of topical framycetin in the form of a spray. This investigation was based on the use of superficial nasal swabs, as these had been demonstrated to be as accurate as deep swabs in the detection of staphylococcal carriers. Certain advantages in the use of superficial nasal swabs in assessing the effectiveness of topical antibiotics are discussed.

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CROCODILE TEARS

BY

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With the doubtful exception of the elephant, man is the only animal capable of weeping in sorrow (Darwin, 1894). Legend, however, has credited the crocodile with shedding hypocritical tears before it devours its victims.

The term "crocodile tears" (Krokodils-tränen) was aptly chosen by Bogorad (1928) to describe the unusual phenomenon of profuse lacrimation occurring only when food is eaten. This bizarre symptom is a well-recognized, if unusual, sequel of facial palsy. Despite much speculation its mechanism has remained obscure and its treatment unsatisfactory. The recent discovery of collateral sprouting of autonomic nerve fibres (Murray and Thompson, 1957) has provided the basis for these observations. It is hoped they serve both to explain the mechanism of crocodile tears and to point to simple and successful treatment.

The phenomenon of crocodile tears has generally followed facial paralysis, either of Bell's type or the result of herpes zoster, head injury, or intracranial operative trauma (Ford, 1933). It is generally held to be rare, and most authors have been able to cite only two or three cases. Tumarkin (1936a, 1936b), however, found that it occurred in 13 out of 18 cases of Bell's palsy failing to recover: an incidence of some 14% of all cases of Bell's palsy in his series.

The condition must be differentiated from the simple epiphora typically associated with Bell's palsy. This is due to laxity of the lower eyelid hampering normal mechanical drainage. It disappears as recovery of the orbicularis oculi secures normal apposition of the lacrimal punctum to the eyeball, unless the lacrimal ducts have meanwhile become clogged with epithelial debris. Such epiphora is not associated with hyperlacrimation and is unaffected by eating or gustatory stimuli of any kind. It is, however, enhanced by such irritants as exposure to wind or cold or bright light.

Lesions of the facial nerve at or proximal to the geniculate ganglion do not produce this epiphora, as involvement of the lacrimal secreto-motor fibres induce a dry eye. Crocodile tears, if they develop at all, do so after an interval of six months or more from onset of the facial paralysis. As Tumarkin emphasized, they point to earlier involvement of the geniculate ganglion.

The essential gustatory stimulus is the chewing of hot or spiced foods, although apples or chocolates are particularly provocative. When severe, the affected eye

waters profusely at every meal. Secondary blepharitis may ensue. Tears running uncontrollably down the cheek occasion much embarrassment, particularly in restaurants, etc., and most patients are thereby forced to forgo dining out to avoid unwelcome comment.

Usually they are accompanied by some facial asymmetry, the result of earlier facial palsy, the incomplete recovery of which is marked by some facial contracture and synkinesia. The facial muscles may, however, show a remarkable recovery and the face appear normal in repose or on voluntary or emotional movement (Gottesfeld and Leavitt, 1942; and present series).

Rarely, crocodile tears have occurred without antecedent facial paralysis. They have been described following a syphilitic lesion of the geniculate ganglion (Singer and Kellner, 1930) and after section of the greater superficial petrosal nerve for headaches (Boyer and Gardner, 1949).

The obvious analogies this syndrome presents with the auriculo-temporal syndrome described by Frey (1923), whereby eating is associated with flushing and sweating about the parotid area, has been noted by many. A similar explanation, with successful therapy, has been offered elsewhere (Golding-Wood, 1963).

Anatomical Considerations

The Lacrimal Pathway.—Both lacrimal and nasal secreto-motor fibres arise in the superior salivatory nucleus, part of the general visceral efferent column of the mid-brain, and emerge in the nervus intermedius at the lower border of the pons. Thereafter they run with the facial nerve to the geniculate ganglion. Here the fibres emerge as the greater superficial petrosal. This runs through a short canal in the petrous temporal, here receiving a twig from the tympanic plexus, thence forward under the dura towards the foramen lacerum, uniting with the deep petrosal (sympathetic) fibres from the internal carotid plexus (Fig. 1). These conjoined parasympathetic and sympathetic fibres form the vidian nerve. This runs forward through the pterygoid canal to enter the pterygopalatine fossa and joins the sphenopalatine ganglion where the parasympathetic fibres relay. The post-ganglionic lacrimal fibres join the adjacent maxillary nerve and enter the orbit with its zygomatic branch, reaching the gland through the zygomatic-

temporal offshoot or through a communicating twig to the lacrimal nerve.

