



SESSION III

Advances in Risk Assessment for Allergic Contact Dermatitis

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DR. KEMPER: It is my pleasure to open the afternoon session, Session III of the Tox Forum in Brussels this year, and it is, also, my pleasure to remind you, ladies and gentlemen, all of you that the old Romans were wrong when they said “Plenus venter non studet libenter”, in English “a filled stomach doesn’t like to work”.

I hope you agree, as I said, they were wrong. Allow me to introduce myself. My name is Fritz Kemper. I am a medical doctor and professor of pharmacology and toxicology and environmental medicine. I am very interested in all sayings of nowadays, toxicology, especially risk assessment.

I am a member of the Scientific Steering Committee of the European Community, as well as the Chairman of the SCCNFP, abbreviated which means Scientific Committee Cosmetology and Non-Food Products Intended for Consumer, a long name, hopefully for good work. If good work is done, my colleagues do so.

Ladies and gentlemen, let me begin this session with good news, good news for those of you who are engaged in experimental toxicological work. The good news is that last Friday the Committee for the Adaptation of Technical Progress that are the delegates of the 15 member states of the European Community, of the European Union, convened here in Brussels and agreed with the draft of the commission directive which was not mentioned today, and which is a commission directive of postponing for a second time the date under which animal tests are prohibited for ingredients or combinations of ingredients in this case of cosmetic products. But you can apply more or less in the same direction all of your fields of toxicological interest.

That means that, at least at the moment, the directive which ends by the thirtieth of June this year, that means in a very few days will be postponed to the thirtieth of June 2002 and hopefully meanwhile the so-called Seventh Amendment to the cosmetic directive is coming into the force which brings us to the year 2006.

If at that time the aim of the commission has been reached, that means that all, I repeat all animal experiments can be replaced by alternatives, from my point of view of today, is rather questionable. But the audience here is a younger generation, and I am very glad to see so many young people who will have an enormous task to fulfill, whereas on the other side some intellectual reasons are against that you can reach this aim.



Now, negative prophetism, let us add to this good news for the toxicological family, also, bad news. Bad news is that Professor Antonella Tosti, University of Bologna who was foreseen for the introductory lecture of this session, unfortunately and unexpectedly has withdrawn attending the Toxicology Forum and that means that the announced overview on allergic contact dermatitis with emphasis on clinical and epidemiological aspects cannot be presented.

Hopefully we will have the manuscript to be published in the proceedings of this Toxicology Forum and my advice to my good old friend Dr. Jerry Brunton is ask her for the manuscript. Probably you will get it because I think her thoughts and her figures and her experience will be very valuable for all of us.

In context with the affiliations of your moderator it seems to be necessary to point to the fact that we don't speak solely and exclusively about cosmetic products. This is wrong. I am of the opinion that allergic contact dermatitis or let us use the abbreviation ACD is imminent for all fields of protecting human health, food, goods of daily use like household products, cosmetics but, also, the large variety of substances and compounds which come into contact with the consumer and, also, where the environment targets the consumer again.

As a toxicologist overlooking the last 50 years of my own professional life as a medical doctor and a reasonable part of this more than three decades as toxicologist I see with some concern the growing importance of allergic phenomena.

With some intention I did not speak about the growing number of allergic manifestations because I am not sure if the observed raise in figures of allergic manifestations is real or due to better diagnostic measurements. Allergy and allergic contact dermatitis is a cell-mediated immune response to small molecular weight chemicals that contact and penetrate the skin.

ACD is a typical pathophysiological answer of type IV hypersensitivity mostly triggered by immunogenic agents such as chromate, nickel and organic agents as picric acid or ingredients of plants, for instance in poison ivy or oak but, also, a variety of other plants can mediate the clinical symptoms of ACD.

ACD requires between 24 to 72 hours as to our knowledge today until full development of the respective lesions, thus ACD is referred to as "delayed type of hypersensitivity".

Contact induced allergy can be triggered as already mentioned by a multitude of allergens, amongst them detergents, medical substances, household and environmental agents. Occupational medicine has a large variety of these substances at hand, cement or whatever else, and one reflection to the famous jeans or trousers which by tradition have a button which is near the umbilical area and as they are worn without anything else on the naked skin it can happen that this leads to a typical ACD.



It is recognized that genetic causes influence the susceptibility to type IV hypersensitivity. We will hear about this later on by experts in the field which I am not.

