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Rehabilitation in Allergy

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A definition of allergy “in a nutshell”

Allergy is an altered state of the immune system – the “defense system” of the body against infections – of an individual. Allergy leads to certain more or less typical signs and symptoms after contact with materials which are not causing these signs and symptoms in non-allergic subjects under similar circumstances of exposure. The specific materials capable of causing allergy are termed allergens.

Characteristics of Allergy

In the degree of detail necessary to understand the implications of allergy for secondary prevention and rehabilitation the following characteristics of allergy are explained; however, for a deeper understanding of the mechanisms, signs and symptoms, and treatment of allergy the reader is referred to standard textbooks and authoritative (systematic) reviews available in the international or national literature:

Allergenic Potency

The proportion of people affected by an allergy to a certain material varies greatly between different materials, which depend on the potential of the material for causing allergies. “Strong allergens” include, for instance, epoxy resin components or ragweed pollen, while “weak allergens” include, for instance, lanolin (wool fat) or pine tree pollen.

Extent of exposure

Obviously, the extent of exposure is crucial for the frequency of allergy in the population as well: if a strong allergen is only found in a confined working or other special environment, fewer persons will be affected than if the same allergen was found in everybody's daily life. One example is “poison ivy” (Gladman 2006). In North America, up to 70% of the population has been estimated to be allergic to this plant, whereas in Europe, or other regions of the world where this plant is found in botanical gardens only, allergic people are accordingly rare.

Individual susceptibility

Only certain individuals, i.e. not everybody, are affected by a certain allergy. This is in contrast to so-called toxic effects, which are an obligatory consequence after contact with a certain material (e.g. Poisons such as arsenic or physical exposures such as radioactivity). The effect of these noxious agents depend much more or exclusively on dose (amount and time) than on individual characteristics. It is a longstanding observation that a “family” of allergic diseases comprising hay fever, bronchial asthma and atopic eczema clusters in families, which points to a certain genetic background, in addition to the sharing a family's micro environment. For another family of allergies affecting the skin, like the poison ivy dermatitis example quoted above, research has not yet identified the determinants of susceptibility there may be – considering the observation that, e.g., in a group of construction workers doing the same job for decades, only one or two will develop cement dermatitis (chromate allergy).

Different general mechanisms of allergy

"Allergy" comprises a number of quite different mechanisms of unwanted immune reactions. The two most important mechanisms are described in the following sections.

Immediate type hypersensitivity

The reaction is caused by proteins contained in biological material such as pollen, mites, animal dander, insect venoms, foodstuffs and the like, and more rarely by small molecules (chemicals) that are capable of binding to "innocent" proteins occurring in the human body, changing their appearance so that they are recognized as "foreign", that is, as allergens. The spectrum of disease, occurring within a few minutes to a few hours after contact with the offending material, includes (i) hay fever (allergenic rhinitis or allergenic conjunctivitis, often combined) with itchy, stuffed or runny nose, and itchy and watering, crusted eyes, respectively, (ii) allergic bronchial asthma with wheezing, chest tightness and shortness of breath, which can be so severe as to be life-threatening, and (iii) atopic eczema (atopic dermatitis). Regarding the latter disease, two important subgroups have been identified: (a) intrinsic atopic eczema, with no conceivable environmental triggers in terms of allergens, and (b) extrinsic atopic eczema, which is much more common, and in which allergens may play an important role (Brenninkmeijer et al. 2008). Allergens comprise, in this setting, food allergens (particularly in children), but also airborne allergens coming into contact with the skin, such as pollen or house dust mite. Hives, i.e. immunological (contact) urticaria, with itching and wheals, following skin contact or ingestion of proteinaceous material, appearing and vanishing within a few hours, sometimes associated with swelling of the lips or other parts of the body, are another manifestation of immediate type hypersensitivity. If the mucosa of the airways is affected, this condition may be life-threatening. The most dramatic and potentially fatal consequence of immediate type hypersensitivity is anaphylactic shock.

