

PAPAIN IN THE TREATMENT OF BILATERAL CLEFT PALATES

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THE incidence of clefts of the lip and palate in South Africa is not known, but investigations in other countries point to an increase in the frequency. Reports dating back to the early part of this century gave figures of approximately one in 1,700 live births with this deformity, whereas recent studies show a ratio of about one in 700 births (Fogh-Anderson, 1942). Half of these affected individuals have a complete cleft lip and palate.

In spite of the characteristic displacement of the palatal shelves, alveolar ridges, lip segments and nostrils in patients with complete cleft lip and palate, it is possible to get good, and in many cases excellent results, using existing methods of treatment. Where the results have not been satisfactory the main problem has been the relationship between premaxilla, nose tip and lateral segments of the maxilla in the antero-posterior dimension. This is usually combined with a downward rotation of the premaxilla.

Embryologically the lack of union occurs between the sixth and 12th week *in utero* for complete bilateral clefts of the lip and palate, at which time the premaxilla is located between the anterior ends of the maxillary lateral segments. Because of its attachment to the rapidly growing vomer and nasal septum the premaxilla is carried forward into a position which, at birth, is often beyond the tip of the nose. If untreated, this unrestrained growth may continue postnatally.

The repair of the lip of a bilateral cleft tends to bring the premaxilla into a better relationship with the lateral maxillary segments. This is possibly due to some degree of premaxillary repositioning as a result of buckling of the nasal septum and vomer, and to the growth of the lateral segments enabling them partly to catch up, as it were, with the premaxilla.

In addition to the repair of the lip, other procedures have been suggested to

improve the end result. The prominent premaxilla may be moved posteriorly by extra-oral strapping. Ideally, this treatment should be started as shortly after birth as possible (Graf-Pinthus 1964). Apart from this strapping, an appliance to control the position of the lateral segments and to aid feeding may be worn.

Such early treatment may give a closer to normal upper arch form, a more satisfactory profile, and aid in the surgical repair (Dreyer and Gavron 1962). Despite this treatment the results obtained in many bilateral clefts still leave a lot to be desired, particularly in the horizontal and vertical position of the premaxilla.

Lip repair or early orthodontic (orthopaedic) treatment seems to produce similar effects:

First, a bulging of the nasal septum in a vertical plane may occur. It takes the form of an S-shaped distortion of the septum which appears to be more evident after a two-stage lip repair. Such septal distortion may contribute to the partial nasal obstruction present in many of our treated patients.

Secondly, there usually is a downward rotation of the premaxilla. This adds to the undesirable relationship of the premaxilla to the lateral maxillary segments which is already present in the vertical plane.

Thirdly, the improvement of the relationship between the tip of the nose, columella and the upper lip is minimal.

Our clinical observations indicate that these effects commonly occur in combination; and that they may be due to a resistance to change of the tissues in the area between the tip of the nose and the pre-vomerine suture.

These observations also imply that the distortion in the septal cartilage adjacent to the tip of the nose and premaxilla cannot be adequately controlled by means of early orthodontic treatment or lip repair. It therefore is necessary to seek other or additional methods of treatment. In his early work Thomas (1956) pro-

