V. Staphylococcal nasal carriers treated with framycetin-gramicidin nasal spray.

A. Previous investigations.

Nasal carriers play a considerable part in the development of staphylococcal infections. Danbolt (28) demonstrated this in the case of furunculosis as early as 1931. Later, this was shown to apply both to furunculosis (126, 130), and to other staphylococcal skin lesions (27, 35, 65, 108, 126). Perinatal pyodermias and puerperal abscesses may also be due to nosocomial infections (78, 88, 120) and postoperative septic lesions are often thought to result from autoinfection with staphylococci from the nose (23, 95, 140, 148).

Local treatment of the nasal mucosa with antibiotics can reduce the frequency of recurrent staphylococcal skin lesions among nasal carriers (27, 46, 65, 127). This treatment also seems to reduce the frequency of staphylococcal infections in maternity wards (4, 40, 72, 75, 121). In surgical wards, however, the results are not quite so uniform and encouraging (42, 43, 63, 110, 121, 140). In several investigations, other measures have been taken concurrently with antibiotic therapy and the individual effect has been difficult to assess.

Various antibiotics have been used in the treatment of staphylococcal nasal carriers and a definite reduction in nasal carriage has usually been demonstrated during and just after treatment (33, 44, 45, 129, 141). But in some investigations less favourable results have been obtained (90, 102).

In recent years, framycetin has been used alone or in combination with gramicidin in order to reduce the frequency of nasal carriers. In several investigations the results have been good (8, 71, 115, 123) but not in all (102).

The efficiency of intranasal application of antibiotics in reducing skin contamination and aerial dissemination of staphylococci by nasal carriers has seldom been studied (98, 132), and little is known of the quantitative side of the problem. The results of investigations of this aspect of the problem will be reported here.

B. Personal investigations.

1. *Material and methods.*

Nasal samples from the nurses and doctors in the department were obtained every other week for $1^1/_2$ years. Thirty individuals who had been carriers of the same staphylococcal strain for 2—6 months were selected, and the incidence and quantity of these organisms in the vestibule of the nose were determined once daily for 3 days before treatment with framycetin-gramicidin nasal spray. Nasal cultures were obtained the day after completing therapy and again at 1 week intervals.

Forty of the 100 nasal carriers in chap-

ter IV were also treated with framycetin-gramicidin nasal spray. The numbers of staphylococci on the skin and the dispersal into the air on bed making were examined once daily for 3 days before treatment (the results are reported fully in chapter IV) and on the day after completing therapy.

Twenty of the 40 patients remained in the department for at least a further 10 days, the incidence and quantity of staphylococci in the nasal vestibule being determined on the 4th and 10th days after completing treatment. In 3 of these patients, skin and air samples were obtained several times after treatment.

In order to keep experimental conditions approximately equal before and after treatment, the 40 patients were bathed or washed on a stretcher, and received clean clothes and bedclothes 2 days before the first pre-treatment examination and 2 days before the post-treatment examination.

The framycetin-gramicidin nasal spray[1] was used 4 times daily. The spray fluid was an isotonic solution containing 1.25 per cent framycetin, 0.005 per cent gramicidin, 0.25 per cent metaoxedrin and 0.002 per cent phenylmercurinitrate. The patients were treated for 3 days and the personnel for 7 days.

The methods of investigation are described in chapter II. In assessing the frequency of nasal carriers, nasal cultures which did not yield staphylococci in the first dilution (1 : 40) were regarded as negative.

2. *Results.*

Tables 33 and 34 give the frequency of nasal carriers of Staph. aureus among the personnel and patients after treatment. The frequency was lowest for the personnel who had been treated longest, and in both groups it was lowest on the day after completion of treatment and rose rapidly in the course of the following 1—2 weeks. Antibiogram determinations and phage typing were performed on 1—2 colonies from all positive nasal cultures. Only 3 individuals in each group yielded different strains after therapy.

Figs. 11 and 12 illustrate the mean nasal counts from the personnel and patients before and after treatment. In both groups, there was a marked reduction from high pre-treatment values to less than 0.01 per cent of the original numbers the day after completion of therapy. The nasal counts from the majority of individuals in both

[1] The preparation was supplied by "Nyco", Oslo.

Table 33. *Staphylococcal nasal carriage after treatment with framycetin-gramicidin nasal spray for seven days.*
(30 members of the personnel).

