

ALLERGIC CONTACT DERMATITIS DUE TO NEOMYCIN

CROSS-SENSITIVITY WITH OTHER ANTIBIOTICS; AND POSITIVE PATCH TESTS WITH THE ISOMERIC COMPOUNDS NEOMYCIN B AND NEOMYCIN C AND WITH NEAMINE

R.KOOIJ, M.D., *Department of Dermatology, University of Cape Town and Groote Schuur Hospital, Cape Town*

Formerly it was thought that locally applied neomycin had a low sensitizing index. Judging from the increasing number of publications of contact dermatitis due to neomycin, it seems that its sensitizing index is much higher than was believed. As early as 1952 contact dermatitis due to neomycin was reported by Kile *et al.*¹ in 1 out of 722 patients treated with neomycin. In the same year Baer and Ludwig² described another case, in a middle-aged housewife, with dermatitis of the ears. She had been treated with eardrops containing neomycin, 5 mg. per ml. of sterile distilled water; 5 months after the inception of this treatment there was a sudden unexplained recurrence of signs and symptoms. A patch test with a neomycin solution, 5 mg. per ml., was positive, while a patch test with a bacitracin solution, 500 units per ml., was negative.

Epstein³ reported 10 cases of contact dermatitis due to neomycin. In an addendum he mentioned that, at the time his paper was going to press (September 1956), the number of cases of contact dermatitis had risen to 25, including some caused by eardrops and eyedrops containing neomycin. Patch tests with the ointments as well as with a 0.5% solution of neomycin were only occasionally positive. Proof of allergic sensitivity to neomycin was demonstrated by intradermal tests with 0.05 ml. of 1 in a 1,000 or 1 in a 100 solution of neomycin, which produced papular reactions in 48 hours.

Epstein pointed out that neomycin contact dermatitis is often not recognized because it resembles an apparent aggravation of the pre-existing dermatitis, which might show improvement after the use of ointments containing neomycin and hydrocortisone. Patch tests with ointments are often negative at the same time.

In a later publication, Epstein⁴ reported on 40 cases of contact dermatitis due to neomycin, of which only 11 showed positive patch tests to the drug, while intradermal tests were uniformly positive. With McCormick⁵ he described 4 cases of conjunctivitis caused by eyedrops or ointments containing neomycin.

Pirilä and Wallenius,⁶ in Finland, reported 28 cases of contact dermatitis from neomycin and bacitracin. Eighteen of their neomycin-sensitive patients reacted positively to patch tests with bacitracin (in concentrations up to 3%) while, of 25 cases in which patch tests with 3% neomycin were performed, all except 1 were strongly positive.

Sidi *et al.*⁷ reported 8 cases of neomycin contact dermatitis which also gave positive patch tests to streptomycin (concentrations not mentioned). They state that in a number of cases patch testing was insufficient to elicit a reaction; however, light scarification before the testing regularly yielded positive tests in sensitized patients.

Calnan and Sarkany,⁸ who described 14 cases of contact dermatitis from neomycin, found that negative patch tests were frequent, but intradermal tests with a 1% solution of neomycin were always positive in their patients. Cross-sensitivity to 1% streptomycin was found in 2 patients, but no allergic neomycin sensitivity was encountered in 7 other streptomycin-sensitive patients. Neither was there evidence of an associated hypersensitivity reaction to bacitracin and framycetin.

Reynolds *et al.*⁹ observed a total of 28 patients and described illustrative cases. Patch tests with 0.1% and 1% isotonic solutions of neomycin sulphate were positive in 24 of the 28 patients.

Kooij¹⁰ reported a case of contact dermatitis due to both hydrocortisone and neomycin. Positive patch tests were obtained with a 1% and 6% solution of hydrocortisone sodium succinate in sterile water, with a 0.5% prednisolone cream, with 3% neomycin in paraffinum molle and with 6% 'chloromycetin' and 6% 'achromycin' in paraffinum molle.

In a later article Pirilä and Rouhunkoski¹¹ collected 184 cases of hypersensitivity to bacitracin and/or neomycin with positive epicutaneous tests, probably due to the frequent use of these drugs. They state that in Finland in the last few years 2 million packages of preparations containing the above antibiotics were sold. A total of 101 patients were tested with both neomycin and bacitracin.

