Invagination of Human Palatal Epithelium Prior to Contact

M. MATO, M.D., Ph.D.
E. AIKAWA, M.D.
G. R. SMILEY, D.D.S., M.Sc.
Chapel Hill, North Carolina 27514

Bergengrün (*2*) and Peter (*9*) were among the first investigators to examine the midline palatal epithelium and to draw attention to the persistence of epithelial remnants after its breakdown. A recent theory of cleft palate formation implicated the occurrence of epithelial pearls or epithelial remnants in the palatal shelves of human abortuses with cleft palates (*4*). Epithelial pearls were thought to indicate the original site of fusion of the two palatal shelves, and it was presumed from this evidence that most cleft palates in man resulted from post-fusion rupture. This theory was perpetuated by Kraus (*5*) on the basis of similar evidence. He proposed that viral infections or anti-organ antibody reactions could cause degeneration of palatal tissue, and combined with the rapid increase in breadth of the face, rupture of the palate would result.

Most of the histological investigations on palatal development have been concerned primarily with the breakdown of the midline palatal epithelium. Recently, Mato, Aikawa and Katahira (*7*) and Mato, Smiley and Dixon (*8*) discussed epithelial changes in the presumptive regions of nasal and palatal fusion of human fetuses at the light and electron microscope levels. Their results emphasized that the cellular changes which were observed, including epithelial cell degeneration and disarrangement, appeared prior to contact of palatal processes and nasal septum. The present investigation presents new findings on the possible method of formation of epithelial pearls in the presumptive areas of palatal fusion in human fetuses.

Materials and Methods

Human fetuses from therapeutic abortions, of approximately 9 weeks menstrual age, were fixed in 10% formalin solution for two days. The

Dr. M. Mato is a Visiting Associate Professor in the Dental Research Center collaborating with Dr. G. R. Smiley. He is from the University of Gunma, School of Medicine, at Maebashi, Japan.
Dr. E. Aikawa is affiliated with Tsurumi Women's University, School of Dentistry, Tsurumi, Japan
Dr. G. R. Smiley is affiliated with the Dental Research Center, School of Dentistry, University of North Carolina, Chapel Hill, North Carolina.
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specimens were decapitated and the heads were post-fixed with Helly's solution for three days, dehydrated, paraffin embedded, sectioned in the coronal plane at 4 microns and stained with Mallory's trichrome technique. Fetal heads with palatal processes in a horizontal position but not in contact with each other were selected for observation.

Results

The epithelium of the oral and nasal surfaces of the palatal processes consisted of cuboidal, regularly arranged cells, from 2–4 cells thick, and clearly lined with a basement membrane (Figure 1). The epithelium was compact, while the mesenchymal tissues were loosely arranged. In all specimens studied, the medial edges were covered with epithelial cells in varied degrees of disorganization (Figures 1–3). Extreme disarray of epithelial cells along the medial edge in some specimens resulted in marked invaginations of epithelium into the mesenchyme, with a concentration of mesenchymal cells in close association with the epithelial invaginations. Careful observation of the regions showed such alterations were limited to that part of the palatal process destined to make contact and ultimately fuse. The invaginated epithelium always consisted of hypertrophied and disarranged epithelial cells and frequently occurred in a mirror-image fashion on the opposing processes.

At a higher magnification, the cuboidal cell layer was obscure, due to the epithelial disorganization, and flattened, irregularly arranged epithelial cells piled up in these areas (Figures 2 and 3). Similar epithelial changes were also observed in the inferior edge of the nasal septum (Figure 1). The basal lamina of the palatal processes was continuous from the oral and nasal surfaces onto the medial edge and surrounded the epithelial invaginations into the mesenchyme. At this early stage the invaginations became rounded and appeared to separate from the epithelium covering the medial edge (Figures 2 and 3). There was no evidence of keratin formation at the light microscope level at this stage of development.

