STSM Report

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Host: Finnish Institute of Occupational Health, Control of Hypersensitivity Diseases Helsinki, Finland.

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Purpose:
In general: exchange experience and wide knowledge concerning recognition and diagnosis of occupational skin diseases and identification of their causal factors

In particular:

1. To study methods of patch testing patients' own materials and products from the workplace in order to improve and extend these methods in Nofer Institiute of Occupational Medicine, Poland.
2. To study methods of identification of new work-related allergens.
3. To study metal-working fluid allergens, particularly the most recent ones, comparing patch testing of these chemicals in Nofer Institute and FIOH.
4. Participation in exposure assessment of individuals with contact allergy, establishment of relevance of patch test reactions.

Work carried out and main results:
During the STSM at the Finnish Institute of Occupational Health (10 working days) I participated in diagnostic procedures carried out in patients referred with skin diseases of presumed occupational origin. I got insights into the results of interviews and clinical examinations of patients and in all performed diagnostic tests, including patch testing, prick tests and open tests. I got familiar with patch test series used in FIOH and had a possibility to compare them with my institute where almost exclusively series manufactured by Chemotechnique Diagnostics are applied. In FIOH, patch tests are performed not only with commercially available allergens (TROLAB, Chemotechnique Diagnostics) but also with numerous in-house substances prepared in local laboratory and with patients' own products handled at work or at home. Numerous series of allergens are used, depending on a patient's occupational exposure. Selection of allergens in series is based on long-term FIOH own experience in diagnosing contact allergy and results of research on current significant allergens.

Furthermore, I participated in patch test readings and in assessment of relevance of test reactions. I had an opportunity to discuss many current issues on occupational and non-occupational contact allergy, in particular allergy to metalworking fluids (MWF) components, epoxy hardeners, acrylates and methacrylates, epoxy (meth)acrylates, oxidized limonens, coconut oil acids derivatives, isothiazolinones, sulfites, isocyanates. I got acquainted with FIOH research results recently published in medical journals on those topics. The knowledge gained during participation in diagnostic procedures, discussion and reading will result in modifications of patch test series used in my institute, among others, inclusion of limonene and linalool hydroperoxides to baseline series or tris-DMP to epoxy series. It will enable us to detect and study the sensitization to some allergens of recently growing significance. It will also improve the diagnostics of contact allergy in my institute, make it closer to European standards and will facilitate the comparison of future research results of our institutes.

One of the most important tasks of my STSM was to study methods of patch testing patients' own materials with the aim to improve and extend them in my institute. The reason for testing patients' own materials is primarily due to the fact that commercially available test substances do not include all possible allergens and sometimes commercial preparations of chemicals fail to reveal contact allergy (for example because of their instability). Testing with own materials significantly helps to establish the proper diagnosis as well as indicates causative factor of skin disease and products responsible for elicitation of allergic contact dermatitis.

Testing materials handled at work (and also hygiene and care products) is an integral part of occupational skin diseases diagnostics in FIOH but it is neglected in Poland. The selection of patient-supplied materials for patch testing is based on careful exposure anamnesis. Information regarding the products is analysed before testing, using material data safety sheets (MSDS), other available product information, list of ingredients, additional data obtained from the manufacturer or supplier, chemical and toxicological handbooks etc. Patch testing is not performed with materials that are known to be hazardous for skin (strong acids and alkalis, pH below 4 or above 9) or whose composition is unknown. On the basis of the information on toxicity and the composition of the material, the proper test concentration and the best vehicle for tested products is chosen.

The test concentration for the product should not exceed the previously recommended test concentration for any of its components. Usually a series of dilutions are applied (for example 10 - 3.2 – 1% or 10 – 5 - 2.5%) which helps in the interpretation of the test results. Buffering is often used, particularly in testing substances with pH beyond acceptable range. Some materials such as cosmetic preparations and topical medications can be tested as is. Some compounds are especially difficult for patch testing, for example acrylics and other highly reactive chemicals such as intermediates in chemical syntheses. Testing with these materials is recommended only in case of negative reactions to commercially available substances. Concentrations considered as safe should not be exceeded (for example 0.1% for acrylate-based products).

The selection of the appropriate vehicle depends on the solubility and other properties of the product. Petrolatum or distilled water are the most recommended but also acetone, ethanol or oils can be used for water non-soluble chemicals. Solid non-irritant materials or powders may be tested usually as is with a drop of vehicle (water for textiles and paper, organic solvents for rubber and plastics) or using extracts. The extraction in solvents or with the use of ultrasonic bath improves the release of allergens and their penetration into the skin.