The Salivary Pathways.—These are variously derived from the nervus intermedius or from the glossopharyngeal nerve. The former continue in the facial

FIG. 1.—Lacrimal and salivary secretomotor pathways.

nerve, then in the chorda tympani, which runs across the middle-ear cleft behind the drum and leaves the temporal bone to join the lingual nerve; after relay in the submandibular ganglion they join the submandibular salivary gland. Secretomotor fibres for the parotid leave the skull with the glossopharyngeal nerve, but just beyond the jugular foramen they enter the temporal bone in its tympanic branch (Jacobson's nerve). This courses over the inner tympanic wall, giving minor branches. The salivary fibres pass on to form the lesser superficial petrosal nerve and thus to the otic ganglion just below the foramen ovale (Fig. 2). Here they relay

FIG. 2.—The tympanic plexus and its connexions.

before being distributed to the parotid gland with sensory fibres of the auriculo-temporal nerve. It is important to note that at the skull base just antero-superior to the tympanic cavity the lesser and greater superficial petrosal nerves run for a short distance in close proximity. Here the lesser gives a communicating twig to the greater.

Collateral Nerve Sprouting.—It is now established that the process of nerve degeneration stimulates adjacent healthy nerve fibres to produce small collateral sprouts that grow into the tubes of degenerating fibres. Originally demonstrated in denervated skin (Weddell *et al.*, 1941), this sprouting has since been shown in motor fibres (Edds, 1953), in autonomic nerves (Murray and Thompson, 1957), and in the central nervous system (Liu and Chambers, 1958). In contrast to its limited effectiveness elsewhere, within the autonomic system this collateral sprouting is enormously efficient. Here sprouting is not merely intraneural; sprouts excited from adjacent nerves may also serve to make functional connexions (Murray, 1959). Vagal re-innervation of

denervated superior cervical ganglion has been demonstrated in the cat (Murray and Thompson, 1957). Similar events have been held responsible for bizarre sweating after sympathectomy in man (Herxheimer, 1958). Murray and Thompson's experimental observations have been confirmed by Guth and Bernstein (1961). It is reasonable to conclude that whenever an autonomic nerve degenerates, whether from injury or disease, any closely adjacent normal autonomic fibres will give out sprouts which can connect up with appropriate cholinergic or adrenergic endings (Fig. 3). This may

FIG. 3.—The reflex arc of crocodile tears.

result in useful function or quite bizarre phenomena. Crocodile tears appear to be an instance of this, as shown by the clinical observations here recorded.

Case 1

A girl aged 13, with severe and intractable perennial vasomotor rhinitis, was subjected to greater superficial petrosal neurectomy in May, 1956. Operation on the right side was conducted by an extradural approach through the middle cranial fossa. Petrosal neurectomy gave immediate and dramatically successful relief of incapacitating nasal symptoms (sneezing and persistent rhinorrhoea) that has endured. The nasal aspects of this case and of others were reported elsewhere (Golding-Wood, 1961).

Similarly, lacrimal secretion was suspended, and the right eye became dry. The conjunctiva remained sufficiently moistened by unimpaired accessory secretion for its goblet cells to avert symptoms of keratoconjunctivitis sicca. The operative result, however, was marred by immediate onset of facial palsy, but this gradually recovered, leaving only slight facial asymmetry.

At follow-up examination five years later the right eye was found to have remained persistently dry to all emotional and sensory stimuli. Over the previous six months, however, profuse "crocodile-tearing" developed from this eye practically with every meal, and this occasioned her considerable distress.

In the hope of relieving the crocodile tears it was decided to resect the tympanic branch of the ninth nerve: this on the hypothesis that the gustatory reflex arc had been completed by sprouts from lesser to degenerated greater superficial petrosal nerve. Tympanic neurectomy was performed in July, 1961. It gave immediate and complete relief from the crocodile tears, and the eye has since remained dry to all stimuli.

Case 2

A woman aged 40 had sustained a severe Bell's palsy eight years previously. During the paralysis of the right side of her face she had not noted any of the usual epiphora. The palsy had lasted about a year, but recovery had been astonishingly complete. The face gradually recovered a full range of symmetrical voluntary and emotional movement, without trace of contracture or synkinesia. Virtually complete normality had been restored.