All showed a positive reaction to neomycin (10% solution) and in only 5 cases tests with a 5% bacitracin solution were negative. Out of 79 patients tested with a mixture of streptomycin and dihydrostreptomycin only 2 reacted positively. They used as high a concentration as 50%.

They also describe a case in which there was a flare-up of dermatitis after using throat tablets and after oral administration of tablets containing these antibiotics. It seems worth while to give full particulars of this instructive case.

The patient, who was hypersensitive to bacitracin, had pharyngitis and he inadvertently treated it with tyrothacin throat tablets ("star") containing tyrothricin and bacitracin. As a result, the oral and lingual mucosa became intensely inflamed and swelling of the lips and rhagades at the angles of the mouth also developed. The patient stopped using the tablets and was cured in 5-6 days. He decided to be more careful in the future in avoiding exposure to neomycin and bacitracin. In spite of this he experienced another unpleasant surprise, which occurred after little more than a week. He had toothache and the dentist diagnosed gangrene of the pulp. The pulp cavity and root canal were opened up to the apex and cleaned. The cavity was then filled with neotrasin paste. Neotrasin "dentale" contains neomycin and bacitracin. Powder containing both these drugs is now almost routinely used for root-canal treatment in Finland. The patient, naturally, could not know that he had again been exposed to these antibiotics.

The toothache increased in severity, and after a lapse of one-and-a-half hours the palms of the patient's hands began to itch. Erythema and swelling of the face soon appeared, and itching in the popliteal folds and on the stump of an amputated leg. The oral mucosa also became inflamed. The dermatitis involved the same area as that following the local application of neomycin and bacitracin preparations. Four hours later the root canal was re-opened and the neotrasin removed. Nevertheless, aggravation of the eczema with oozing occurred during the first 24 hours. Thereafter, under cortisone and antihistamine treatment, the eczema cleared up in one week. Roentgenograms showed that a guttapercha filling, later inserted into the tooth, penetrated through the root canal into the periapical focus. In the same way neotrasin had reached this focus, whence the allergen was probably carried to the skin by the blood stream, thus explaining the flare-up of his eczema as due to the use of neotrasin in the root canal.

Neomycin was later tried internally on the same patient. As smaller doses did not produce a clear reaction he was given 2 tablets (165 mg. each) 4 times during one day, making a total of 1.3 G. (daily doses, 5-10 times as high, have been used for pre-operative medication). About 6 hours after the patient had taken the first 2 tablets he had loose stools but no other symptoms. After 24 hours the skin in the popliteal folds began to itch and after 2 days a follicular eczema developed at the site as well as on the thighs, in addition to oedema of the face. As there was no improvement on the third day, cortisone treatment was started.

PRESENT STUDY

In a few patients with a dermatitis in whom the probability of neomycin being the causal factor was suspected, patch tests with several brands of neomycin ointment were carried out. The results were negative. By using higher concentrations, as suggested by Calnan and Sarkany,³ positive results were obtained.

MATERIAL AND METHODS

Patch tests were performed on the backs of the patients, and the results were read after 48 hours and again after 96 hours, and often also later.

In the beginning we used, empirically, 3% and later 6% neomycin in paraffinum molle for patch testing.

These concentrations were used for patch testing with 'aureomycin', chloromycetin, achromycin, and bacitracin, all in paraffinum molle. For patch tests with 'soframycin' (containing framycetin) 1.5% soframycin ointment (Roussel) in a water-soluble base was used.

Streptomycin (sulphate) and dimycin were applied in an aqueous solution of 25%. Dimycin contains equal parts of streptomycin sulphate and dihydrostreptomycin.

In some cases the isomeric compounds neomycin B and neomycin C, and also neamine, in a concentration of 6% in paraffinum molle, were tested.

The 'neomycin complex' contains the isomeric compounds neomycin B and neomycin C and a third entity, originally called neomycin A, now designated as neamine, which arises from the hydrolytic cleavage of either neomycin B or C.¹²

Other patch tests are mentioned in the case reports (see addendum).