Day after treatment	No. of samples		Per cent of samples positive
	Positive	Negative	
1	3	27	10
7	17	13	57
14	23	7	77
21	25	5	81
28	27	3	90

Table 34. *Staphylococcal nasal carriage after treatment with framycetin-gramicidin nasal spray for three days.*
(20 patients).

Day after treatment	No. of samples		Per cent of samples positive
	Positive	Negative	
1	8	12	40
4	11	9	55
10	18	2	90

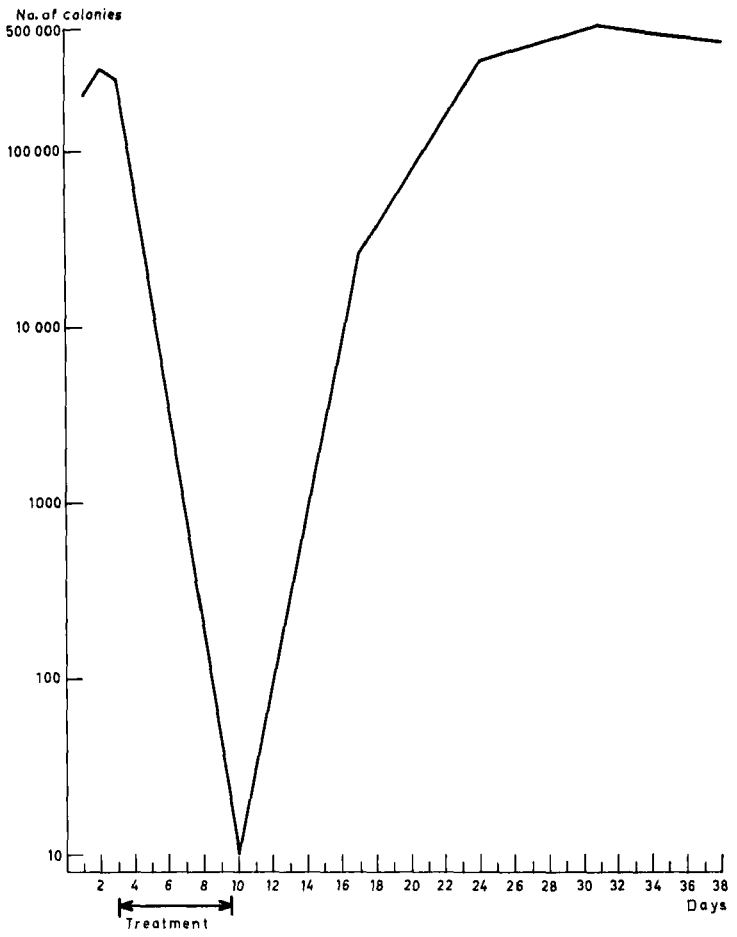

Fig. 11. Staphylococcal nasal counts before and after treatment with framycetin-gramicidin nasal spray (mean counts, 30 nasal carriers).

groups were still low 4 and 7 days later, but during the subsequent week the mean counts for both groups rose to about the same level as before treatment.

Quantitative nasal cultures were obtained for 10 days from 10 untreated subjects (patients and personnel) who had been shown by weekly examinations (covering 1 to 2 months) to be persistent staphylococcal nasal carriers. Fig. 13 illustrates the mean numbers of Staph. aureus in daily samples from these individuals. Only minor variations were observed.

Table 35 gives the frequency of staphylococcal positive nasal, throat, skin and air samples from 40 nasal carriers before and after treatment. From the throat, staphylococci were isolated almost as frequently after treatment as before, but in the other samples the organisms were seldom demonstrated after treatment.