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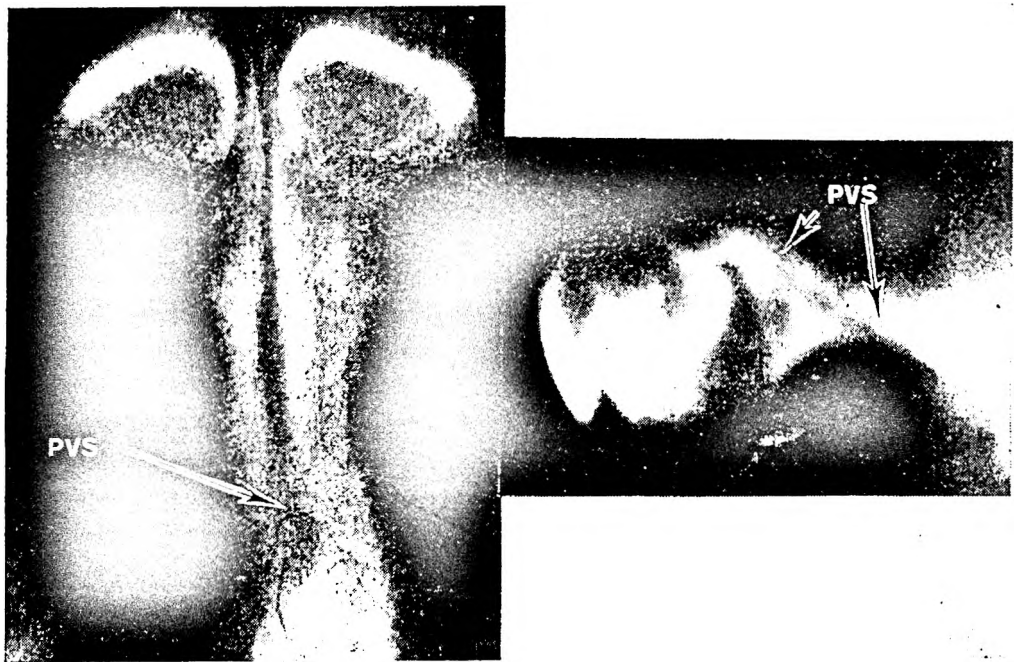


FIG. I. Occlusal and lateral X-ray views of the premaxilla and vomer of a patient showing the prevomerine suture (P.V.S.)

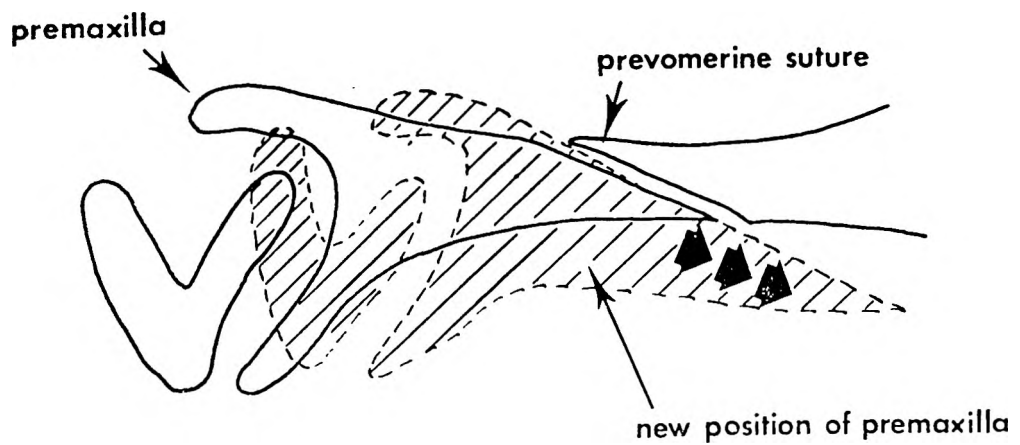


FIG. II. Diagrammatic representation of the premaxilla and vomer showing the desired repositioning of the premaxilla.



FIG. III. Patient E.S. prior to treatment.



FIG. IV. Patient E.S. one day after papain and pressure therapy.

posed that certain enzymes be used for this purpose. He found that the parenteral administration of a plant enzyme, papain, causes a reversible softening of the cartilage of rabbits without any other apparent adverse effect.

Dreyer and Cleaton-Jones (1969) reported similar findings in their work on rabbits and rats. Further, their study on the local effects of papain indicated that the softening of cartilage, after local injection, starts within a few hours and reaches its maximum effect within 24 hours; and that thereafter the affected cartilage rapidly returns to normal. They suggested that inactivated crystalline papain be used in the early treatment of bilateral cleft palates if the resistance of the vomer can be overcome. From the X-rays of the pre-vomerine suture in infants with bilateral cleft palates, it appeared that the suture might allow movement between its components (Fig. 1). If this movement could be induced by manipulation or mechanical pressure while the cartilage above it was softened by papain, the desired repositioning of the premaxilla could be obtained within days (Fig. II).