In this study most of the patients tested were those suspected of being hypersensitive to neomycin. About 60 controls, White and non-White, were also tested.

RESULTS

Patch tests were carried out in 7 patients with a contact dermatitis due to neomycin (cases 1-7) and in 1 patient with allergic sensitivity to streptomycin (case 8) — see case reports.

Table I shows the main results in these patients of the various patch tests with neomycin, chloromycetin, achromycin, aureomycin, bacitracin, streptomycin, dimycin, the isomeric compounds neomycin B and neomycin C, and neamine.

Each of the 7 patients with neomycin contact dermatitis showed a positive patch test with 3% and 6% neomycin in paraffinum molle. The persistence of the reactions to the patch tests with neomycin for several weeks, and also to patch tests with other antibiotics (see case 7, Fig. 2), has already been noticed by others.

Cross-sensitivity occurred to all the antibiotics tested with the exception of streptomycin, which, however, was found positive by others in cases of contact dermatitis due to neomycin. Case 8, with allergic sensitivity to streptomycin, did not show positive patch tests to the other antibiotics. As is obvious, each case has its own pattern of reaction.

The patch tests with the isomeric compounds, neomycin B and neomycin C, and with neamine, were positive in the cases tested, the strongest reactions being obtained with neamine.

During the course of the investigation the impression was gained that the activity of the patch-test material was diminishing, because in 2 patients (cases 6 and 7) known to be hypersensitive to neomycin, patch tests with 6% neomycin, 6% chloromycetin, 6% achromycin, and 6% bacitracin in paraffinum molle were negative.

The material used in both these patients had been prepared at least 6 months earlier and had not been kept in the ice chest. However, with freshly-prepared material positive results were obtained in both cases.

The 1.5% soframycin ointment used for patch testing still gave positive, although weaker, reactions. This proprietary preparation in a water-miscible base was

TABLE I. RESULTS OF PATCH TESTS IN PATIENTS WITH CONTACT DERMATITIS DUE TO NEOMYCIN (CASES 1 - 7) AND STREPTOMYCIN (CASE 8)

Cases	Patch tests															
	3% Neomycin	6% Neomycin	3% Chloromycetin	6% Chloromycetin	3% Achromycin	6% Achromycin	3% Aureomycin	6% Aureomycin	3% Bacitracin	6% Bacitracin	1.5% Soframycin	25% Streptomycin	25% Dimycin	6% Neomycin B	6% Neomycin C	6% Neamine
1	++		±		±	+		+		+	-		++	++	
2*	+++	-	++	-	+		-				-				
3	+	+	-		-		-	-		+	-		++	++	+++
4		+	-		-		-		+	±	-				
5		+	-		-		-		-	++	-**	-**	++	++	±**
6		++	-		-		-	-		-	-	-	++	++	+++
7		++	+		+		+		-	+	-	-	++	++	+++
8		-	-		-		-		-	-	++				

* Also hypersensitive to hydrocortisone.

** While under oral treatment with steroids (medrol).

manufactured in November 1957; the date of expiry was November 1959. It was used to test various patients between February 1959 and September 1960.

The influence of steroid treatment on the results of the patch tests was noted in case 5. Formerly positive patch tests with 6% neomycin in paraffinum molle became negative after patients had been under oral 'medrol' treatment for several weeks. Also, the previously strong reaction to the waterproof 'elastoplast', used for patch testing, was much weaker.

DISCUSSION

According to the literature, which bears out our own experience, there has been an increase in the number of cases of contact dermatitis due to neomycin. This is partly due to the enormous increase in the use of neomycin preparations for local application and partly to a better recognition of neomycin as a cause of allergic sensitivity.

At first it was not known that the clinical features of neomycin dermatitis can differ from the usual type of allergic contact dermatitis. For instance, instead of an acute, vesicular, oozing process at the site of contact, the reaction to neomycin can be of the dry, desquamative type. I observed it in case 4 in this series.

The improvement often observed when changing from a neomycin ointment to an ointment containing both neomycin and hydrocortisone has also contributed to the failure to recognize neomycin contact dermatitis. Most confusing is the fact that patch tests done with the neomycin ointments are actually often negative, even in cases of contact dermatitis due to this antibiotic. By increasing the concentration of neomycin in the ointments used for patch testing, however, and also by means of intradermal tests with solutions of neomycin, more positive results can be obtained. I prefer patch tests to intradermal tests because intradermal injections are not without danger in very sensitive patients.