Emotional and reflex lacrimation was normal, but for the past six years she had suffered marked crocodile-tearing from the right eye with every meal. Within a minute of starting to eat, tears would well up in the right palpebral fissure, and shortly thereafter would overflow. These tears trickled down her cheek and dripped from her chin.

There was no other abnormality. The lacrimal punctum was normally effective and the ducts were patent. "Argyrol" instilled into the lower conjunctival fornix was cleared at normal speed on either side. Ordinary lacrimation judged by Schirmer's test was normal and equal in both eyes. Reflex lacrimation to noxious nasal stimuli was normal.

Resection of the tympanic branch of the ninth nerve by permealatal tympanotomy immediately abolished gustatory lacrimation. Normal lacrimation has been left unimpaired.

Case 3

A woman of 28 had suffered from right Bell's palsy one year previously. There had been no epiphora until some eight months after onset, when it developed solely with eating. At first, tears would overflow and trickle down the cheek with meals. Meanwhile facial recovery had been almost complete. There was no evidence of synkinesia, but some laxity of the lower eyelid remained. This, too, was recovering, and two months later she found that, by blinking, she could divert most of the gustatory tears to the natural channels.

Though she was still conscious of the event, this gustatory lacrimation ceased to be a major embarrassment, though it could readily be discerned when eating an apple. She did not wish to undergo operative treatment, and her symptoms scarcely merited this.

The nerves at the right jugular foramen were blocked with lignocaine. Temporary paralysis of the ninth, tenth, and eleventh nerves was induced. Clearly the ninth nerve was blocked immediately proximal to the origin of its tympanic branch. During the period of effective block no lacrimation could be induced by eating provocative foods that characteristically induced it immediately before and shortly afterwards.

Case 4

A male business executive aged 50 had sustained a left Bell's palsy three years previously. Recovery had been slow and incomplete. Considerable contracture and synkinesia of the left side of the face had resulted, though closure of the eyelids was satisfactory despite some laxity of the lower lid.

Crocodile-tearing developed eight months after onset of paralysis, the right eye having hitherto been dry. This crocodile-tearing occasioned him great embarrassment, particularly during business lunches.

Under local anaesthesia the left tympanum was explored. The tympanic branch of the ninth nerve and the chorda tympani were faradically stimulated separately by bipolar electrode. Stimulation of Jacobson's nerve induced brisk lacrimation from the left eye. Stimulation of the chorda tympani gave no detectable response.

The tympanic branch of the ninth nerve was resected. This brought immediate relief from crocodile tears. Gustatory stimuli have since failed to produce any lacrimation.

Operative Technique

A technique for resecting the tympanic plexus was originally proposed for the relief of tinnitus by Lempert (1946), but it has not gained any general acceptance. Recently I have found other cogent indications for this operation, sometimes resecting the chorda tympani also (Golding-Wood, 1962).

Under general or local anaesthesia the tympanic cavity is exposed by permealatal incision parallel to but some

distance from the annular margin of the drum, extending from 11 o'clock to 5 o'clock (Fig. 4). The meatal skin is raised and the posterior and inferior part of the drum is reflected in continuity with this meatal skin-flap. All otologists are familiar with this approach in modern stapes surgery.

The tympanic nerve courses upwards over the promontory a little anterior to the round window niche. Generally it lies on the bone, covered only by the fine layer of mucosa, and is readily visible under the operating microscope. In some 20% of cases it is enclosed in a bony canal that gives no surface indication of its presence. This canal, however, is easily defined and opened with a fine pick, and the nerve exposed.

After adequate exposure the nerve is resected as far as possible. The canaliculus by which it enters the tympanum can generally be closed by careful use of a micro-drill, operation being under 16 or 24 magnification.

The drum and skin flap are replaced and held in position with a simple meatal pack.

This operation involves no discomfort, and the patient can be discharged after two to three days, the meatal pack being removed in a week. This neurectomy being but a trivial extension of the exploratory tympanotomy now routinely part of otology, it may be considered to be entirely safe. Hearing is unaffected.

There is evidence that the chorda tympani often contributes to parotid secreto-motor activity (Reichert and Poth, 1933). Thus tympanic neurectomy alone does not necessarily terminate parotid secretion, although it may do so (Golding-Wood, 1962). In either event this occasions no disability.

