B.C.G. organisms were widely disseminated, and it is difficult to assess the significance of this. Some degree of systemic spread must be accepted as a normal sequel to B.C.G. vaccination. The extensive spread in this child seems to have been the consequence of his ill-health rather than the cause. In some of the cases of "B.C.G.-itis" to which reference has been made there appeared to be no predisposing illness. However, three of the five reported cases in infants had a family history of hypogammaglobulinaemia. It is clearly desirable that any future cases should be thoroughly investigated with this possibility in mind. B.C.G. has already had to live down one scandal for which it was not responsible: it would be unfortunate if it were to be blamed for deaths which should be laid at another diagnostic door.

With regard to the liability of hypogammaglobulinaemic patients to *Pneumocystis carinii* pneumonia, it is suggested that the cellular defect is more important than the deficiency of γ -globulin. In adults with this infection the level of γ -globulin has been found normal whenever it has been estimated, but in most instances there has been malignant disease of the reticulo-endothelial system.

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EFFECT OF TOPICAL FRAMYCETIN ON STAPHYLOCOCCAL NASAL CARRIAGE

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The carriage of coagulase-positive staphylococci by patients and hospital personnel is one of the important factors contributing to the development of infection by these organisms. Many studies have demonstrated the prevalence of nasal carriage in hospital patients and the close association between this carrier state and the occurrence of staphylococcal infection (McNeill *et al.*, 1961). To reduce the incidence of staphylococcal sepsis attempts have been made, by the use of antibiotic nasal creams, to eradicate nasal staphylococci in patients admitted to hospital and to prevent the development of nasal carriage of these organisms, particularly of antibiotic-resistant "hospital" types, during the period of hospitalization. These attempts, however, have been only partially successful in the elimination of nasal carriage and in the prevention of infection (Henderson and Williams, 1961). The report from Australia of Stratford *et al.* (1960) that framycetin sulphate ("soframycin") spray (containing framycetin 1.25% and gramicidin 0.005%) rapidly and completely cleared staphylococci from the nose suggested that an effective method of treating nasal carriage was available. Some of the findings in this report, however, differ from those of other workers.

Stratford *et al.* (1960) used deep nasal swabs to detect the presence of the carrier state and to assess the results of treatment with topical antibiotics. This technique was employed because a survey of 103 patients had indicated that deep swabbing was 17% more effective than superficial swabbing in the detection of nasal carriers. This finding, however, is not in accord with other reports which claim that superficial swabbing

more frequently demonstrates the presence of nasal staphylococci. Indeed, Williams *et al.* (1960) state that "nothing will be gained by swabbing the higher reaches of the nose, and in fact mistakenly swabbing beyond the vestibule may produce artificially low carrier rates."

Other studies on the effectiveness of framycetin, such as that of Barber and Warren (1962), have shown that not all patients carrying staphylococci ceased to do so under treatment with framycetin, and although in many cases the staphylococci disappeared from the nares they subsequently returned despite continuation of treatment.

As Stratford and his co-workers did not carry out phage-typing of the staphylococci isolated from nasal swabs it is not possible to ascertain whether nasal recolonization after cessation of framycetin was due to environmental contamination by different strains of staphylococci or to persistence of the same organisms in the nose. The investigation of Jarvis and Wigley (1961) would suggest that the latter explanation is the more likely.

In the investigation reported here evidence is presented on the frequency with which nasal carriage of staphylococci occurs in the hospital environment; on the accuracy of superficial as compared with deep nasal swabbing in the detection of the carrier state; and on the effectiveness of topical framycetin in the prevention and treatment of nasal carriage.

Materials and Methods

The investigations detailed below were carried out in a male general surgical ward in which staphylococcal infection had already been studied (McNeill *et al.*, 1960).

Superficial nasal swabs were taken from 457 patients on admission to and discharge from the ward in order to demonstrate the frequency with which nasal carriage occurred in this hospital environment.

We studied 179 patients in order to compare the accuracy of superficial and deep nasal swabbing in the detection of the carrier state. Superficial swabs were taken from the nasal vestibules of the patients. Deep swabs were obtained from the mucosa of the middle meatus and middle turbinate. To prevent contamination from the vestibule the mucosa was swabbed under direct vision through a sterile Thudichum nasal speculum. Alternatively, the swab was protected by a sterile glass tube.

The effects of topically applied framycetin were examined in 116 patients. The presence of nasal carriage in these patients was assessed by superficial nasal swabs taken on admission to the ward, the day after admission, and on every fourth day thereafter, including the day of discharge. The preparation containing framycetin 1.25%, gramicidin 0.005%, and phenylephrine hydrochloride 0.25% in isotonic saline was sprayed daily into each patient's nares from a plastic container so that the vestibule as well as the deeper parts of the nose were adequately treated.

All swabs were moistened with 7.5% salt broth prior to their introduction into the nares. On withdrawal from the nose the end of each swab was broken into a bottle of the same medium, which was incubated at 37° C. for 24 hours before plating out on horse-blood agar. Suspected colonies of staphylococci were examined for coagulase production, and then the phage pattern and antibiotic sensitivity, including sensitivity to framycetin, was determined. No strain of staphylococcus isolated during the course of these investigations was found to be resistant to framycetin.