With a concentration of 6% neomycin in paraffinum molle in the above 7 cases of contact dermatitis from neomycin, positive results were obtained, while these concentrations did not evoke positive reactions in about 60 controls. It is not impossible that with higher concentrations, more positive cases would have been found. Patch testing with antibiotics is not used as a routine in the Groote Schuur Hospital Skin Department, but only in suspected cases of hypersensitivity. This method was also used in a number of controls for the determination of the correct concentration for patch testing. Recently, Piriä and Rouhunkoski,¹¹ used 50% neomycin ointments, which gave positive reactions in some cases that had not reacted to a 10% solution of neomycin. In a control series of 150 persons, no positive reactions were observed.

The persistence for several weeks of the reactions to the patch tests with neomycin is very striking, and it should be remembered that patients might complain about it. This persistence of the neomycin patch-test reaction is on a par with the often long duration of contact dermatitis itself due to the same cause.

Of practical importance is the finding that the antibiotic test material in paraffinum molle, kept out of the ice chest, decreased considerably in activity in about 6 months, resulting in negative patch tests in previously positive reactors. In consequence it has been decided to preserve all the patch-testing preparations in the ice chest and to renew them from time to time. It is wise, also, to bear in mind that neomycin-sensitive patients who are being treated systematically with steroids might conceivably show negative patch-test reactions to this antibiotic.

CROSS-SENSITIZATION

Seeing that many antibiotics may contain similar chemical compounds in their structural formulae, the possibility of cross-sensitization was investigated. By means of patch

tests, chloromycetin, achromycin, aureomycin, bacitracin, soframycin (framecytin) and streptomycin were investigated with this in view. Cross-sensitization is a phenomenon where allergic sensitization of human skin produced by a compound (the primary allergen) is associated with allergic eczematous sensitization to one or more compounds.¹² It occurs between immunochemically related substances or between two or more apparently unrelated substances which, by conversion in the human tissues, are broken down into products which are immunochemically related.

In the above investigation positive patch tests to chloromycetin, achromycin, aureomycin, bacitracin and soframycin were found in patients with a contact dermatitis due to neomycin. No positive patch tests were noted in this series with streptomycin, although cross-sensitivity between neomycin and streptomycin has been described.

Case 8, with allergic sensitivity to streptomycin in a high degree, did not show positive patch tests to any of the other antibiotics tested.

As is shown in Table I, every patient reacted characteristically, individually, and had his own pattern of reaction, as has been shown among others by Kooij and van Vloten¹⁴ in cases of allergic sensitivity to sulphonamides.

The above results point to the possibility that in cases of allergic sensitivity to neomycin the use of other antibiotics, even systemically, might lead to reactions. One of the reasons for the choice of neomycin for topical use was that it was hardly ever used systemically and when used orally it was only slightly absorbed.

The above-mentioned illustrative case described by Pirilä and Rouhunkoski,¹¹ however, shows that even the oral administration of neomycin can cause a dermatitis in sensitive persons.

Several of the antibiotics, which this investigation showed to possess a cross-sensitivity with neomycin, are used systemically on a large scale. It might easily happen that, for this reason, the use of any one of them might have to be denied in cases where a life was at stake.

A warning against the indiscriminate use of neomycin is therefore justified. It should not be forgotten that most cases of impetigo and pyoderma can easily be cured with the old galenicals, such as sulphur, salicylic acid and other medicaments, without the aid of antibiotics.

ACTIVE CHEMICAL COMPOUND CAUSING SENSITIZATION

A beginning has been made in the search for the active chemical compound causing the allergic sensitization in the case of neomycin. As mentioned above, neomycin is not a single substance but it is a 'neomycin complex' containing the isomeric compounds neomycin B and neomycin C and a third entity called neamine. Neamine arises from the hydrolytic cleavage of either neomycin B or C.

