

Partial Fusion Between Upper and Lower Lips in the Rat: A Report of a Case

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Congenital abnormalities of the lips and circumoral structures are comparatively common in humans. The most frequent abnormalities are unilateral, bilateral, and median clefts of the upper lip and micro- and macrostomia. These defects are the result of abnormal fusion between the medial and lateral nasal, maxillary, and mandibular processes which contribute to the formation of this area of the face (7). Other malformations are labial pits in the lower lip which are from persistence of some or all of the lateral and medial sulci in the mandibular process (13) and double lip which occurs almost always in the upper lip (11). These lip and circumoral defects may occur alone, in association with other facial abnormalities, or with generalized defects of the body (3).

Most of these abnormalities occur spontaneously or can be induced in experimental animals. This has been of great benefit in determining the etiology and site of lip abnormalities in the developing embryo. However, care must be taken in extrapolating findings from animal to humans in the facial region, for, though the developmental processes are similar, they are not the same. In particular, the median structures of the upper lip are distinctly different between humans, which have a philtrum, and experimental animals such as the macaque monkey, rat, and mouse, in which the philtrum is absent (6).

Fusion of the upper lip to the lower lip is very rare. Review of the literature revealed no previously reported cases in either humans or experimental animals. This paper is a report of an isolated case of paramedial fusion between the lips in a Sprague-Dawley rat embryo which had been subjected to amniotic puncture at in utero age of fifteen days sixteen hours. The abnormality is described and possible etiologies discussed.

Amniotic puncture operations were performed using a previously de-

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scribed technique on pregnant Sprague-Dawley rats at 15 days 16 hours of pregnancy (12). This procedure produces a number of congenital deformities including cleft palate, micrognathia and malformed extremities. Characteristically, but not always, the embryos simulate a Pierre-Robin syndrome. On subsequent days after operation the pregnant rats were sacrificed and the cleft palatal shelves used in *in vitro* fusion experiments. This particular litter was sacrificed at in utero age 20 days 16 hours. To obtain the palatal shelves the head of the embryo is severed from the body. When this procedure was performed the mouth usually opened, though it was noted that in one embryo the mouth did not open. Closer inspection revealed a fine band of tissue passing from the left paramedial eminence of the upper lip to the lower lip. The band was triangular in shape with the apex attached to the upper lip and the base from the lower lip being about two millimeters wide. It was not connected posteriorly to the tongue or alveolus. Following fixation for 48 hours in 10% Peters Buffered Formalin a 40 silk suture was passed behind the band (Figure 1).

No other deformities of the face were noted and specifically the embryo did not have the characteristic Pierre-Robin facies, though on subsequent sectioning it was found that the hard palate was cleft. The body was large and stocky but still within the range of normal size for rats of this age. The only gross malformation of the body was the hind limbs which were underdeveloped; they were short with the toes still webbed together (Figure 2).

The head was embedded in paraffin, sectioned in the sagittal plane, and stained with haematoxylin and eosin (Figure 3). The band passing between the two lips was entirely epithelial, being composed of a keratinized stratified squamous epithelium continuous with that of the skin of the embryo. The inner aspect of the band appeared to have been separated from the mesenchyme of the upper lip as this surface was denuded of epithelium. The inner aspect of the band spanning the gap between the lips was not keratinized. The base of the band attached to the lower lip was broad but rapidly tapered to a thin band only 5-6 cells thick. Unfortunately the upper attachment of the band had been ruptured by removal of the silk suture used to demonstrate the band.

The malformation is of interest in that it is very rare and does not follow the expected pattern of developmental anomalies in this region. It has not been reported in previous amniotic puncture studies (2, 8, 12), nor has it been noted in the extensive embryological experiments performed at this laboratory. The etiology of the malformation is obscure, as it could have arisen at two distinct stages in embryological development; first, at the time of lip formation, or, second, it could have been a result of the amniotic puncture procedure.

In normal lip development in the rat, the mouth is open until the 13th day. The upper and lower lips are in contact on the 14th day but open



FIGURE 1. 4.0 silk suture behind band. Triangular shaped band passes from mandible to left paramedial eminence.

again on the 15th day, with the tongue protruding between the lips (1). Hence the band could have been formed on the 14th day. But this does not answer the essential question of how the fusion occurred.