Table 36 and figs. 14 and 15 give the mean counts in nasal, skin and air samples

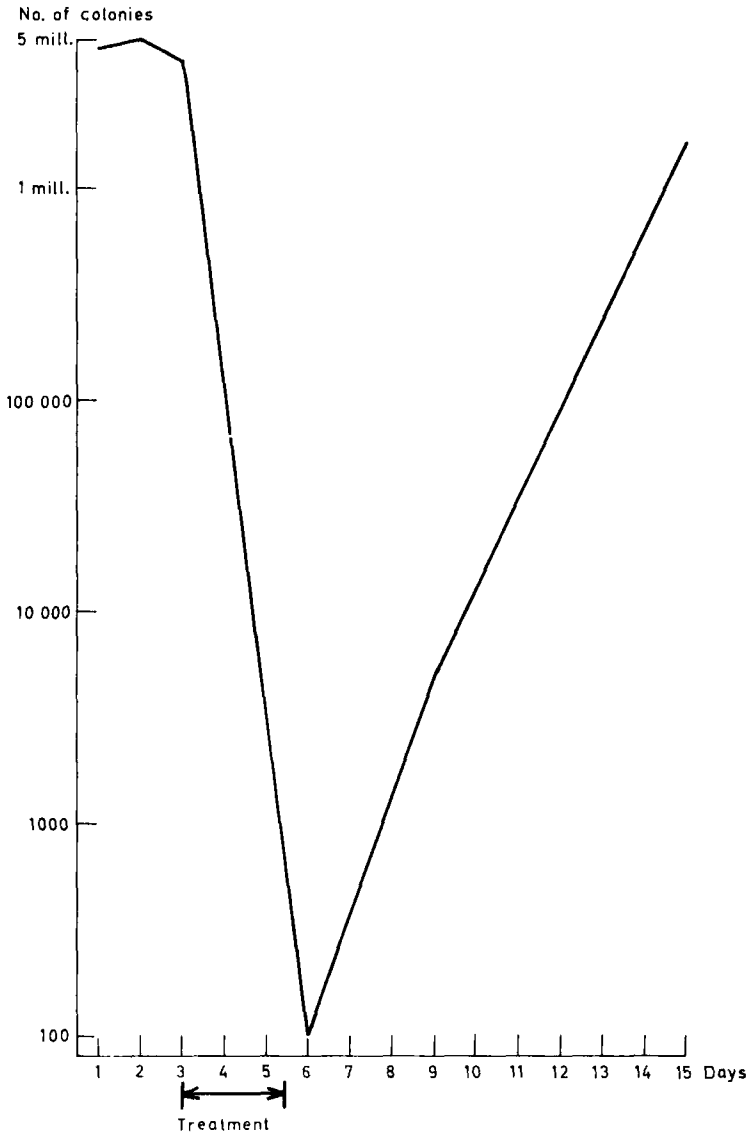

Fig. 12. Staphylococcal nasal counts before and after treatment with framycetin-gramicidin nasal spray (mean counts, 20 nasal carriers).

from 40 nasal carriers before and after treatment. For all samples, a marked reduction was demonstrated from high values before treatment to extremely low values the day after treatment was completed.

Three patients had positive perineal samples (from 2,000 to 8,000 staphylococci) the day after completing treatment.

Sixteen of the 40 patients yielded positive post-treatment nasal cultures. Antibiogram determinations and phage typing were performed on 18 colonies from these

Table 35. *Frequency of staphylococcal positive samples before and after treatment with framycetin-gramicidin nasal spray for three days.*
(40 nasal carriers).

Day of treatment	Nose		Throat		Upper lip		Fingers		Hands		Air contam.	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
−3	40	100.0	13	32.5	36	90.0	40	100.0	39	97.5	40	100.0
−2	40	100.0	12	30.0	35	87.5	40	100.0	39	97.5	40	100.0
−1	40	100.0	11	27.5	37	92.5	40	100.0	39	97.5	40	100.0
+1	16	40.0	8	20.0	8	20.0	5	12.5	1	2.5	9	22.5

− = before treatment, + = after treatment.

Table 36. *Mean staphylococcal nasal, skin and air counts before and after treatment with framycetin-gramicidin nasal spray for three days.*
(40 nasal carriers, mean counts in thousands).

Day of treatment	No. of bacteria*				
	Nose	Upper lip	Fingers	Hands	Air contam.
−3	4,614.650	2.380	13.925	64.163	4.280
−2	3,746.500	3.182	13.986	51.263	4.433
−1	4,600.080	2.302	17.291	57.100	3.888
+1	0.155	0.009	0.003	0.013	0.012

* Calculation method I, − = before treatment,
+ = after treatment.

samples. In all cases, identical strains were demonstrated before and after treatment. Altogether, 25 staphylococcal colonies were demonstrated in the 14 positive samples from upper lip, fingers and hands of the 40 patients after treatment. Antibiogram determinations and phage typing were performed on 15 colonies. Only 1 colony differed from the corresponding nasal strain. Seventeen Staph. aureus colonies were demonstrated in the air samples after treatment. Seven colonies were different from the respective nasal strains. Skin and air sample colonies which differed from the respective nasal strains were assumed to be due to environmental contamination and were not included in the calculations of skin and air contamination.

Eight patients had positive throat samples after treatment. Antibiogram determinations and phage typing were performed on 10 colonies from these samples. Five patients had identical throat strains before and after therapy. Staphylococci were not demonstrated in skin and air samples from 3 patients who yielded positive throat cultures and negative nasal cultures after treatment.

