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TERMINOLOGY OF CONTACT DERMATITIS

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From the International Contact Dermatitis Research Group

"There is almost nothing, good or bad, you cannot do with words, if only you know how to use them" (2).

It is apparent to anyone studying the literature of contact dermatitis that there is a great confusion in the terminology and conventions employed. The Members of the International Contact Dermatitis Research Group have aimed at a standardization of terms used to describe the phenomena of contact dermatitis and the results of patch testing. Discussion about this has been prolonged and arduous and the members of the Committee are under no illusion that their suggestions will be universally accepted. It is obviously important to attempt to standardize the methods used in the patch test procedure, but the benefit of this would be limited if the results could not be communicated in a manner that was accurate and universally comprehensible. In time computerization will doubtless reduce all communications to an agreed set of symbols; meanwhile we must make do with the language and with signs. But these involve national and cultural differences that are not easily altered. We are aware that our suggestions may evoke traditional or emotional objections. We hope that these will be abandoned in the interests of uniformity in a field where accuracy in reporting, as in recording, is the best counterbalance to the vagaries of the human test subject.

In attempting to find an agreed definition and nomenclature of terms used, the Committee had also to bear in mind the different meanings imposed by usage within the same basic language and felt that these should not be sacrificed unnecessarily. "Use familiar words rather than the far-fetched, if they express your meaning equally well; for the familiar are more likely to be readily understood" (5). Those members of the Committee involved in editorial duties were particularly aware of the need for the symbols to be clear, short and unequivocal; where two alternatives existed, that one which took less printed space was preferred. The recommendations, therefore, represent a compromise, but we have been at pains to avoid introducing new terms and have preferred to accept one of two established conventions rather than to mix these to produce a hybrid. This solution will not satisfy everyone but it is hoped that many of the suggestions may become generally acceptable and that others may be the subject of an informed and constructive dialogue which may lead to further improvements or a wider measure of agreement.

The terms and symbols in question fall into three groups:

(i) Symbols used to record patch test techniques and results.

(ii) General terms used to describe delayed, contact-types sensitivity.

(iii) Specific terms used to describe the mode and variants of the sensitization process.

Symbols Used to Record Patch Test Techniques and Results

The notation used in recording patch tests varies throughout the world and even within the same national cultures. It is usual to describe results in terms of $-$ and $+$. But there is no universal agreement on the exact meaning of the symbols used; particularly the sign $\pm$ and $+++$. In the USA these algebraic symbols are replaced by the Arabic 0 to $4+$; these save space

but are difficult to translate into visual terms and may invite confusion with numbers used to denote the subjects involved. After considerable discussion the Committee favoured the following:

NT not tested
?+ doubtful reaction
+ weak (non-vesicular) reaction
++ strong (oedematous or vesicular) reaction

It was agreed that

+++ extreme reaction

might sometimes be required. This would normally signify a bullous or ulcerative reaction.

IR should be used to denote an irritant reaction.

The sign − should be used for negative reactions in preference to 0, which may be construed as meaning 'not tested'.

Photopatch tests should be graded in the same way as allergic reactions, with the prefix Ph; thus:

Ph?+ Ph− Ph+ Ph++ Ph+++ Ph NT

Duration of application of the patches should be stated in the original account of the method used (e.g. one or two days).

Time of reading tests. This is usually given as 48 hour (1st) and 72/96 or 72–96 hour (2nd) after application. The joint European study (4) showed that the first reading is often performed at 72 hour and that this might be regarded as a 'first reading' (equivalent to a 48 hour reading) or as 'second reading' (equivalent to a 96 hour reading). It was, therefore, decided to recommend the *day of reading* instead of the hours, to avoid giving a misleading impression of an exact time of reading which, in fact, was not always the case. Thus:

D1 = 24 hours (particularly for phototests)
D2 = 48 hours
D4 = 96 hours
D7 = 1 week