Discussion

Hitherto the only explanation of crocodile tears after facial palsy was that proffered by Ford (1933) and Tumarkin (1936b). These authors pointed out that it arose only when facial palsy involved the geniculate ganglion. After neural degeneration, misdirection of regenerating fibres occurred, as evidenced by synkinesia. In this process salivary fibres normally passing to the submandibular salivary gland via the chorda tympani were thought to become misdirected during regeneration and to reach the lacrimal gland. Motor fibres might also do so, but as lacrimation is not induced by voluntary facial movement they must fail to excite secretion.

Clearly this explanation, rational as it then appeared, will not serve for many cases, although it cannot be wholly disputed. It is dependent on evidence of fibre misdirection, clinically detectable as synkinesia. Not all cases exhibit this, as shown in Cases 2 and 3 above, and in another recorded by Gottesfeld and Leavitt (1942). As is obvious, crocodile tears not associated with antecedent facial paralysis (Singer and Kellner, 1930; Boyer and Gardner, 1949) require other explanation.

FIG. 4. — Operative approach in tympanic neurectomy.

In all these cases degeneration of the greater superficial petrosal nerve could be shown or reasonably presumed. In Case 1 of this series this nerve has been sectioned and there had been no regeneration of activating fibres along it from the facial nerve—as shown by the persistent dryness of the eye to all normal stimuli. Degeneration of the greater superficial petrosal nerve near the geniculate ganglion might be expected to induce collateral sprouting from the lesser superficial petrosal. All the conditions found provocative by Murray (1959) exist. At the appropriate point just beyond the geniculate ganglion these two nerves lie in extremely close proximity. The communicating twig from lesser to greater petrosal may facilitate the passage of repairing sprouts. The time interval, generally six months or more before crocodile tears follow the nerve injury, is consistent with such reparative process. Salivary secretory fibres are appropriate for lacrimal excitation and a gustatory reflex arc may well become established.

Boyer and Gardner (1949) had found that intracranial section of the glossopharyngeal nerve relieved crocodile tears in their two cases. This fact, with the results obtained in this series by stimulating and by resecting the efferent pathway at a more convenient point, appear to provide conclusive evidence of this hypothesis.

If this be accepted, then tympanic neurectomy would seem the most suitable form of treatment. For the skilled otologist it is a safe operation requiring only two days' hospitalization, and local anaesthesia will often suffice. Normal emotional lacrimation, if it persists, as it may, is preserved. Lacrimal adenectomy or vidian neurectomy (Golding-Wood, 1961) would abolish this. Intracranial glossopharyngeal rhizotomy (Boyer and Gardner, 1949) is unnecessarily hazardous.

Summary and Conclusions

Paroxysmal lacrimation while eating is a well-recognized sequel that may arise six months or more after severe lesion of the facial nerve at or proximal to the geniculate ganglion. It is generally but not necessarily associated with facial synkinesia. It may arise after intracranial section of the greater superficial petrosal nerve without facial palsy.

Hitherto the pathological mechanism of crocodile tears has remained speculative and obscure. From analysis of four cases and relevant literature a new hypothesis is advanced. Degeneration of the greater superficial petrosal nerve excites collateral sprouts from the lesser superficial petrosal, normally subserving salivary secretion; these make functional connexion with the lacrimal glands. Thus a reflex arc provoking lacrimation on chewing food is established and thereafter it will persist indefinitely, to the patient's great embarrassment.

The most convenient point to sever the efferent arc is in the tympanic cavity by resection of the tympanic branch of the glossopharyngeal nerve; with modern otological technique this is a trivial operation for the patient and appears likely to give uniform relief while preserving normal lacrimation if such persists. This operation is offered as the most suitable treatment.

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ETHACRYNIC ACID: A NEW ORAL DIURETIC

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Safe, effective oral diuretics are now available, and the treatment of oedema, although often empirical, is generally satisfactory. There are occasional patients who do not respond adequately to these diuretics, and it was with these "resistant" patients in mind that we investigated the diuretic properties of a new drug, ethacrynic acid (MK-595). MK-595 is an unsaturated ketone derivative of aryloxyacetic acid and is not structurally related to hydrochlorothiazide (Fig. 1) or other diuretics (Schultz *et al.*, 1962).

FIG. 1.—Structural formulae of MK-595 (left) and hydrochlorothiazide.

This drug has been shown to have potent diuretic activity in animals (Baer *et al.*, 1962, 1963), and preliminary observations of the dose-response in oedematous patients have recently been reported (Foltz, 1963). We have compared the action of MK-595 with that of hydrochlorothiazide in normal volunteers and in oedematous patients.

Methods

Dose-response.—The dose of MK-595 which would give maximal diuretic response was determined in three