MATERIALS AND METHODS

A two per cent solution of crystalline papain (British Drug Houses) was prepared using a phosphate buffer of pH 7.0*. This was sterilized by tyndallisation as was a 0.01M iodoacetamide solution.

Immediately prior to use equal quantities of the papain and iodoacetamide solutions were mixed to form a one per cent solution of inactivated papain, which was then incubated for 30 minutes at 37°C. This solution to a total dosage of 1.0 mgm was introduced into the sub-mucosa of the nasal septum on both sides, radiating from the prevomerine suture area while the patients were under general anaesthesia.

CASE REPORTS

1. E.S. was born with a bilateral cleft lip and palate (Fig. III). On the 25th day

*(24 ml solution containing 2.388 gm Na HPO₄ per 100 ml was added to 16 ml of a solution containing 0.907 gm KH₂PO₄ per 100 ml).

post partum the inactivated papain solution was introduced submucosally as already described. Immediately after the injection pressure was applied to the premaxilla using a wad of gauze strapped in position under tension by means of elasticsized adhesive plaster. This pressure was intended to remain active during the entire period that the physical properties of the cartilage were altered. Unfortunately after some 6 - 8 hours of pressure the pad became dislodged and was replaced only some 12 hours later. The degree of posterior movement of the premaxilla obtained is shown in Fig. IV. No mucosal ulceration or any other obvious pathological change was observed at the injection sites. The postoperative recovery was uneventful.

2. H.V.T. was born with a complete bilateral cleft palate and an incomplete bilateral cleft lip (Fig. V). On the 10th day the inactivated papain solution was introduced alongside the nasal septum. The prevomerine suture was manipulated in order to slide its anterior part below the posterior section (Fig. II). As this was unsuccessful, the area was exposed surgically (Fig. VI) and a segment of bone

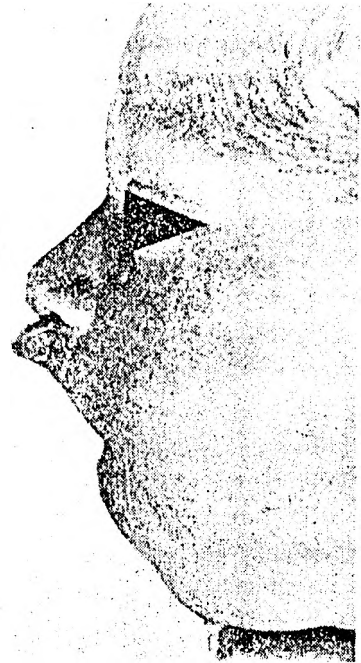


FIG. V. Patient H.V.T. prior to treatment.



FIG. VI. Patient H.V.T. showing the exposed prevomerine suture area.

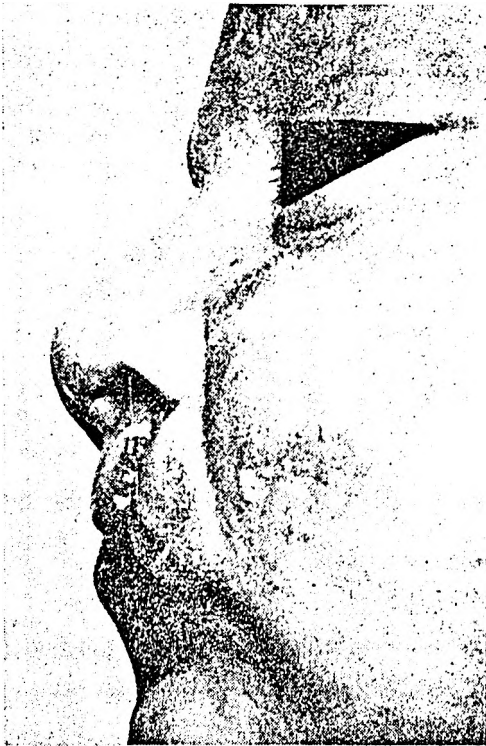


FIG. VII. Patient H.V.T. seven days after papain and pressure therapy but prior to repair of the lip.