The patch test. When used without qualification, it should be written thus, without hyphen, and refers to the standard 'closed' 48 hour method of testing a presumed allergen (4). If qualification is needed, the words 'standard' or 'conventional' can be used without fear of confusion but the term '*open*' *must* be used when this exceptional method of testing is used. '*Photopatch*' or 'phototest', though coined adjectives, are the shortest terms available in English to describe a patch test irradiated by natural or artificial light. The terms do not imply the use of any particular method, which must be described in full. The terms '*patch test readings*' and '*patch test results*' are self-evident. '*Patch*' refers to the single piece of material or unit on which the allergen is applied to the skin. It should be fully described, e.g. "Al-test IMECO, Stockholm, in strips of five patches were used . . ." (4). The vehicle and concentration of allergen used must also be specified, Vaseline®, or yellow soft paraffin are best abbreviated as '*pet.*' (yellow petrolatum). '*Test substance*' is the preferred term for the agent used in testing and does not prejudice the issue of sensitization.

Where the standard method of patch testing is compared with *intradermal* or *intracutaneous* tests, the terms '*epidermal*' and '*epicutaneous*' are synonymous. The latter is more widely used at present. The choice depends on style and syllogy.

A number of allergens grouped together for the purpose of testing can be referred to as a '*test series*' or a '*battery*', e.g. the '*standard test series*' used in the Committee's investigation of sensitivity reactions in eight centres (4); or a '*shoe battery*', '*medicament battery*', etc.

If this military metaphor were to be enlarged, one could refer similarly to '*aimed*' patch tests, e.g. where bichromate alone is applied in suspected cases of chrome sensitivity; or '*random*' testing, e.g. when chrome and other metals, but not a complete battery, are applied in cases of suspected metal allergy.

General Terms Used to Describe Delayed-type Sensitivity

Irritants and Sensitizers. The terms 'toxic' and 'irritant', whether relating to substances or forms of dermatitis, are interchangeable. But 'toxic', in English, has wider implications as in 'toxicology', the 'toxic' effect of a drug, etc. This can lead to confusion, whereas the term 'irritant' implies, more exactly and correctly, the local effect of a substance on a part of the body with which it is in contact and is therefore the preferred term. The Committee recognise that this semantic difference is particular to English and that the term 'toxisch', for instance, may remain the correct term in German.

'*Primary irritant dermatitis*', retained by usage, is pleonastic and the word '*primary*' should be omitted. Thus:

Irritant (contact) dermatitis describes the effect caused by a strong irritant on the skin, e.g. that caused by a strong alkali. The term '*acute irritant dermatitis*' may be used in contrast to '*cumulative insult dermatitis*', which, though cumbersome, is exact in the description of a dermatitis developing 'after repeated insults by weak primary irritants over a long period' (7). It is to be preferred to '*traumiterative dermatitis*' (6). '*Wear and tear dermatitis*' is an acceptable alternative (9). '*Allergen*' and '*sensitizer*' are synonymous and the Committee expressed no preference. Choice will depend on context, style and euphony. '*Allergenic*' is self-evident.

'*Primary allergen*'. The prime substance inducing sensitization.

'*Secondary allergen*'. Substances closely related to or partly identical with the primary allergen which evoke a reaction in patients sensitized to this.

'*Hapten*', indicating an incomplete allergen, should be used only to convey this exact meaning.

'*False positive reaction*'. A positive patch test reaction not due to allergic sensitivity. Such reactions are usually irritant in nature; some are characteristic, e.g. the punctate or pustular reaction of metals; the 'glazed' reaction of hexachlorophane, etc.

'*False negative reaction*'. A negative reaction occurring in a person in fact sensitive to the substance tested. This is usually due to insufficient concentration or inadequate penetration.

'*Prophetic (or 'predictive') patch test*'. A term used to describe the deliberate assessment of the sensitization property of a new substance or its comparison with that of known substances of a similar type. The particular techniques used should be exactly specified (3, 8).

A '*lost reaction*' is one which was previously positive and found subsequently to be negative under identical environmental and experimental conditions.