It is very difficult to obtain these compounds in the pure state. Through the courtesy of S. B. Pennick and Company, New York, we recently obtained pure neomycin B, neomycin C and neamine. Positive patch tests were obtained in cases of contact dermatitis due to neomycin, not only with the isomers B and C, but also with neamine (case 3, Fig. 1). The reactions with the latter were severe.

The immediate interpretation of these results is difficult,

since the elucidation of the exact chemical structure has not progressed to the point where an unequivocal formula can be drawn. These investigations for the active compound causing allergic sensitivity to neomycin are only in the first stage. They will be continued and the results will be reported in a separate article.

SUMMARY

1. Seven cases of allergic contact dermatitis due to neomycin, and 1 case due to streptomycin are reported.

2. Patch tests with the usual neomycin ointments were often negative; by increasing the concentration to 6% in paraffinum molle, positive reactions were obtained in all 7 cases.

3. In the 7 patients with allergic contact dermatitis due to neomycin, cross-sensitivity has been observed with chloromycetin, achromycin, aureomycin, bacitracin and soframycin, but not with streptomycin. The patient hypersensitive to streptomycin did not show cross-sensitivity to the other antibiotics. The implications of these findings are discussed.

4. Diminishing activity of the test material, when not preserved in the ice chest, was found.

5. Previously positive patch-test reactions became negative while the patient was under oral treatment with steroids (medrol).

6. A warning against the indiscriminate local use of neomycin is given, since this might make it difficult, because of cross-sensitivity, to use other antibiotics systemically in circumstances where they might be life-saving.

ADDENDUM—CASE REPORTS

Case 1

A White shopkeeper, aged 23 years. Recurrent weeping eczema, chiefly of legs and hands since 1953. Treated, among other preparations, with ointments containing aureomycin, erythromycin and neomycin, and with neocortef and 'florinef' preparations, the florinef containing graneodin. In February 1959, following treatment with neomycin and 'neocortef' ointment, the skin condition worsened and the patient was admitted to a dermatological ward.

Date	Patch tests	Results
February 1959	Neomycin ointment, 0.5%	—
	3% neomycin in paraffin. molle	++
	Neocortef ointment, 1%	+
	Terramycin ointment	—
	Iloctin ointment	—
	Soframycin ointment, 1.5%	+
	Chloromycetin, 1%, in paraffin. m.	—
	Chloromycetin, 6%, in paraffin. m.	±
	Achromycin, 1%, in paraffin. m.	—
	Achromycin, 6%, in paraffin. m.	±
	Bacitracin, 3%, in paraffin. m.	+
	Aureomycin, 3%, in paraffin. m.	+
March 1960	Sulfanilamide, 5%, in paraffin. m.	—
	Anthisan cream	—
	Neomycin B, 6%, in paraffin. m.	++
	Neomycin C, 6%, in paraffin. m.	++
	Hydrocortisone succinate in water, 6%	—

Case 2

A garage hand, non-White, aged 19 years. At the beginning of July 1958 he developed weeping eczema on his face and hands. He was treated, among other preparations, with 1% neomycin ointment on the skin round the eyes. The condition improved, but relapsed after 10 days and became worse than before. Neocortef ointment, 1%, was then applied, and this was again followed by an improvement. About 10 days later the condition worsened and a 1% hydrocortisone ointment was tried but the skin condition became even worse.

Date	Patch tests	Results
March 1959	Neomycin, 3%, in paraffin. m.	+++
	Neocortef ointment, 1%	++
	Chloromycetin, 3%, in paraffin. m.	-
	Chloromycetin, 6%, in paraffin. m.	++
	Achromycin, 3%, in paraffin. m.	-
	Achromycin, 6%, in paraffin. m.	+
Nov. 1960	Aureomycin, 6%, in paraffin. m.	-
	Neomycin, 6%, in paraffin. m.	+
	Hydrocortisone sodium, 6%	+

In addition, this patient was proved to be hypersensitive to hydrocortisone. Patch tests with 1% and 6% hydrocortisone sodium were positive, as was prednisolone, but not cortisone and triamcinolone.

