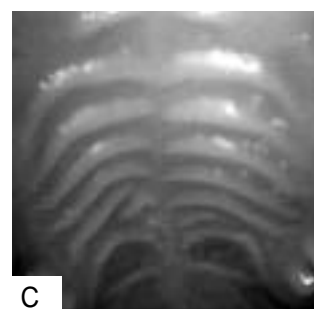
Figure 3 Palatal rugae in stillborn offspring A: No. 10, control; caudal rugae are still not fully developed. B: No. 37, 300 ng/kg; teeth are precociously erupted and rugae are hyperplastic and rugged. C: No. 43, 300 ng/kg; rugae are slightly hyperplastic and rugged with asymmetric patterns.



A



B



C

Figure 4 Palatal rugae in surviving offspring A: No. 2, control; some variant patterns are noted in the caudal rugae. B: No. 31, 300 ng/kg; rugae 2-6 seem slightly hyperplastic and edematous; rugae 7 are bilaterally short and hypoplastic. C: No. 66, 300 ng/kg; rugae 1-5 are hyperplastic; right ruga 5 is divided; rugae 7 are bilaterally short and hypoplastic.

Table 1 Tooth anomalies and palatal ruga hyperplasia in stillbirths and early postnatal deaths in the 300 ng/kg group

| Offspring No. | Tooth anomalies | Ruga hyperplasia |
|---------------|---|------------------|
| 34 | - | - |
| 37 | <u>A</u> <u>AD</u> <u>A</u> <u>A</u> precocious eruption, dysplasia, <u>B</u> missing | + |
| 40 | <u>D</u> precocious eruption, incomplete calcification, <u>A</u> <u>A</u> missing | + |
| 43 | - | - |
| 57 | <u>BA</u> <u>ABD</u> <u>A</u> <u>A</u> precocious eruption, incomplete calcification | + |
| 103 | - | + |

-: Not detected +: Detected

Table 2 Tooth anomalies and palatal ruga hyperplasia in surviving offspring in the 300 ng/kg group

| Offspring No. | Tooth anomalies | Ruga hyperplasia |
|---------------|---|------------------|
| 31 | <u>542</u> <u>24</u> missing, <u>5</u> cone-shaped, <u>5</u> maldirected | + |
| 33 | - | - |
| 35 | - | - |
| 39 | <u>542</u> <u>245</u> missing | - |
| 42 | <u>5</u> <u>5</u> missing, <u>4</u> cone-shaped | - |
| 44 | <u>54</u> <u>45</u> maldirected | - |
| 60 | <u>542</u> <u>245</u> , <u>5</u> <u>5</u> missing | - |
| 66 | <u>52</u> <u>2</u> , <u>1</u> <u>1</u> missing, <u>45</u> cone-shaped, maldirected, <u>54</u> <u>45</u> maldirected | + |
| 102 | - | - |
| 106 | <u>A</u> <u>A</u> , <u>4</u> <u>24</u> missing | - |
| 109 | - | - |

-: Not detected +: Detected

These results indicate that variant palatal ruga patterns are frequent even in controls, and that it is difficult to separate variants in the normal range and really abnormal patterns. However, hyperplastic rugae seem to indicate abnormal development of oral structures including teeth. To establish the range of "normal" variant patterns, we are examining a large number of adult palates.

Acknowledgments

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