ALLERGENS IDENTIFIED BY PATCH-TESTING IN THE CRAIGAVON AREA 1972-73

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JADASSOHN OF BRESLAU has been hailed as the originator of the patch-test (Jadassohn, 1896). But it is largely due to the work of Bonnevie (1939) in Copenhagen that the patch-test, particularly when exhibited in battery form, has come to hold its present important place in modern dermatology. Bonnevie also established a tradition for excellence in the technique of patch-testing throughout Scandinavia which has been maintained to the present day.

A number of investigations employing batteries of patch-tests has now been reported, but the largest of these studies was one carried out by ten European dermatologists and involved applying a battery of twenty common allergens to more than four thousand patients referred for a variety of reasons to dermatology clinics in Denmark, England, Germany, Holland, Italy and Sweden between March 1967 and June 1968. The results of this investigation were analysed and published by Fregert and colleagues (1969). For convenience this work will hereafter be referred to as the European study.

We felt it would be of value and interest to record the contact allergens currently prevalent in this area. Accordingly arrangements were made to patch-test all patients referred to our clinics over a period of time whom we clinically suspected to be suffering from contact dermatitis. Exactly the same standard battery was employed as had been used in the European study, but with additional patch-tests when it was considered these were indicated.

MATERIAL

The investigation ran from 1st January, 1972, until 30th April, 1973. In this period we saw 136 patients clinically suspected to be suffering from contact dermatitis. There were 60 males and 76 females of whom 58 males and 71 females were patch-tested with the standard battery, either with or without additional tests. In the remaining 2 male and 5 female patients only a number of additional patch-tests was possible. The mean age of the male patients was 44 (SD ± 19) years and of the female patients 39 (SD ± 18) years.

METHOD

The usual closed patch-test and, when indicated, the photo-patch-test, were performed in accordance with the principles at present accepted as standard (Hjorth and Fregert, 1968). The substances exhibited in the tests were applied on a 2 cm square fabric patch in the centre of a 4 cm square waterproof microporous plastic wound dressing (BPC) supplied as Airstrip Elastoplast by Smith and Nephew Pharmaceuticals Limited. In retrospect a 1 cm square fabric patch would probably be large enough to allow a satisfactory reading and would reduce the
risk of active sensitization. Controls were applied as necessary. The closed patch-tests (hereafter referred to simply as patch-tests) were removed and read at 48 hours, and as far as possible again at 72 hours. Photo-patch-tests were removed at 24 hours and the sites irradiated with a sub-erythema dose of light either as ultraviolet light from a mercury vapour arc lamp, or as natural sunlight. The photo-patch-tests were read at 24, 48 and 72 hours as far as was practicable. Twenty-four out of the 1,260 patch-tests (2 per cent) read at 72 hours were then positive, though they had been negative at 48 hours. Similarly 9 (0.7 per cent) of the tests read at 72 hours were then considered definitely negative though they had been graded as doubtful at 48 hours.

In order to increase certainty in interpretation of the tests, and precision in diagnosis, testing was carried out, as far as was possible, with single allergens. Some tests were carried out with complex materials, such as samples of proprietary applications and rubber gloves, but since interpretation of such tests is empirical and often uncertain we have confined our attention in this article to tests performed with what were, for practical purposes, single identifiable allergens.

RESULTS

Standard Battery

Table I sets out the allergens which constituted our standard battery, together with their concentrations, vehicles, usual sources and percentage of positive results by sex. In the Craigavon area 41 per cent of males and 42 per cent of females gave no positive results with the standard battery. Corresponding figures in the European study were approximately 60 per cent for each sex. The higher incidence of positive results in the Craigavon study is probably due to the fact that this was limited to patients who clinically were suspected to be suffering from a contact dermatitis, a constraint which did not apply so strictly in the European study.

Table II sets out the allergens by ranking order of positive results in both the Craigavon and European studies. While at first glance there appears to be little concordance, on closer inspection a tendency to a common pattern becomes apparent. Metals, balsams and tars are high in ranking order in both sexes in both studies. In the European study, however, chromium sensitivity was much commoner than nickel sensitivity in males, while in females this order was reversed. Sensitivity to balsams and tars probably represents a wide range of cross sensitizing allergens, including perfumes, essential oils, flavouring agents and medicaments (Hjorth 1961; Fregert and Hjorth, 1968). The total number of patch-tests carried out by means of the standard battery in the Craigavon area was 2,580 and of these 165 (6 per cent) were positive, the corresponding figure in the European study was 4 per cent.