For further particulars of this patient, reference may be made to an earlier article of mine.¹⁰

Case 3

A housewife, aged 31 years, had suffered from 'boils in the ears' from 1954. She was treated, among other preparations, with florinef and neocortef eardrops. She used neocortef ointment

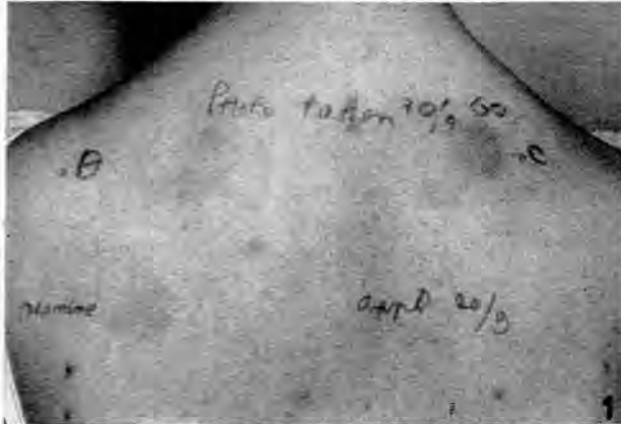


Fig. 1. Case 3. Positive reactions to patch tests with 6% neomycin B (n B), 6% neomycin C (n C), and 6% neamine, all in paraffinum molle. The photograph was taken 10 days after the application of the patch tests

for more than a year, initially with satisfactory results. Later on, in June 1959, the condition worsened and spread to both eyelids. Fig. 1 is a photograph, taken on 30 September 1960, of the patch tests performed on 20 September.

Date	Patch tests	Results
June 1959	Neomycin, 3%, in paraffin. m.	+
	Neomycin, 6%, in paraffin. m.	+
	Chloromycetin, 6%, in paraffin. m.	-
	Achromycin, 6%, in paraffin. m.	-
	Aureomycin, 6%, in paraffin. m.	-
	Bacitracin, 3%, in paraffin. m.	-
	Soframycin ointment, 1½%	+
	Streptomycin, 25%, in water	-
	Hydrocortisone succinate in water, 6%	-
	6%	-
20 September 1960	Neomycin B, 6%, in paraffin. m.	++
	Neomycin C, 6%, in paraffin. m.	++
	Neamine, 6%, in paraffin. m.	+++

Case 4

A European policeman, aged 22 years. He suffered from a generalized eczema from the beginning of 1959. He was treated with ointments containing various antibiotics, among others aureomycin, chloromycetin, and neomycin, and also with neocortef ointment. After temporary improvement the skin condition worsened.

Date	Patch tests	Results
September 1959	Neomycin, 6%, in paraffin. m.	+
	Chloromycetin, 6%, in paraffin. m.	-
	Achromycin, 6%, in paraffin. m.	-
	Aureomycin, 6%, in paraffin. m.	-
	Bacitracin, 6%, in paraffin. m.	+
	Soframycin ointment, 1.5%	±
	Streptomycin, 25%, in water	-
	Hydrocortisone succinate in water, 6%	-

Case 5

A Coloured female, a cook general, aged 46 years. She was admitted to the dermatological ward in September 1959 with seborrhoeic dermatitis. Her skin complaints had started in 1953 and had worsened for the last 6 months. She had local treatment with various ointments containing aureomycin, chloromycetin and neomycin, and with neocortef ointment. The condition gradually became worse.

After withdrawal of the neocortef ointment and administration of 4 mg. medrol tablets, 6-2 daily for several weeks, the skin condition improved. She was discharged in December 1959. Because of a recurrence, probably due to neomycin, she was again admitted to a dermatological ward and again needed medrol orally.

Date	Patch tests	Results
September 1959	Neomycin, 6%, in paraffin. m.	+
	Chloromycetin, 6%, in paraffin. m.	-
	Achromycin, 6%, in paraffin. m.	-
	Bacitracin, 6%, in paraffin. m.	-
	Aureomycin, 6%, in paraffin. m.	-
	Soframycin ointment, 1.5%	++
	Hydrocortisone succinate in water, 6%	-
June 1960	Neomycin B, 6%, in paraffin. m.	++
	Neomycin C, 6%, in paraffin. m.	++

In September 1960, while under medrol treatment with 4 mg. twice daily for several weeks, a repeat of the patch tests with the following freshly-prepared substances gave uniformly negative results:

Patch tests	Results
Neomycin, 6%, in paraffin. m.	-
Chloromycetin, 6%, in paraffin. m.	-
Achromycin, 6%, in paraffin. m.	-
Aureomycin, 6%, in paraffin. m.	-
Bacitracin, 6%, in paraffin. m.	-
Soframycin ointment, 1.5%	-

The patient, who formerly showed severe reactions to the waterproof elastoplast used for patch testing, reacted, under medrol treatment, only slightly to this material on this occasion. She was treated with medrol for several weeks, starting with 6 tablets a day and tapering down to 2 at the time of the patch tests.