However, it should be mentioned that all signs and symptoms mentioned can also occur without proven underlying allergy; in these cases "intolerance" as a more general term is often used – which does, from a practical point of view, not make much difference for the affected patient. Moreover, allergic bronchial asthma may become chronic relapsing in the sense that it will, after some duration, be triggered not only by the original allergen(s), but also by non-specific factors such as exercise, cold air and the like. One difference, however, exists at the level of diagnosing allergy versus intolerance: the former can usually be proven by skin tests (prick test) or blood analysis (specific IgE antibodies). In contrast, the latter can only be verified by controlled exposure tests with defined, minute amounts of the incriminated substance(s), which is both cumbersome and not without risks. Both diagnostic procedures have to be performed by specialist doctors only.

Delayed type hypersensitivity

This is a much slower reaction mostly confined to the skin, i.e., rarely affecting the conjunctivae, oral mucosa or other mucosal areas. The onset of symptoms (itching) and signs (redness, swelling, vesicles (little blisters in the uppermost layer of the skin), crusts, oozing, later fissuring) is only after several hours to few days following skin (or mucosal) contact with the offending material. The resulting disease called allergic contact dermatitis is sometimes easy to recognize, if the affected skin area corresponds to a previous characteristic contact area, e.g., to jeans, earrings or deodorant. In other cases, the clinical picture is less suggestive, making it more difficult to arrive at a hypothesis regarding the culprit allergen(s). In most cases, a diagnostic skin test called patch test is necessary to confirm suspected causes or, if history and clinical pattern are not characteristic, to find a hint or even a full explanation. During the patch test, the skin is exposed to minute amounts of well-defined substances known to cause contact allergy. Usually, the patch test includes a "baseline" series (a collection of those contact allergens which have been proven to be most important – in the respective country or region) supplemented with more special allergens as selected according to the patient's history. If the causative substance has been identified, it will be necessary to avoid skin

contact with this substance to avoid relapses of allergic contact dermatitis (see below).

Diagnostics, the first step to successful secondary prevention and rehabilitation

Allergy is a very specific condition in terms of the substance(s) which act(s) as allergen in the individual case, even if the resulting disease, be it “hay fever”, bronchial asthma, urticaria or contact dermatitis, appears relatively uniform, that is, the signs and symptoms are independent of the actual cause. This implies that the signs and symptoms themselves are not helpful in finding the cause of disease (the allergen(s)). However, the time course or, in case of contact dermatitis, the anatomical site (first) affected may give important clues to the experienced allergy specialist, or sometimes to the patient. Such clues can guide the selection of allergens employed in skin or laboratory testing in terms of special series or batteries of allergens, which are usually tested in addition to a baseline series of the overall most important allergens.

Still, despite greatest care and broad experience it may happen that an actually existing allergy is not reflected by a positive test to the culprit allergen, or the panel of tests did not include the particular allergen. This unfortunate result is called a “false-negative” test. The opposite may also be true: a test is unequivocally positive to a substance which is actually not an allergen for the patient – either it has never been an allergen (then it is a “false-positive” test result), or it has been responsible for a past episode of disease, but not for the current episode the patient presents with (hence this would be a test result with “past relevance”, but not current clinical relevance). In the ideal case, which is probably also the most common case, the test does identify the culprit allergen and thus “explains” the current episode of disease. This alone can be an achievement, after possibly weeks, months or even years of health problems and previous attempts to solve them.

However, beyond the value of retrospectively elucidating the individual health problems, diagnosing allergy has another, even more important aspect of enabling future avoidance of the allergen(s) identified, or, where this is not possible, at least targeted strategies to lessen the burden of individual disease. This double benefit renders appropriate diagnostic allergy testing an indispensable cornerstone of allergy secondary prevention and rehabilitation.