We agree with Fregert and associates (1969) that the degree of relevance attributed to a positive result depends to a large extent on the subjective opinion of the attending clinician. Accepting that this is so, it is considered that approximately half (84) of the positive results obtained with the standard battery in the Craigavon area were relevant to the patients’ disease. Positive results with neomycin,
### Table I

*Allergens exhibited as a patch-test battery in respect of fifty-eight male and seventy-one female patients*

| Allergen                                      | Usual Sources                                                      | Positive results (per cent*) |
|-----------------------------------------------|-------------------------------------------------------------------|----------------------------|
|                                               |                                                                   | Male | Female |
| Potassium dichromate 0.5%                     | Builder's cement                                                  | 9    | 8      |
| Cobalt chloride 1%                            | Cross reactions with chromates and nickel, possibly builder's cement | 5    | 13     |
| Nickel sulphate 2.5%                          | Nickel plated objects                                             | 9    | 11     |
| Formaldehyde (in water) 2%                    | Plastics, textiles, medicaments, preservatives, etc.              | 3    | 3      |
| p-Phenylenediamine 2%                         | Dyes                                                              | 0    | 7      |
| Mercaptobenzthiazole 1%                       | Rubber chemical                                                   | 3    | 4      |
| Tetramethylthiuramdisulphide 1%               | Rubber chemical                                                   | 7    | 7      |
| Phenylcyclohexyl-p-phenylene-diamine 1%       | Rubber chemical                                                   | 0    | 3      |
| Diphenyl-p-phenylenediamine 1%                | Rubber chemical                                                   | 2    | 1      |
| Balsam of Peru 25%                            | Cross reactions with related cmpds., balsams, perfumes, medicaments, etc. | 7    | 17     |
| Turpentine peroxides (in olive oil) 0.3%      | Paints, polishes, liniments                                       | 3    | 0      |
| Neomycin sulphate 20%                         | Medicaments                                                       | 5    | 7      |
| Benzocaine 5%                                 | Medicaments                                                       | 0    | 6      |
| Chinoform 5%                                  | Medicaments                                                       | 2    | 7      |
| Chlorquinaldol 5%                             | Medicaments                                                       | 3    | 6      |
| Wool alcohols 30%                             | Topical applications (lanolin)                                    | 7    | 13     |
| Parabens (methyl-, ethyl-, propyl-, butyl-, benzyl-) 3% each | Preservative in topical applications                              | 9    | 10     |
| Coal Tar 5%                                   | Tar products, medicaments                                         | 9    | 8      |
| Wood tars (pine, beech, juniper, birch) 3% each | Tar products, medicaments                                         | 10   | 13     |
| Colophony 20%                                 | Adhesive tape, Polishes                                           | 9    | 6      |

The allergens, dispersed in petroleum Ph.Nord.63 except where indicated, were supplied by Trolab, Denmark.

* Percentages based on totals for each sex independently.
**Table II**

*Ranking order of positive reactions from standard battery in males and females*

| Rank | MALES | FEMALES |
|------|-------|---------|
| **MALES** | Craigavon | **FEMALES** | Craigavon |
| 1 | Chromate | Wood tars | Nickel | Balsam of Peru |
| 2 | Wood tars | Chromate, nickel, parabens, colophony, coal tar | Wood tars | Cobalt, wood tar, wool alcohols |
| 3 | Cobalt | TMTD, balsam of Peru, wool alcohols | Balsam of Peru | Nickel |
| 4 | PPD | Cobalt, neomycin | Cobalt | Parabens |
| 5 | Turpentine | Formaldehyde, MBT, chlorquinaldol, turpentine | Turpentine | Chromate, coal tar |
| 6 | Balsam of Peru | Diphenyl—PPD, chinoform | Benzocaine | PPD, TMTD, neomycin, chinoform |
| 7 | Neomycin | PPD, benzocaine, phenylcyclohexyl—PPD | PPD | Benzocaine, chlorquinaldol, colophony |
| 8 | Coal tar | Formaldehyde | Neomycin | Formaldehyde, phenylcyclohexyl—PPD |
| 9 | Benzocaine | Neomycin | Formaldehyde | MBT |
| 10 | Formaldehyde | Chromate | Diphenyl—PPD |
| 11 | Colophony | Colophony | Turpentine |
| 12 | Wool alcohols | Coal tar | |
| 13 | Nickel | Wool alcohols | |
| 14 | Phenylcyclohexyl—PPD | TMTD | |
| 15 | MBT | Parabens | |
| 16 | TMTD | MBT | |
| 17 | Chinoform | Chinoform | |
| 18 | Parabens | Phenylcyclohexyl—PPD | |
| 19 | Diphenyl—PPD | Chlorquinaldol | |
| 20 | Chlorquinaldol | Diphenyl—PPD | |

*Abbreviations:*
- Mercaptobenzthiazole (MBT)
- Paraphenylenediamine (PPD)
- Tetramethylthiuramdisulphide (TMDT)
parabens (esters of p-hydroxybenzoic acid), lanolin (wool alcohols) or rubber chemicals are thought particularly likely to be relevant. In the European study the positive results most often considered relevant were those obtained with chromium, lanolin (wool alcohols), neomycin, nickel, parabens esters and rubber chemicals.

Additional Allergens

An additional 142 tests were carried out on 43 patients. These tests were performed in the light of patients' individual histories and clinical findings. Table III sets out the positive results which were obtained with the additional tests together with an indication of the suspected source. The positive results obtained with these allergens were found to have a high degree of relevance, 36 out of the total of 40 positive results (90 per cent) being considered relevant to the aetiology of the skin disease under investigation.