On 20 September 1960, a recent patch test with 6% neamine in paraffin. m. was only slightly positive (±), becoming positive (+) after a week. Streptomycin, 25% in water, and dimycin, 25% in water, were negative.

Case 6

A European male, an auditor, aged 34 years. From the end of 1957 he suffered from dermatitis of both hands. His hobby is angling, which he carries out under the strong South African sun at the seaside. This hobby was probably the cause of the dermatitis.

In November 1958 a neocortef ointment was prescribed, and he kept the skin condition under control with this ointment, without medical supervision, until April 1960. Then a severe dermatitis of both hands developed. The neocortef ointment was withdrawn and the dermatitis gradually, although slowly, improved.

Date	Patch tests	Results
June 1960	Neomycin B, 6%, in paraffin. m.	++
	Neomycin C, 6%, in paraffin. m.	++
July 1960	(Test material prepared in January 1960)	
	Neomycin, 6%, in paraffin. m.	-
	Chloromycetin, 6%, in paraffin. m.	-
	Achromycin, 6%, in paraffin. m.	-
	Aureomycin, 6%, in paraffin. m.	-
	Bacitracin, 6%, in paraffin. m.	-
	Soframycin ointment, 1.5% (from 1957)	-
August 1960	(Repeat with freshly-prepared test material)	
	Neomycin, 6%, in paraffin. m.	++
	Chloromycetin, 6%, in paraffin. m.	-
	Achromycin, 6%, in paraffin. m.	-
	Aureomycin, 6%, in paraffin. m.	-
	Bacitracin, 6%, in paraffin. m.	-
	'Nivemycin' ointment (Boots) containing 0.5% neomycin sulphate in a bland, non-irritant anhydrous base	++

September 1960	Neamine, 6%, in paraffin. m.	..	+++
	Streptomycin, 25%, in water	..	-
	Dimycin, 25%, in water	..	-
	Hydrocortisone succinate in water, 6%	-

Case 7

A housewife, aged 61 years.

She had chronic otitis externa for several years. She was treated in 1957 with 2.5% neocortef ointment for the ears and a neocortef solution for the eyes. For some time she was also treated with aureomycin ointment.

In July 1960 she came to the dermatological outpatient department with an acute dermatitis round the left eye after application of a neocortef ointment for blepharitis of that eye. After withdrawal of this ointment the dermatitis showed improvement.

Date	Patch tests	Results
18 July 1960	Neomycin B, 6%, in paraffin. m.	++
	Neomycin C, 6%, in paraffin. m.	++
25 July 1960	(Patch tests with material prepared in January 1960)	
	Neomycin, 6%, in paraffin. m. ..	-
	Chloromycetin, 6%, in paraffin. m.	-
	Achromycin, 6%, in paraffin. m.	-
	Aureomycin, 6%, in paraffin. m.	-
	Bacitracin, 6%, in paraffin. m. ..	-
	Soframycin ointment, 1.5% (from 1957)	+
30 August 1960	(Repeat of patch tests with freshly-prepared material)	
	Neomycin, 6%, in paraffin. m. ..	++
	Chloromycetin, 6%, in paraffin. m.	+
	Achromycin, 6%, in paraffin. m.	+
	Aureomycin, 6%, in paraffin. m.	+
	Bacitracin, 6%	-
20 September 1960	Neamine, 6%, in paraffin. m. ..	+++
23 September 1960	Streptomycin, 25%, in water ..	-
	Dimycin, 25%, in water	-
	Hydrocortisone succinate in water, 6%	-

Patch tests performed on 30 August 1960 were still positive on 23 September (Fig. 2).