Secondary prevention of allergy

The avoidance of future relapses of allergic manifestations is secondary prevention on the individual level. It is a basic strategy to be followed before any measures of tertiary prevention, i.e. rehabilitation, are recommended or taken. In other words: there is no (should be no) rehabilitation without underlying secondary prevention. Hence, secondary prevention is given some room in this article.

Secondary prevention has to take into account a multitude of individual or societal factors to be both feasible and effective:

The exposure context

Evidently, an allergen encountered at the workplace should prompt secondary preventive measures in terms of occupational hygiene (e.g., personal protective systems for a baker with wheat flour allergy or a painter with bronchial asthma due to diisocyanates or a turner with allergic contact dermatitis due to industrial preservatives in the cutting oil he has been using, or re-allocation to work without exposure to his or her allergen(s), as possible). If feasible and successful, this preventive action will result in a complete resolution of disease.

Conversely, an ubiquitous environmental allergen like birch or ragweed pollen would necessitate a different avoidance strategy: moving to a non-exposed area for the blossoming season. This is, for

most people, hardly possible at least on a regular basis, so that therapeutic and rehabilitation strategies are the only realistic option here (including use of antihistamines or other medications, or hypo sensitization, see below). If the source of the allergen is found in the home environment, as in the case of furred pets, house dust mites, mould spores and the like, a removal or containment of these sources is evidently an important part of the overall strategy.

Who will pay

There may be implications regarding which institution (mostly some sort of insurance) will have to pay for the tangible costs of allergic disease. These include, above all, medical diagnostics and advice, treatment, possibly lost working days, potentially personal protective equipment or additional costs for the employer resulting from the need to rearrange the production or service process around a worker affected by allergic disease, to enable further employment. In the occupational setting, costs might ultimately include worker's compensation or funds for professional retraining, if the present workplace turns out to be intolerable even after modifying it. In those societies that have implemented insurance schemes covering occupational accidents and diseases, insurance is often a driving force, side by side with governmental or state regulatory institutions and researchers in this field, of setting up and promoting or enforcing suitable occupational hygiene measures in terms of primary prevention. This is, as long as primary prevention is cost-effective, a “win-win” situation for all stakeholders.

Regarding secondary prevention, which is the focus of this section, the degree of coverage of costs by occupational accident (employers liability) insurances may greatly vary between countries and is thus not discussed further here. A similar world-wide variability can be noted beyond the occupational context, i.e. regarding health insurance systems, which may or may not refund costs incurred during the treatment and rehabilitation of allergic disease. For instance medical costs may be covered at least to some extent, but not costs for special requirements at home, such as mite-proof mattress covers and the like.

Allergen characteristics

Allergens may differ regarding how easily they are recognized in the individual environment – both in the field of respiratory or skin “immediate type” allergens and in the field of (skin) contact “delayed type” allergens. Expert advice on the occurrence of these allergens, after a thorough and comprehensive allergy test procedure (see above) will be a first step. However, a severe, partly threatening problem are hidden sources of the allergen, which is a well-known problem in peanut allergy, where minute amounts in foodstuffs normally not containing peanut may cause severe allergic reactions, at least in highly allergic persons. Generally, food (especially if it is industrially processed) requires special care in the avoidance of food-related allergens. Another problem is the fact that, for instance, pollen allergy often implies not only symptoms after inhalation or other contact with the respective pollen, but also after ingestion of certain foodstuffs containing allergenic structures related to those causing allergy by pollen. One example is the “oral allergy syndrome” (Kondo and Urisu 2009); for instance in people sensitized to birch pollen who develop itching, burning and swelling of the oral mucosa or even more generalized and severe symptoms after eating apples and similar fruit. This is just one of several “clusters” of allergen families comprising seemingly diverse plant species. Hence, expert advice should address such issues of so called “cross-sensitivity” or “cross-reactivity” as well.