FIG. VIII. Patient H.V.T. fifteen months after the initial papain and pressure therapy and subsequent surgical repair of lip.

posterior to the vomerine suture excised. The wound was closed and sutured and a pressure pad was applied to the premaxilla as in Case 1. Pressure was continued for the crucial first 24 hours post-operatively and thereafter the strapping was used to maintain the position until the lip was repaired surgically 14 days later.

The results obtained are shown in Figs. VII and VIII. As in Case 1, no side effects were noted. In fact this baby took its full bottle feed three hours postoperatively.

DISCUSSION

CASE 1. E.S.

The structure of the prevomerine suture as seen in Fig. 1 suggested that the suture would allow a sliding of the component bones over each other (Fig. II). After the papain injection had been given, manipulation of the premaxilla indicated that the suture offered a greater amount of resistance than was anticipated; and this resistance was maintained in spite of the force exerted by the pressure pad during the period of action of the papain. This is indicated by the minimal repositioning that resulted (Fig. IV).

Although maintained pressure on the premaxilla is important for repositioning, and there was dislodgement of the pressure pad, the deciding factor in the amount of repositioning achieved in this patient probably was the resistance of the suture.

Therefore the total amount of repositioning of the premaxilla in the first 24 hours could not be attributed to cartilage softening. There was a similar degree of repositioning in previous work by applying pressure without the use of papain. While the results obtained in this patient were not those hoped for, a number of important points emerged:

First, the absence of any obvious local or systematic side-effects due to the injected papain indicated that it could be safely employed in this age-group.

Secondly, it was realised that if papain was again to be used for any rapid controlled movement of the premaxilla, the

resistance of the prevomerine suture had still to be overcome,

Finally, the dislodgement of the pressure pad underlined the need for adequate supervision by nursing staff during the first 24 hours when the nasal septum cartilage is softened.

CASE 2. H.V.T.

After the papain solution had been injected manipulation of the prevomerine suture was attempted. As this again proved impossible, the alternative plan was used.

The surgical exposure of the region showed that the structure of the suture at this age already was more complex than the X-rays disclosed.

In view of this a segment of bone equivalent to the desired amount of repositioning was excised posterior to the suture. Now that the splinting action of the vomer had been removed, some manual repositioning was possible. The pressure pad then applied to the premaxilla was so constructed that the forces exerted could produce in it a posterior bodily displacement.

The nature of the movement obtained resulted in a good profile with minimal downward rotation (Fig. VII). The satisfactory appearance of the patient fifteen months after the initial papain and pressure therapy and subsequent surgical repair of the lip is shown in Fig. VIII.

The pleasing profile, the lack of downward rotation and the apparent absence of bulging of the nasal septum point to this as a possible additional method for the treatment of selected bilateral cleft palates.

SUMMARY

In many cases of cleft lip and palate good results may be obtained with existing methods of treatment. In some cases, however, the end result is unsatisfactory.

A new method of treatment is described for bilateral cleft palates: the injection of a proteolytic enzyme, papain, into the nasal septum. This softens its cartilage which, combined with pressure and surgery, allows easier repositioning and a better premaxillary relationship with the adjacent structures.

The rationale of the method and the results obtained in two human patients are described.

ACKNOWLEDGMENTS

The authors are grateful to Professor D. Walker and Mr. P. Hugo for making their patients available for this study and for their help and co-operation.

All surgical procedures in patient H.V.T. were performed by Professor D. Walker, head of the department of plastic and reconstructive surgery, University of the Witwatersrand.

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