'*Sensitizing index*', (or '*potential*'). "The relative capacity of a given agent to induce sensitization in a group of human beings and animals" (10).

'*Index of sensitivity*'. "The incidence of positive reactions in a population of a previously acquired sensitivity to a given agent as compared with other agents" (10).

'*Latent period*'. The interval between first contact with a sensitizer and the observed onset of sensitization.

'*Refractory period*'. A period of patch test unresponsiveness following a severe allergic reaction.

'*Reaction time*'. The time between exposure of a previously sensitized subject to the specific sensitizing allergen and the development of the clinical reaction. This may vary from 8–120 hours.

'*Eliciting threshold concentration*'. In the context of patch testing this denotes the lowest concentration of a test substance that will detect a positive patch test response. This is preferred to 'degree of sensitivity' and 'level of sensitivity'.

Specific Terms Used to Describe the Mode and Variants of the Sensitization Process

The exact definition of terms used to describe the various phenomena and relationships of the sensitization process are often loosely construed.

'*Sensitization*' is the process of being sensitized.

'*Sensitivity*' indicates that this process has occurred in the fully sensitized state.

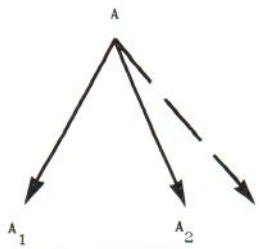
The term '*latent sensitivity*' is a confusing one and should be abandoned in the interests of clarity. It has been used to describe a state in which a patient is sensitized (clinically or by patch test) but who has not yet had sufficient contact with the allergen to develop clinical signs of sensitivity. The term '*unrevealed sensitivity*' would be more accurate.

A positive patch test is considered 'relevant' if the allergen is traced. If it reflects a past episode of contact dermatitis it should be referred to as '*sensitivity with past relevance*'. This is synonymous with '*immunological scar*', a striking term which is not, however, recommended for use in this context.

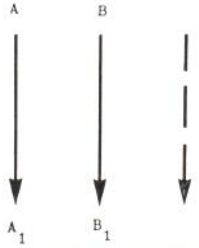
If the source of a positive patch test is not traced, the term '*unexplained positive*' should be used.

A '*photoreaction*' is a reaction dependant upon the transformation of a substance (usually of low molecular weight) into an irritant or an allergen by irradiation with light.

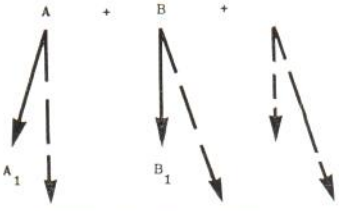
'*Phototoxicity*' is concerned when a non-immunological photo-irritant reaction can be elicited in most individuals on first exposure to a suffi-



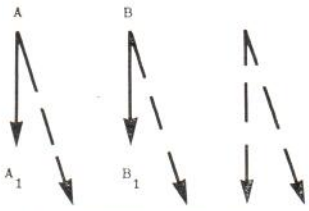
1. Single sensitization.



2. Multiple sensitization.

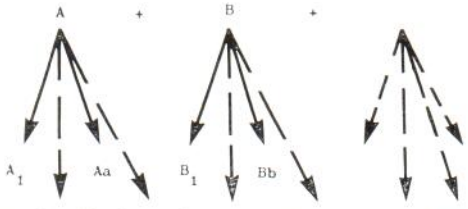


3. Concomitant sensitization.



4. Simultaneous sensitization.

5. Cross-sensitization.



6. Combination of cross- and concomitant sensitization.

Fig. 1. Modes of Contact Sensitization (reproduced from Contact Dermatitis Newsletter (1969) p. 109 by kind permission of the Editor).

cient concentration of a phototoxic agent and a sufficient intensity of light of the correct wavelength. It thus corresponds broadly to an eliciting *'irritant reaction'*. *'Photosensitivity'* or *'photo-allergy'* is an immunological state requiring exposure to a photosensitizer and to the appropriate wavelength of light followed by a latent interval for the development of the immunological response, a photo-allergic reaction; and then by a rash evoked by light but not necessarily confined to the light-exposed areas.