The large number of positive results (26) obtained with quindoxin (Grofas) made this the most frequently diagnosed sensitivity in the entire investigation. Quindoxin has been widely added to animal feeds in the order of 20 to 50 mg per kg as a growth stimulant. Attention has previously been drawn to the fact that quindoxin is a potent photosensitizer and individuals who are allergic to it develop a

| Allergen                              | Usual Sources                  | Positive results | Male | Female |
|---------------------------------------|--------------------------------|-----------------|------|--------|
| Epoxy resin 1%                        | Adhesive                       | 2               | 1    |        |
| Triethylenetetramine 0.5%             | Epoxy curing agent             | 1               | 0    |        |
| Tetramethyli thiurammonosulphide 1%  | Rubber chemical                | 1               | 1    |        |
| 1, 3-diphenylguanidine 1%             | Rubber chemical                | 1               | 0    |        |
| Cinchocaine chloride 1%               | Medicament                     | 0               | 1    |        |
| Amethocaine 1%                        | Medicament                     | 0               | 2    |        |
| Cyclomethycaine chloride 1%          | Medicament                     | 0               | 1    |        |
| Gentamicin 1%                         | Medicament                     | 0               | 1    |        |
| Butyl parabens 3%                     | Preservative in topical applications | 1           | 0    |        |
| Quindoxin 0.1% (photo-allergen)       | Growth stimulant in animal feeds | 13             | 13   |        |
| Chrysanthemum leaf                    | Plant                          | 1               | 0    |        |

The allergens listed from epoxy resin to cyclomethycaine inclusively were obtained from Trolab, Denmark, dispersed in petrolatum Ph. Nord. 63. The remainder were prepared in yellow soft paraffin (BP) apart from the chrysanthemum leaf. Samples of gentamicin, parabens, and quindoxin were obtained by courtesy of Roussel Laboratories Ltd., Upjohn Ltd., and Imperial Chemical Industries Ltd. respectively.
photocontact dermatitis on coming into skin contact with animal feeds in which it has been incorporated (Dawson and Scott, 1972; Scott and Dawson, 1973). It is hoped that quinoxin dermatitis will now cease to be a problem in the agricultural community as there has been an announcement in the press that Imperial Chemical Industries Limited, who manufactured it, have withdrawn it from the market as they have reason to suspect it can be carcinogenic in experimental animals when fed to them in high dosage.

Contact allergy to gentamicin is usually considered to be uncommon so that our one patient found to have this sensitivity is perhaps worthy of special mention.

The patient with the contact sensitivity to butyl parabens had previously shown a positive reaction to the parabens mixture in the standard battery. He had used a single preparation for many years in the treatment of regional eczema, and it was known that this contained butyl and methyl parabens only as preservatives. On testing with each type of parabens individually it was interesting to find that a positive result developed with butyl parabens only.

**DISCUSSION**

As there is no instrument which can read a patch-test, any reaction which develops must be interpreted by the clinician either as a direct irritant effect, a true contact allergy, or possibly a combination of both. The relevance of a positive result to the patient’s disease is also a matter of clinical judgement, for by no means all the contact allergies an individual may have are necessarily relevant in respect of a contact eczema from which he may be suffering. The hazards and possible sources of error inherent in the exhibition and interpretation of the patch-test have been well reviewed by Hjorth and Fregert (1968). Among these the possibility of actually inducing sensitization, and the difficulty posed by false negative results are particularly important.

In spite of the difficulties, labour and hazard associated with patch-testing, it remains a most powerful tool with which to investigate cases of contact dermatitis; without its use many misdiagnoses might be made and even injustice in the medico-legal sense perpetrated. Nevertheless the diagnosis must ultimately rest on clinical observation, with the patch-test acting as an ancillary aid. We subscribe to the belief which has previously been so eloquently expressed in these pages, that the school of Cnidus still yields the palm to the school of Cos (Biggart, 1971).

Finally, in view of the number of cases in which sensitivity to medicaments was detected, both in the Craigavon and European studies, and the possibility that the patch-test may itself sensitize, it seems not inappropriate to end by recalling that noble exhortation handed down to us from the Father of the Art: “primum non nocere.”

**SUMMARY**

Patients seen at dermatology clinics in the Craigavon area 1972-73 who were clinically suffering from contact dermatitis were patch-tested with a standard battery of twenty common allergens and in selected cases also with additional allergens. The results of this investigation are presented and compared with those reported from other European clinics.
In general, experience with the standard battery in the Craigavon area was similar to that obtained elsewhere in Europe. Positive results with the standard battery were most often found with balsams, esters of p-hydroxybenzoic acid, metals, tars and wool alcohols (lanolin). The sensitivities demonstrated by the standard battery considered to have greatest relevance were due to esters of p-hydroxybenzoic acid, neomycin, rubber chemicals and wool alcohols (lanolin).

The most frequently diagnosed sensitivity in the entire series however was due to quindoxin (Grofas) which was included among the additional allergens. Twenty-six patients were found to have a photosensitivity in respect of this substance which has been used in agriculture as a growth stimulant incorporated in animal feeds. The manufacturers have now announced withdrawal of quindoxin from the market on the grounds that they suspect it may be a carcinogen and it is therefore hoped no further case of photosensitivity from this source will arise.

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