Results

The admission and discharge nasal swabs from 457 patients gave an indication of the normal pattern of staphylococcal nasal carriage in the ward being studied. The results obtained are summarized in Table I. In 271 of these patients no nasal staphylococci were demonstrated on admission to hospital, but 27% of this group became nasal carriers. The majority (79%) of these newly acquired organisms were antibiotic-resistant "hospital" types. Of the 186 patients entering hospital carrying nasal staphylococci 50% retained the same type and 25% lost these organisms during their stay in hospital. The remaining 25% changed their type of nasal staphylococci, the majority of these (91%) acquiring antibiotic-resistant organisms. An important point not illustrated in Table I was that 56 (30%) of the patients admitted with nasal staphylococci were already carrying antibiotic-resistant types. The carriage of resistant organisms at the time of admission could be

TABLE I.—*Nasal Carriage of Coagulase-positive Staphylococci Assessed by Admission and Discharge Swabs in 457 Patients*

Negative on admission		197 (73%)	271 (59%)
Remaining negative		74 (27%)	
Becoming positive			
Antibiotic-sensitive staphylococci	15 (21%)		
Antibiotic-resistant "hospital" staphylococci	59 (79%)		
Positive on admission		92 (50%)	186 (41%)
Retaining same type		46 (25%)	
Changing type			
Antibiotic-sensitive staphylococci	4 (9%)		
Antibiotic-resistant "hospital" staphylococci	42 (91%)		
Becoming negative		48 (25%)	

accounted for in almost all instances by previous hospital admission in this group of patients.

A comparison of superficial with deep nasal swabbing in 179 patients is presented in Table II. In the patients with negative superficial nasal swabs deep swabbing showed the presence of staphylococci in 13%. In the patients with positive superficial swabs 17% had a negative deep swab. Where superficial and deep nasal

TABLE II.—*Nasal Carriage of Coagulase-positive Staphylococci Assessed by Superficial and Deep Nasal Swabbing in 179 Patients*

Superficial Swabs		Deep Swabs	
Negative	 120 (67%)	{ Negative 104 (87%)	
		{ Positive 16 (13%)	
Positive	 59 (33%)	{ Negative 10 (17%)	
		{ Positive 49 (83%)	

swabs were both positive the organisms isolated were identical in phage pattern and antibiotic sensitivity with one exception. In this study, therefore, 59 (33%) carriers were detected by superficial swabbing and 65 (36%) by deep swabbing. This difference of 3% between the two methods is not significant. It was therefore decided to assess the effectiveness of framycetin using the more easily performed technique of superficial swabbing.

The pattern of nasal carriage of staphylococci as presented in Table I was derived from admission and discharge nasal swabs only. Table III shows the pattern of nasal carriage in the framycetin-treated group of patients, when assessed by admission and discharge nasal swabs. In the framycetin-treated group only 11% of those entering hospital free from nasal carriage

TABLE III.—*Nasal Carriage of Coagulase-positive Staphylococci Assessed by Admission and Discharge Swabs in 116 Patients Treated with Topical Framycetin*

Negative on admission		74 (64%)
Remaining negative on discharge	 66 (89%)	
Becoming positive	 8 (11%)	
Positive on admission		42 (36%)
Retaining same type	 9 (21%)	
Changing type	 8 (19%)	
Becoming negative	 25 (60%)	

acquired nasal staphylococci during their stay in the ward, as compared with 27% of the untreated patients. Of those patients who were nasal carriers on admission 60% lost the organisms in the framycetin-treated patients as compared with 25% in the untreated group. These results indicate that framycetin is effective in reducing nasal carriage of staphylococci.

In considering these results it must be recognized that the more often nasal swabs are taken the greater is the demonstrable carrier rate. In Table IV, where the results of framycetin treatment are assessed by more frequent swabbing, the effectiveness of framycetin is less marked. It will be seen that 74 (64%) of these patients entered hospital free of nasal staphylococci—a similar finding to that given in Table I. Of these, 68% remained free throughout their stay on the ward; 24 (32%), however, acquired nasal staphylococci, of which 50% were resistant hospital types; these acquired organisms were subsequently lost in 18 patients.

Of the 42 patients who were admitted with nasal staphylococci, 9 (21%) retained these organisms and 28 (67%) lost them. Fifteen of the patients losing their nasal organisms acquired staphylococci again prior to discharge from hospital, and in 60% of cases these were resistant hospital strains. In 10 of the 15 patients in whom recolonization occurred during treatment with framycetin the staphylococci responsible were of the

same phage type as those that the patient had previously carried. Although this could have resulted from contamination of the nares from other sites of carriage on

TABLE IV.—*Nasal Carriage of Coagulase-positive Staphylococci Assessed by Frequent Swabbing in 116 Patients Treated with Topical Framycetin*

	Negative on Admission. 74 (64%)			Positive on Admission. 42 (36%)			
	Remaining Negative. 50 (68%)	Becoming Positive. 24 (32%)	Again Becoming Negative. 16	Retaining Same Type 9 (21%)	Changing Type 5 (12%)	Becoming Negative. 28 (67%)	Again Becoming Positive 15
Antibiotic-sensitive staphylococci	—	12 (50%)	6 (33%)	—	1 (20%)	17 (61%)	6 (40%)
Antibiotic-resistant "hospital" staphylococci	—	12 (50%)	12 (67%)	—	4 (80%)	11 (39%)	9 (60%)

the body, it was more probably due to persistence of the organisms in the nose. During framycetin treatment five patients changed the type of their nasal staphylococci, four of them acquiring antibiotic-resistant strains.