Three patients were examined several times after completing treatment with nasal spray. Table 37 shows the results of these post-treatment examinations, which

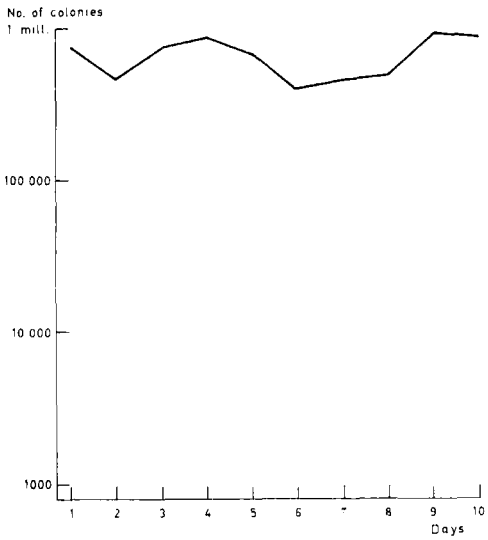

Fig. 13. Mean staphylococcal nasal counts from 10 untreated nasal carriers.

demonstrated that the number of organisms on the skin, and the dispersal into the air increased with increasing nasal counts.

Antibiogram determinations and phage typing were performed on a total of 68 Staph. aureus colonies from the samples of these 3 patients. Apart from 2 colonies in the air samples, all strains from each patient were identical.

One patient had mild side-effects from the treatment in the form of nasal stenosis and mild dyspnoea. The symptoms disappeared as soon as treatment was discontinued.

Staphylococcal strains resistant to framycetin and gramicidin were not observed during the investigation.

3. *Discussion.*

Nasal spray therapy has only a temporary influence on the carrier status. Staphylococci are often demonstrated after the completion of treatment, the interval before the nasal samples become positive varying considerably (71, 102, 115, 123). This may partly be due to differences in technique (71, 102) and in the staphylococcal nasal counts before treatment. It has in fact been shown that patients who were recolonized after nasal application of antibiotics, yielded higher pre-treatment nasal counts than patients who became non-carriers (132). The individuals in the present investigation were accounted persistent carriers — carriers with high nasal counts (117) — while in other investigations (71, 123), there were probably more occasional carriers — individuals yielding few nasal staphylococci. The results are probably also dependent on the duration of treatment and the care with which it is carried out (115). In the present investigation, checks were made once or twice daily to see that the spray bottle was used correctly.

In the majority of cases, the demonstration of staphylococci after treatment was probably due only to persistence of the original strains in the vestibule of the nose. Stratford et al. (123) surmised that the recolonization was due to exogenous staphylococci but as phage typing was not performed, they were unable to prove this. In the majority of patients in the present study the pre- and post-treatment nasal strains were identical. There were very few or no staphylococci on the skin and bedclothes after treatment so that dispersal to the nose from these sites was most unlikely. Re-infection from the throat was, on the other hand, possible in some cases. In the majority, however, persistence of the original organisms in the vestibule of the nose was the most reasonable explanation. This is in accordance with the results of other investigations (71, 102).

One of the 3 individuals in the personnel group who changed strains had negative nasal cultures for 22 days, but the day after