Discussion

Epithelial pearls in humans are normally found in the midline of the secondary palate after mesenchymal fusion. Most of these pearls develop from epithelial remnants that remain after degeneration of the midline epithelial seam. Scott (*10*) suggested that the epithelial pearls in the midline of the palate could undergo proliferation to form cysts. He believed that in certain circumstances these cysts may be related to the developmental processes concerned with the etiology of clefts of the palate. According to Wood and Kraus (*13*), epithelial pearls are selectively located in the human secondary palate, as they were observed only in the hard palate and not in the soft palate in that particular study. Since Burdi and Faist (*3*) found epithelial remnants only in the hard palate of human fetuses they concluded that the hard palate had formed by fusion

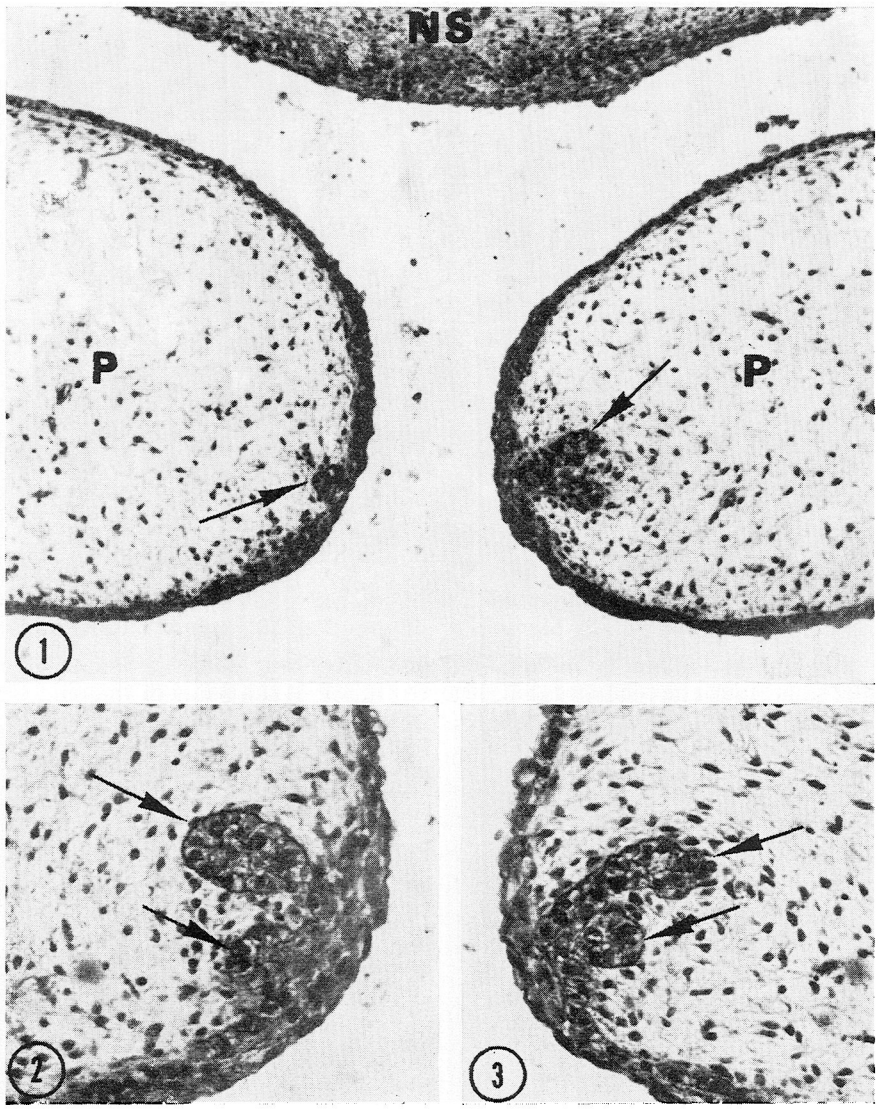

FIGURE 1. Coronal section of the palatal processes (P) and nasal septum (NS) of a human embryo. The epithelium is thickened and disarranged on the medial edges of the palatal processes and the inferior border of the nasal septum. Epithelial invaginations are observed (arrows). Mallory's trichrome stain. × 135.

FIGURE 2. Rounded, cyst-like epithelial invagination surrounded by a basal lamina that is continuous with that of the epithelium (arrows). The epithelium appears thickened due to accumulation of superficial flattened cells. Mallory's trichrome stain. × 245.