Discussion

A comparison of the data included in Tables I and IV shows that when nasal carriage is assessed by frequent swabbing, framycetin has little effect on the pattern of nasal carriage of staphylococci in this particular hospital environment. Of those patients entering hospital without nasal organisms, 73% remained free from nasal carriage in the untreated group and 68% remained free in the framycetin-treated group. Of those patients entering hospital with demonstrable nasal staphylococci 25% spontaneously lost the nasal organisms in the untreated group and only 31% lost the organisms and remained free from carriage in the treated group. Moreover, 21% of the patients being treated with framycetin acquired nasal staphylococci of the resistant "hospital" type during their stay in the ward. Of the untreated patients 22% acquired nasal carriage of resistant organisms. Although the use of framycetin seemed to have little effect on the overall pattern of staphylococcal nasal carriage it may be that topical antibiotics of this type reduce the density of nasal organisms and so decrease the environmental contamination from this source.

These results are in marked contrast to those reported by Stratford *et al.* (1960), who showed 100% success in the treatment of nasal carriers with framycetin. Their assessment of the carrier state in the framycetin-treated group of patients by deep nasal swabbing does not take into account, however, the possibility of vestibular carriage in these patients. The present investigation confirms the persistence of vestibular staphylococci during treatment with framycetin. It is suggested, therefore, that topical framycetin is a more effective method of treating mucosal carriage of staphylococci than of treating carriage of these organisms on the squamous epithelium of the nasal vestibule. Other studies on the effects of topical framycetin, such as those of Barber and Warren (1962) and Jarvis and Wigley (1961), confirm the persistence of vestibular staphylococci during framycetin treatment. As staphylococcal contamination of the environment can follow superficial nasal carriage as well as deep nasal carriage it is concluded that the assessment of the effective carrier rate during framycetin

treatment is more accurately determined by superficial swabbing.

This contention pertains even when the carrier rate demonstrated by deep swabbing exceeds that detected by superficial swabbing as in Stratford's report. In the present investigation we have been unable to confirm his finding, although we realize that differences in ward population, climatic conditions, and swabbing technique may explain the disparity in the results. As Stratford used unguarded swabs it was possible that his high percentage of deep carriers was in part due to the contamination of the swabs from the anterior nares. This explanation, however, seems unlikely in that similar contamination did not occur in swabbing the framycetin-treated patients whose swabs were consistently negative. His failure to isolate staphylococci from his framycetin-treated patients may be attributed to his employment of blood-agar as a primary culture medium. The use of salt broth as a selective medium for the isolation of staphylococci is a technique which yields a higher number of isolates than direct plating on to blood-agar (Jarvis and Wigley, 1961). Thus when framycetin has reduced the concentration of nasal organisms it is possible that the use of blood-agar may have allowed staphylococci to go undetected owing to overgrowth by other organisms.

Temporary nasal carriage is recognized as a common event and may occur in up to 60% of a population (Hutchison *et al.*, 1957). It is only by frequent swabbing that the carrier state is discovered in these individuals. As these temporary carriers also represent a potential source of environmental contamination they cannot be neglected in any study of staphylococcal nasal carriage. This is emphasized by the completely false picture of nasal carriage that is obtained by the consideration of admission and discharge swabs only, as presented in Table III. The significance of positive nasal swabs can be appreciated only when the staphylococci isolated are identified as completely as possible by establishing their phage pattern and antibiotic sensitivity. In this way the persistence of staphylococci in the nose during framycetin treatment can be differentiated from the acquisition of new strains from the patient's environment or from other carriage sites on his body. In this investigation it was possible to show in 66% of the patients who were recolonized during framycetin treatment that the recolonization was due to organisms identical in phage pattern and antibiotic sensitivity to those previously carried. The likelihood is that these staphylococci persisted in the nose during treatment.

In view of the failure of topical antibiotics to eliminate completely the nasal carriage of staphylococci it may be necessary to turn to other methods. Spink (1962), for example, has demonstrated that early colonization of the nares in infants by *Staphylococcus albus* inhibits the acquisition of coagulase-positive staphylococci. It is interesting, therefore, to speculate on the possibility of establishing biological control of nasal carriage by deliberately attempting to colonize the nose with *Staph. albus* and in this way protect the patient from the acquisition of pathogenic antibiotic-resistant hospital strains of coagulase-positive staphylococci.

Summary

Study in a surgical ward ascertained the normal pattern of staphylococcal nasal carriage in patients and showed that it was not significantly affected by the use

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-