Case 8

A female nurse, aged 20 years.

In November 1959 her left eye became itchy and swollen. At that time she was giving many injections of streptomycin. She also had a papular rash on her fingers. When she avoided contact with streptomycin the skin condition cleared. On repeated contact there was a recurrence.

Date	Patch tests	Results
November 1959	Streptomycin, 1/100	+
	Streptomycin, 1/1,000	+
	Streptomycin, 1/10,000	+
	Streptomycin, 1/100,000	-
	Streptomycin, 25%	++

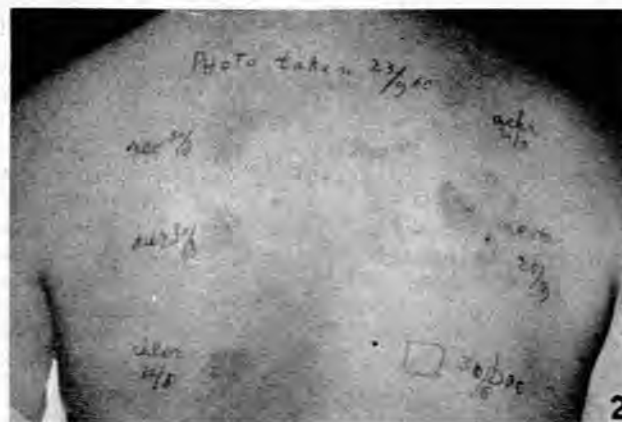


Fig. 2. Case 7. Positive reactions to patch tests with 6% neomycin, 6% aureomycin, 6% achromycin and 6% neamine, all in paraffinum molle. The reaction to 6% bacitracin was negative. All the patch tests were carried out on 30 August 1960, except that with neamine, which was performed on 20 September. The photograph was taken on 23 September 1960.

August 1960 (Patch tests with freshly-prepared material)

Neomycin, 6%, in paraffin. m. ..	-
Chloromycetin in paraffin. m. ..	-
Achromycin, 6%, in paraffin. m. ..	-
Aureomycin, 6%, in paraffin. m. ..	-
Bacitracin, 6%, in paraffin. m. ..	-
Soframycin ointment 1.5% (from 1957)	-

I am indebted to Mr. J. I. Aitken, Senior Pharmacist, Groote Schuur Hospital, and Mr. M. W. Clancy, for the preparation of the test material; to Mr. B. Todt, of the Department of Clinical Photography, for the photographs; and to the Dr. C. L. Herman Research Fund for financial aid.

REFERENCES

- Kile, R. L., Rockwell, E. M. and Schwarz, J. (1952): *J. Amer. Med. Assoc.*, **148**, 339.
- Baer, R. L. and Ludwig, J. S. (1952): *Ann. Allergy*, **10**, 136.
- Epstein, S. (1956): *Dermatologica (Basel)*, **113**, 191.
- Idem* (1958): *Ann. Allergy*, **16**, 268.
- Epstein, S. and McCormick, G. L. (1958): *A.M.A. Arch. Ophthalm.*, **60**, 1000.
- Pirila, V. and Wallenius, T. (1957): *Hautarzt*, **11**, 518.
- Sidi, E., Hincey, M. and Longueville, R. (1958): *J. Invest. Derm.*, **30**, 225.
- Cainan, C. D. and Sarkany, I. (1958): *Brit. J. Derm.*, **70**, 435.
- Reynolds, H., Hildebrand, J. F., Livingood, C. S. and Fosnaugh, R. P. (1959): *A.M.A. Arch. Derm.*, **80**, 455.
- Kooij, R. (1959): *Brit. J. Derm.*, **71**, 392.
- Pirila, V. and Rouhunkosky, S. (1959): *Acta derm.-venereol. (Stockh.)*, **39**, 470.
- Waksman, S. A. (1958): *Neomycin. Its Nature and Practical Application*. Baltimore, Maryland: Williams and Wilkins.
- Baer, R. L. (1954): *Modern Trends in Dermatology*, 2nd series, ch. 13. London: Butterworth.
- Kooij, R. and van Vloten, Th. J. (1952): *Dermatologica (Basel)*, **104**, 151.