FIGURE 3. Cuboidal epithelial cell layer is deeply invaginated into the mesenchyme to form two epithelial cyst-like structures (arrows). Mesenchymal cells are concentrated close to these structures. Mallory's trichrome technique. × 245.

and the soft palate by merging. However, Scott (*10*) showed a group of cysts developing in the anterior part of the soft palate and Kraus, Kitamura and Latham showed (*6*) a pearl in the soft palate of a cleft palate fetus. Also in two 8-week old normal specimens, there appeared to be epithelial lamination of the midline in the soft palate region (*6*). Even though epithelial remnants are not frequently observed in the secondary palate of the rodent, an epithelial seam in the soft palate has been observed, denoting fusion of the soft palate (*11*).

Angelici (*1*) stated that post-fusion reopening had occurred at epithelial interfaces between the lateral palatal processes and median nasal processes in two A/Jax mouse specimens. This post-fusion reopening is significantly different from the theory proposed by Kitamura (*4*) and Kraus (*5*), since in the A/Jax mice there was abnormal persistence of the epithelial wall and mesenchymal fusion did not occur.

The phenomenon of epithelial degeneration and disorganization in the medial edge of palatal processes is similar to that of epithelial changes found in the inferior border of the nasal septum of human fetuses (*8*). Although the changes observed in the previous study indicate that the epithelium of the medial edge varies in the degree of alteration according to the animal species and location, the human fetuses in this study showed more marked epithelial changes than those found in rodents. Even though the same epithelial changes that occurred in the medial edge of the palatal processes occurred in the cells of the inferior border of the nasal septum, epithelial pearls were infrequently observed along the nasal septal border, and the epithelium in this area degenerated more rapidly during its fusion to the palate. Studies of single palatal processes in organ culture have shown that the epithelium of the medial edge underwent complete breakdown without contacting the epithelium from the adjacent palatal process (*12*). Thus, a midline epithelial seam is apparently not necessary for breakdown that would lead to the persistence of epithelial remnants. This experiment also suggested the possibility of migration of epithelial cells into the mesenchyme. It is interesting to note that Kraus, Kitamura and Latham (6) showed what was probably an epithelial remnant in the mesenchyme of the palatal processes prior to its contact in the posterior region. In many of their other 47-day normal specimens, epithelial disorganization was evident on the medial edge of the palatal processes prior to contact; this is similar to appearances seen in this study.

In fetal material, where palatal processes were horizontal but had not made contact throughout their length, over 30% of the material examined showed severe epithelial irregularities (invaginations) along the medial edge of epithelium and all showed some degree of disorganization. Although the epithelial invaginations into the mesenchyme are very similar to those that form the dental lamina during tooth formation or mucous glands in the palate, it is very unlikely that these are dental or glandular primordia. Judging from the menstrual ages of the fetuses, the fact that

the surface of the medial edge was smooth and not torn, the number of cell layers, and the continuity of the basement membrane, it was assumed that these epithelial invaginations were formed from the palatal epithelium prior to contact.

Evidence for a different method of the formation of epithelial pearls in the midline of the palate is presented, since it has been shown previously that the formation of epithelial rests can begin prior to contact of the palatal processes. Therefore, at least in human fetuses, epithelial pearls are not always derived from the degeneration of the epithelial seam between the palatal processes. With this evidence, the theory of post-fusion rupture can be challenged and deserves re-examination.

Summary

Specific epithelial changes along the medial edge of human palatal processes in the presumptive regions of fusion were demonstrated. The histology of the area immediately before fusion showed consistent epithelial disarrangement and marked epithelial invaginations into the palatal mesenchyme. The invaginated epithelium appeared to become isolated into epithelial remnants before palatal contact occurred. Although epithelial pearls are derived in large part from remnants of the breakdown of the midline epithelial seam between fused palatal processes, the results of the present study indicate another possible method of epithelial pearl formation prior to contact of human palatal processes.

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reprints: *Dr. Gary R. Smiley*
Dental Research Center
School of Dentistry
University of North Carolina
Chapel Hill, North Carolina 27514

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