If a patient develops a test reaction to his/her own material, it is important to find the chemical responsible for positive reaction. It is often possible by comparing concomitant positive reactions to an individual test substances in the standard or additional series. Sometimes the sensitizer can be identified by testing separately ingredients of the product. If this is not possible, positive reactions should be confirmed by performing control patch tests, usually in 20 persons, to distinguish allergic reactions from the irritant ones. It is suggested that the concentration for the control test should be ten times higher than the lowest concentration that gave the reaction to the patient (except for highly sensitizing chemicals).

Knowledge and experience in the above-described area will serve to establish patch testing patients' own materials a routine procedure in my institute. It will enable us to improve recognition of the occupational skin diseases, particularly to identify cases which would be overlooked when testing only with commercially available allergens. The knowledge of these methods will be disseminated during courses and trainings on occupational skin diseases for occupational physicians in my institute.

The next goal of my STSM was to study how new allergens are identified in FIOH. Identification of new contact allergens is possible through the patch testing with patients' own materials. Allergic reactions to own materials without concomitant positive reactions to all possible known allergens may indicate sensitization to the chemical which either was not specified in MSDS or is the impurity of the product or is an intermediate formed during application of the product. In rare cases, it is possible to identify an allergic reaction to compound which was not reported before as human sensitizer. To identify this potential allergen, it is necessary to determine thoroughly composition of the material and perform patch tests with all compounds. If information on material composition based on MSDS and the one from a manufacturer or supplier does not reveal the causative compound, chemical analysis of the product is necessary. In some cases thin layer, gas or liquid chromatography and mass spectrometry can be performed. During patch testing of possible new allergens, various dilutions of test substance are used. It enables to observe the relationship between concentration of chemical and intensity of skin reaction. It is believed that in principle the actual allergen produces a test reaction at a concentration as low as 0.01%. As described above, also control patch tests are carried out in at least 20 volunteers. This Knowledge pertaining to the identification of new allergens may be useful in future research work in my institute. It will enable to avoid misinterpreting irritant reactions for allergic ones.

Finally, during my stay in Finland I had also the opportunity to observe the cooperation between doctors and chemists in analysis of patients' exposure to agents possibly harmful for skin (mainly to chemicals with sensitizing or irritant properties, but also to protein allergens). I participated in selection of own materials for patch testing and in choice of appropriate vehicle and dilution for the purpose of testing. I observed how test substances are prepared/made up from various materials and how extraction of allergens is performed using solvents or ultrasonic bath. I also visited FIOH laboratories where advanced methods of identification of chemicals are used, for example chromatography and mass spectrometry. I had the chance to discuss the application of those methods in identification of chemicals in diagnosis of patients with occupational dermatoses. On the basis of this experience, I would like to establish a cooperation between dermatologists and chemists in my institute in the area of selection and preparation of materials for diagnosing contact allergy, especially of occupational origin.

Allergens of MWF were a special field of my interest during STSM in FIOH. In my institute, in workers exposed to MWF, patch tests are performed with Oil and Cutting Fluid Series, supplied by Chemotechnique Diagnostics, consisting of 35 test substances. In rare cases, dilutions of MWF from workplace are also tested. In FIOH, workers are tested, among others, with the following series: Oil and Cutting Fluid (14 test substances), Antimicrobials (30), Ethanolamines and Methylamines (12), Coconut Oil Fatty Acids Derivatives (8). Also patch tests with own MWFs from workplace are always carried out. In recent years, new MWF allergens have been identified in FIOH (i.e. tall oil fatty acids monoethanolamide, capryldiethanolamine, polyolefin ester) and new test substances will be probably soon included in series routinely used. To follow FIOH example, diagnosing of MWF allergy in my institute will be modified and extended. In future, maybe also new allergens identified in FIOH will be included in series in Nofer Institute that would allow to assess the prevalence of allergy to these substances outside Finland.

Conclusions and further collaboration:
The knowledge and experience gained during STSM in FIOH will enable us to improve the diagnostics of occupational skin diseases in Nofer Institute in Poland, specifically by modification and extension of sets of allergens used for patch testing as well as by introduction and development of testing patients' own materials as a routine procedure. All these will allow to reach us European standards in the area of diagnostics of occupational dermatoses and will facilitate the comparison of future research results of my institute with other European centres.

Future collaboration between FIOH and Nofer Institute may include testing new allergens identified in FIOH in Polish patients to assess the prevalence of allergy to these compounds outside Finland.

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