The cascade of events that result in ACD and the precise contribution of T-cells is not well understood yet. It seems to be agreed upon in science it has a sensitizing phase to be distinguished from an elicitation stage. Without going into detail obviously, and that is the knowledge I put out of big books, the Langerhans' cells in the skin play a major role supported by mechanisms which convert, also, as an antigen processing cells from arresting to an activated state induced by cytokines as for instance IL1, beta and IL6 as well as TNF alpha may contribute, also, secreted by the keratinocytes. As always in life, at least in my life, ladies and gentlemen, I am very proud that heaven helps me if the needs are requiring this, and so it happened what I told you already that Professor Tosti is not with us, but in this very moment, heaven helped me, yesterday I got knowledge of the latest issue of "Contact Dermatitis" and in the May number of this journal an excellent review article came out, appeared and I am very proud to announce that most of the authors of this article are in the audience, and later on will refer to their results. That is Dr. Frank Gerberick, that is David Basketter, and that is last but not least Pauline McNamee, and I owe her my personal thanks for being so excellent in assistance in the preparation of this Session III of the program.

This article is entitled "The Importance of Exposures to Estimation in the Assessment of Skin Sensitization Risk", has been published in this May number of Contact Dermatitis, and I encouraged the organizers of Tox Forum, again, my good friend Jerry Brunton, I encouraged them to ask the Copenhagen editors of this journal to give the permission that this article can be added later to the proceedings, for those who do not regularly have this periodical.

For new products or product ingredients that come into contact with the skin, "it is necessary prior to the introduction onto the market to conduct a thorough skin safety testing and risk assessment program to be certain that the product will be well tolerated. One of the critical skin safety testing and risk assessment processes related to development of allergic skin reactions referred to as skin sensitization, the clinical manifestation of which is called allergic contact dermatitis, ACD" (citation). That was from the introduction to the mentioned article, and I think, ladies and gentlemen with this we have an excellent introduction into what we are speaking about in the next few hours, and I think, also, that it should be mentioned that interestingly in the elicitation process which I mentioned for ACD they have clearly shown that there is a dose dependency of the damaging agent which is unusual in allergic reactions and there is a specificity of these allergic skin symptoms.

What first has been regarded as a non-replaceable gap, the absence of our first speaker, therefore, may be an advantage for the next speaker, and I hope that within our program we will hear about the official allergen list which has been published by WHO and the EU where 55 food allergens are listed, and I hope to hear more about these food allergens and their classification as to classical food allergens and polymer-related food allergens. That can be an item for the roundtable at the end of our afternoon.



By the way, that was new for me that more than 35 allergens had been cloned meanwhile and are available. Included are IgE, immunoglobulin E binding capacities and have been certified.

Perhaps a last remark, a very short remark on risk assessment and risk analysis. You learn from the other, and I put it again on the screen, that in July the commission offers under the chairmanship of Professor Dr. Dr. h.c. Arpad Somogyi, highly reputed and responsible within the EU for Risk Assessment, an international conference on risk analysis and this includes the work of a special risk group from the SSC, the Scientific Steering Committee. I am very proud that I am a member of this group which is headed by Professor James Bridges, University of Surrey/UK, who will give his presentation tomorrow morning. Jim has prepared a paper which has good progress now, and hopefully we can present it in July according to the intentions of the commission.

Risk assessment and risk analysis which is dedicated to Session IV of this Tox Forum is in the case of allergic contact dermatitis an estimation of measurements of exposure and again I dare pose the question are there thresholds. An exciting chapter of toxicology and speaking about advances as the title of this afternoon in risk assessment for ACD poses two different questions. The first is: do we speak only about methodology, how to detect ACD and especially to which extent can tests help us here. We have to compare the results of classical tests like Magnusson-Kligman, together with new ones as the lymph node assay or even more which is done in progress in the laboratories, and it was very wise to mention this morning and I underline this, that 95 percent of all this even basic scientific work is done in the laboratories of industry.

It is regrettable but true that universities and independent research institutes can only contribute to a minor extent in this respect.

The second question, and that is my last remark, is: do we only look for methodologies or do we speak about in a wider sense concepts in skin sensitization risk assessment. I, personally, am of the opinion that the latter is the most important. That leads immediately to the first speaker in your program.