Similar phenomena exist in the field of contact sensitivity, where allergy to one compound can imply that a number of other, chemically, or rather “immunologically” related substances will cause the same problems as the original allergen. Examples include oxidative hair or textile dyes and certain antibiotics, to name but a few.

Individual degree of sensitivity

Allergy – both immediate and delayed type – is not an "all or nothing" phenomenon, but a graded one. This means that there are considerable differences between individuals regarding the amount of allergen required to elicit disease (of comparable severity) in them. In case of nickel contact allergy it has been found, for instance, that the so called elicitation threshold varies by a factor of about 1000 (Fischer et al. 2007). The most sensitive persons will most likely develop dermatitis after transient contact with traces of nickel ions or after ingestion of nickel liberated by stainless steel cooking utensils, while the least sensitive will often have no, or limited, problems in everyday life – the patch test may even be the only sufficient contact with nickel "above their individual threshold" capable of eliciting allergic contact dermatitis in these weakly sensitized persons. Evidently, the intensity of allergy (the individual elicitation threshold) will have to be considered in efforts for secondary prevention. In case of a weak sensitization, basic and limited efforts may suffice, whereas in cases of exquisite sensitivity more comprehensive and far-reaching measures have to be taken.

Treatment of allergic disease

As outlined above, allergen identification and avoidance are the most important principles in dealing with allergic disease. However, sometimes avoidance may fail or be impossible to achieve to a sufficient extent, for instance regarding exposure to seasonal or perennial airborne plant allergens causing "hay fever" or bronchial asthma, or similarly regarding ubiquitous plant contact allergens such as those in "poison ivy" (*Toxicodendron species*) in the United States or "congress weed" (*Parthenium hysterophorus*) in India.

In case of the immediate type hypersensitivities a treatment is available for a number of allergens, which can be regarded as "causal", namely, the hypo sensitization therapy (immunotherapy) (Compalati et al. 2009). This therapy aims at gradually reducing sensitivity to a level that alleviates or even eliminates actual disease. However, hypo sensitization is neither available for all allergen (and certainly not for contact allergens, despite anecdotal reports) nor is it effective in each and every case.

Hence, modes of treatment relieving the clinical signs and symptoms (but potentially also the progression of disease), that is "symptomatic treatment", is often an issue. As the symptomatic treatment of the different diseases naturally differs, it is very briefly outlined in the following sections.

On a national level, guidelines for both immunotherapy and symptomatic treatment may exist providing much more detailed and authoritative reference than the crude overview presented here. Moreover, (systematic) reviews and meta-analyses on these issues are available in the international scientific literature. The systematic reviews compiled by the Cochrane Collaboration are particularly useful and authoritative (http://www.cochrane.org/).

Allergic rhinitis/conjunctivitis

A treatment directly aimed at the affected part of the body is the front line approach because this largely avoids exposing the whole body to the drugs. This type of treatment is called topical treatment, and, in case of the nose, means aerosols or drops applied to the nasal mucosa, and in case of the eye – specifically the conjunctivae – the application of drops or ointments to the conjunctival sac. Agents often used include antihistamines, disodiumcromoglycate, corticosteroids (which have to be used with utmost care and only strictly controlled by an ophthalmologist at the eye!). If topical treatment should prove to be not sufficiently helpful, systemic treatment with antihistamines or a number of other drugs will usually be considered.

Allergic bronchial asthma

As bronchial asthma may (i) progress in severity and become life-threatening and (ii) moreover progress in the sense that it will not be triggered only by allergen contact, but by a number of non-specific stimuli after some time, early and strict allergen avoidance and possibly hypo sensitization therapy are particularly important. (Symptomatic) treatment is organized according to age group and severity and may range from a topical treatment with so called beta agonists or parasympaticolytics only in case of symptoms, to a continuous topical therapy e.g. with corticosteroids, to a systemic therapy with corticosteroids, leucotriene antagonists and other special medications – all of these needing adequate medical supervision.