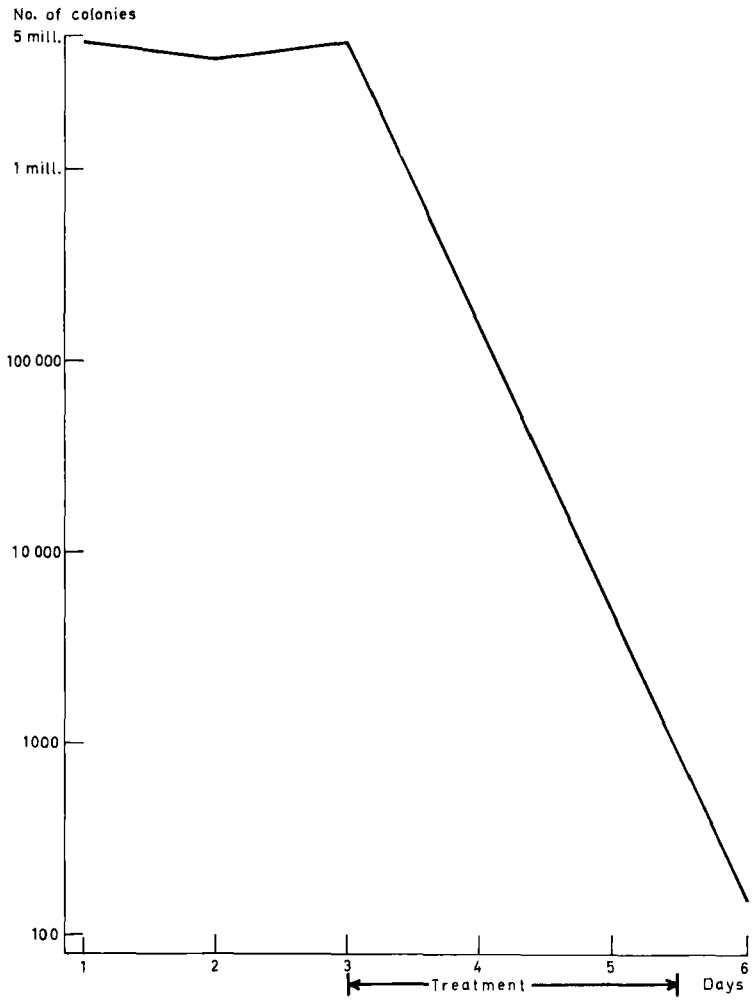

Fig. 14. Staphylococcal nasal counts before and after treatment with framycetin-gramicidin nasal spray (mean counts, 40 nasal carriers).

she began nursing a patient isolated for a severe staphylococcal pyodermia (patient 1, chapter VII), her nasal cultures yielded a strain identical with that harboured by the patient.

In one of the 3 patients who changed strains, the one developed in the nose after treatment was identical with the strain yielded by the perineum. Another of these 3 patients, who was placed in the same room as a perineal carrier who dispersed large numbers of staphylococci, yielded after 3 days positive nasal cultures of a strain identical with that of the perineal carrier.

Routine examination of air contamination in the wards and charting of all staphylococcal carriers among personnel and patients showed that those individuals who changed their strains, were recolonized

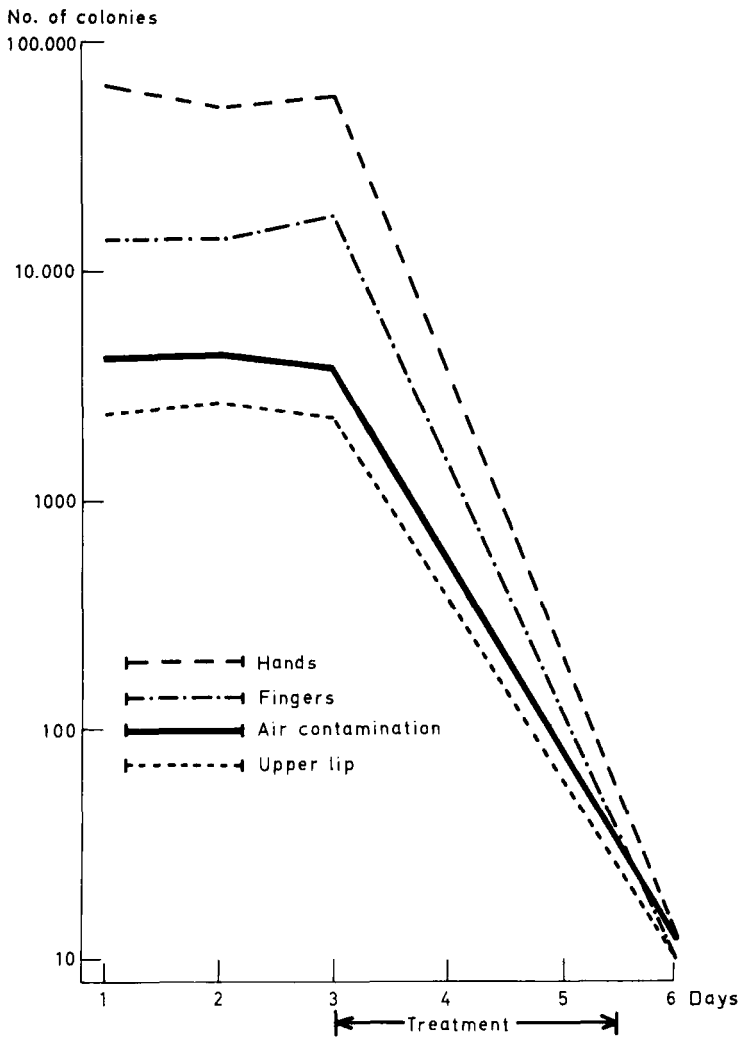

Fig. 15. Staphylococcal skin and air counts before and after treatment with framycetin-gramicidin nasal spray (mean counts, 40 nasal carriers).

with those organisms which appeared in greatest numbers. These observations are few in number, but there is probably a quantitative factor in the transfer of staphylococci from one individual to another.