The left paramedial band could have been formed by excessive fusion of the left maxillary and mandibular processes resulting in a unilateral microstomia; subsequently the lateral part could have broken down leaving a paramedial band. However, the lateral parts of the mouth opening appeared grossly and histologically normal. Fibrous bands, Simonart's bands in humans, do occur between the facial processes which normally fuse together. These are explained on the basis that the processes did initially fuse but were subsequently separated with only a small amount of tissue remaining between them. However, the maxillary process and mandibular process do not normally fuse at any stage during facial development. Other abnormal fusions between

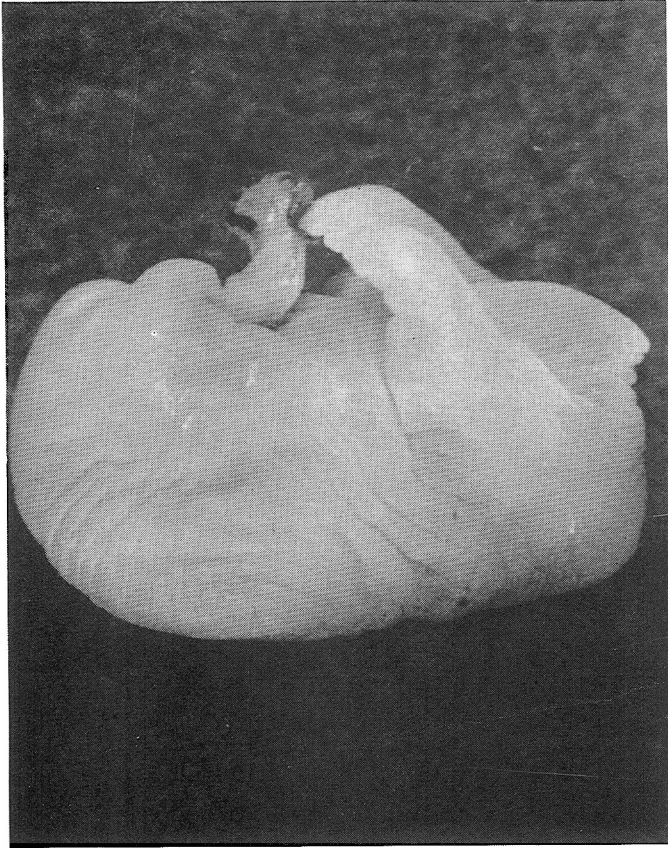


FIGURE 2. Body, upper limbs normal, lower limbs stunted.

processes not normally fused have been reported in humans as occurring between the buccal portions of mandibular and maxillary alveolar processes (9), between the tongue and palate (10), and between the palate and floor of the mouth (5).

Alternatively, the band could have been formed subsequent to normal lip formation at the time of the amniotic puncture procedure. The congenital malformations induced by this procedure are said to be caused by compression of the embryo by the amniotic membrane following the partial loss of amniotic fluid. In particular, the normal extension of the cervical spine is prevented or greatly delayed. The chin is compressed against the sternum and the mandible against the maxilla. This results in micrognathia and cleft palate by mechanical obstruction from the tongue (12). Movements of the embryo in amnion are also markedly reduced. Thus, the upper and lower lips could be compressed together with only minimal movement between them. It has been found in a previous *in vitro* study (4) that, under conditions of close and



FIGURE 3. Photomicrograph. Sagittal section stained with haematoxylin and eosin. Band arising from mandible. Mag. $\times 40$.

immobile contact, fusion will occur between differing oral structures such as palatal shelf to tongue. Hence the lip fusion could have occurred in a similar manner as the shelves were in close contact and the movement of the embryo restricted.

As the band is entirely epithelial and without a nutrient supply, it would presumably shortly break down, leaving only minimal evidence of its presence.

Summary

Fusion of the upper to the lower lip is rare in experimental animals and humans. This is a report of a case of paramedial fusion between the lips in a Sprague-Dawley rat embryo which had been subjected to amniotic puncture at in utero age of fifteen days sixteen hours. This abnormal fusion is of interest as it does not follow the usual pattern of developmental anomalies in the perioral region. Its possible etiology at

either the time of lip formation or as a sequela of the amniotic puncture is discussed.

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