Allergic contact dermatitis

The natural course of allergic contact dermatitis or chronic contact urticaria ("protein contact dermatitis") is self-limited after sufficient allergen avoidance is established. This, however, means several days or often weeks until resolution of dermatitis and some more time until complete recovery of the physiological integrity of the skin. Thus, symptomatic topical, and rarely systemic, treatment with anti-inflammatory agents such as corticosteroids or calcineurin inhibitors is often used to shorten the course of disease and to quickly lessen the symptoms. The choice of the adequate vehicle for treatment is essential, e.g. a "light" lotion (oil in water emulsion) or solution in the acute, vesicular state, and a change to "rich" ointments (water in oil emulsions or pure lipids) in a more chronic, possibly fissured state of the skin. This implies dermatological supervision, if possible. Essentially, the symptomatic treatment of allergic contact dermatitis is not different from the treatment of other types of contact dermatitis (such as irritant contact dermatitis) or dermatitis (eczema) in general.

Rehabilitation

Rehabilitation, sometimes also termed tertiary prevention, is an attempt to lessen the negative consequences of (allergic) disease possibly remaining after following the previously outlined fundamental steps. The actual measures of rehabilitation will depend at least as much on individual and societal factors as secondary prevention does. In fact, virtually the same determinants apply, and are thus not repeated here.

In an occupational setting, rehabilitation could mean compensation for reduced income resulting from chronic / intractable allergic disease, be it due to less specialized and less well paid further employment, possibly after a change of the employer, or even a compensation for complete disability to work. Evidently, the legal or regulatory framework for these processes, if they are formally implemented at all, will more or less vary between countries.

Moreover, rehabilitation of chronic allergic bronchial / obstructive lung disease or chronic dermatitis of whichever origin may include episodes of hospitalization for optimization of chronic treatment or intermittent special treatments. Hospitalization may try to exploit the beneficial effect of a temporary, more or less drastic change of the environment, such as a seaside or mountain setting. The special treatments can include, in particular, the training of supportive coping strategies such as (i) psychological or behavioral therapy, (ii) intensified advice regarding allergen avoidance and treatment and (iii) in an occupational context "skill labs" in which improved application of personal protective equipment is trained. This can be regarded as a special application of ergotherapy. As such measures beyond standard medical treatment require highly specialized expertise, comprehensive rehabilitation is usually offered by specialized institutions, often run or funded by health or occupational accident insurances (Skudlik et al. 2009).

In a pediatric setting, rehabilitation of allergic disease will obviously include one or both parents, who may not only need education in a strict sense on how to manage their offspring's disease, but

possibly, depending on individual factors of the parent(s), supportive (psychological) care. This may be achieved in routine medical care, on a case-by-case basis, or by participation in structured programs. Such programs have been established in some countries for entities such as allergic bronchial asthma in children, atopic eczema (which cannot always be regarded as a strictly allergic disease, see above) in children or adults. The programs may be offered regionally, close to the patients' place of residence, or in the context of a hospitalization period (see above).

Quality control of rehabilitation measures should address not only structural or procedural aspects, but, if possible, also relevant outcomes. These depend on the specific disease(s) covered by the measure and could include aspects such as general or allergy-related quality of life, need for chronic medications, sick leave or need for hospitalization, and occupational outcomes, as appropriate.

In addition to standard care, which may greatly differ between countries, numerous studies address the potential for improvement of disease control, particularly in the field of (pediatric) bronchial asthma, for the obvious reason that this is the most severe and potentially life-threatening of the allergic diseases (and much more common than anaphylaxis, which is also a potentially severe and life-threatening disease). The scope of such new approaches cannot be summarized here; the reader is referred to scientific reports and reviews which can, for instance, be identified using Medline, the online service of the US National Library of Medicine (http://www.ncbi.nlm.nih.gov/pubmed).

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