The term *'active sensitization'* is widely used to denote sensitization induced by patch testing but can be construed in other ways. In order to avoid confusion the Committee prefer the term *'patch test sensitization'*. Several terms are used to describe the reaction occurring at the site of a patch test on day 7 (D7) or later, with no preceding reaction on days 1–6 (D1–D6), e.g. 'delayed flare-up', 'focal flare-up', 'flare-up reaction'. This reaction, the manifestation of patch test sensitization due to the interaction of residues of the allergen with the newly sensitized tissues, is best and most simply called the *'late reaction'*.

'Cross-sensitization' (see below). The Committee preferred the expression 'cross-sensitization *to*' rather than the use of other prepositions.

'Hyposensitization'. An induced increase in the threshold of sensitivity induced deliberately or (sometimes) acquired by natural re-exposure to the allergen.

Multiple sensitivities. The confusion surrounding the use of this expression is partly due to our lack of knowledge of the mechanism or relevance in a given situation. But when this is known, the appropriate term should be used (Fig. 1).

Multiple non-specific reactions. These are multiple reactions which occur especially when testing is carried out in patients with active eczema, on damaged skin or under any conditions in which reactivity is abnormally enhanced.

Multiple primary specific sensitivities. Also referred to as 'concomitant *sensitivity*'. Multiple sensitivities to substances that are unrelated chemically, e.g. lanolin and neomycin. One sensitivity may predispose to the acquisition of another, e.g. by treatment; or there may be a genetic or constitutional predisposition to acquire sensitivities easily.

Multiple secondary specific sensitivities. Allergic sensitization engendered by one compound, the *primary allergen,* extends to one or more compounds, then *secondary allergens,* (1). The allergens are related chemically or are converted to substances that are identical or closely related, so that the sensitized cells are unable to distinguish between them.

Multiple reactions to compounds containing an identical allergen

('False cross-sensitivity'). Positive reactions to substances which are apparently unrelated but which in fact contain an identical or closely related substance, which is the sensitizer. Thus, cobalt may contain traces of nickel and *vice versa;* balsams and other natural substances may contain related or identical substances; the same impurity may exist in widely differing products. It is obvious that these multiple reactions are often a reflection of our ignorance.

Examples of modes of multiple sensitization are illustrated in Fig. 1.

Single sensitization

A induces sensitization. A_1 and A_2 are the same substance as A but occurring in different products and under different guises, e.g. chrome in cement, matches and anti-corrosive agents.

Multiple sensitization

A and B occur in different products and usually induce sensitization at different times. A_1 and B_1 are the same substances as A and B but occur in different products. They may elicit sensitization at the same or at different times, e.g. nickel and rubber additives.

Concomitant sensitization

Here, A and B are present in the same product and both induce sensitization. A_1 and B_1 are the same substances as A and B but are present in different products and may elicit contact dermatitis at the same or at different times, e.g. chrome and cobalt in cement; MBT and TMTD in rubber gloves.

Simultaneous sensitization

A and B are present in different products but may induce sensitization simultaneously. A_1 and B_1 are the same substances as A and B and are present in different products and elicit contact dermatitis separately, e.g. chrome in cement and additives in rubber gloves.

Cross-sensitization

A is the primary allergen, inducing sensitivity. A_a is the secondary allergen, chemically related to A and also capable of eliciting contact dermatitis, e.g. neomycin and Kanamycin.

Combination of cross- and concomitant sensitization

A and B are present in the same substance and induce sensitization. A_1 and B_1 are the same chemical substances as A and B but are present in different substances. They may also elicit contact dermatitis. A_a and B_b are cross-reacting substances, i.e. secondary allergens, present in different substances, but capable of eliciting contact dermatitis. For example, balsams containing many unknown allergens. The distincton between cross- and concomitant sensitization are often difficult to determine.

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