Although staphylococci can be demonstrated in nasal cultures after treatment, a purely qualitative assessment does not give a true picture of the effect of treatment. Porter et al. (102) did not undertake quantitative investigations but they were nevertheless aware of this: "Although the use of framycetin seemed to have little effect on the over-all 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".

In the present study, a marked reduction was demonstrated in the staphylococcal skin and air counts, from high values before treatment to almost negligible numbers after its completion. If there is a quantitative factor in the development of staphylococcal lesions, a simple treatment such as antibiotic nasal spray should therefore contribute to reducing the frequency of infections with these organisms. As mentioned previously, this has been shown in some investigations but not in all (63, 121).

The staphylococcal skin and air counts fell during treatment with nasal spray approximately in parallel with the number of organisms in the nasal samples. This might be due to accidental contact of skin and spray, e.g. when the cap was screwed on and off or via handkerchiefs, but the main reason was probably that the number of dispersable organisms in the nasal vestibule fell to a minimum.

Only one of the individuals in the present study had side-effects from the therapy and these were very mild. In large doses, gramicidin may produce lung infiltrations in rabbits (105). Rubbo (113) and Gremeaux (48) have shown that the quantity used in framycetin-gramicidin nasal spray could hardly give rise to lung symptoms.

4. *Summary and conclusions.*

1. Thirty nurses and doctors and 20 patients who had been shown by repeated examinations (covering periods of 3 weeks to 6 months) to be nasal carriers of the same staphylococcal strain, were treated with framycetin-gramicidin nasal spray 4 times daily for 7 and 3 days respectively.

Table 37. *Reappearance of staphylococci after treatment with framycetin-gramicidin nasal spray for three days.*
(3 nasal carriers).

Pat. no.	Day after treatment	No. of bacteria (in thousands)					
		Nose	Throat	Upper lip	Fingers	Hands	Air contam.
	1	<0.04	<0.04	<0.02	<0.02	<0.5	<0.025
	2	1.60	<0.04	0.02	0.02	<0.5	0.025
1	3	14.00	<0.04	0.02	0.02	<0.5	0.025
	6	84.00	0.04	0.44	0.08	4.0	<0.025
	7	184.00	<0.04	0.44	0.72	11.0	0.300
	4	17.00	<0.04	<0.02	<0.02	<0.5	0.025
	5	36.00	<0.04	0.02	<0.02	<0.5	<0.025
2	6	57.00	<0.04	<0.02	0.18	<0.5	0.100
	7	252.00	<0.04	<0.02	0.12	<0.5	0.300
	11	2,400.00	<0.04	5.60	3.60	12.0	4.900
	1	<0.04	<0.04	<0.02	<0.02	<0.5	<0.025
3	3	0.16	<0.04	<0.02	<0.02	<0.5	<0.025
	29	1,600.00	0.84	0.64	3.92	20.0	1.200
	30	800.00	0.36	0.40	1.78	1.5	0.300

Twenty-seven (90 per cent) individuals in the personnel group and 12 (60 per cent) in the patient group had negative nasal cultures on the day following completion of treatment. However, the frequency of positive cultures increased rapidly in both groups in the following 1—2 weeks.

For both groups, the staphylococcal nasal counts fell from high pre-treatment values to less than 0.01 per cent of the original counts on the day after completion of treatment. They remained relatively low for 4—7 days, then rose during the following week to about the same level as before treatment.

Eighty to ninety per cent of the individuals with positive nasal cultures after treatment yielded the same strain before and after therapy. It is assumed that in the majority of cases the original organisms persisted in the nose.

2. Forty patients who were nasal carriers of large numbers of staphylococci were treated with framycetin-gramicidin nasal spray for 3 days.

The quantity of staphylococci in the nose, on the upper lip, fingers and hands fell from high pre-treatment values to very low values on the day after completion of therapy. The same applied to aerial dissemination of staphylococci on bed making. When the staphylococcal nasal counts began to rise after treatment, the skin and air contamination also rose.

Treatment by framycetin-gramicidin nasal spray is regarded as a valuable measure for preventing the dissemination of staphylococci from nasal carriers.