

THE JOURNAL OF PREVENTIVE MEDICINE
2003; 11 (1): 75-104

THE FIRST ROMANIAN-GERMAN SYMPOSIUM ON OCCUPATIONAL MEDICINE

Between the 18th and 21st of June 2003 in Iasi was held the first Romanian-German Symposium on Occupational Medicine: ***THE EFFICIENCY OF OCCUPATIONAL MEDICINE - SUCCESSES, TENDENCIES, NEW ISSUES***, organised by:

- The Institute of Public Health Iasi
- The Institute of Occupational Medicine of Freie Universität & Humboldt-Universität zu Berlin, Germany
- The German Cultural Centre Iasi

The main topics were:

- The impact of environmental pollution on the respiratory system (asbestos, artificial fibres, organic dusts, respiratory functional investigations, periodic health control)
- Polycyclic Aromatic Hydrocarbons
- Pesticides
- Reference values: limit values in occupational health and environmental health
- Specials
- Industrial units inspection

Round Table: *THE OCCUPATIONAL HEALTH LEGISLATION IN THE CONTEXT OF THE EUROPEAN INTEGRATION*

Moderators:

Prof. Dr. med. Gustav Schäcke

Institute of Occupational Medicine of Freie Universität & Humboldt-Universität zu Berlin, Germany

Dr. Doina Popa, senior researcher

Institute of Public Health Iasi

I. Workshop: *THE EXPERT OPINION IN OCCUPATIONAL MEDICINE. Presentation & Discussion*

Moderators:

o. Prof. Dr. med. Gustav Schäcke

Priv. Doz. Dr. med. Rainer M. Kirchhoff

Institute of Occupational Medicine of Freie Universität & Humboldt-Universität zu Berlin, Germany.

II. Workshop: *REFERENCE VALUES – NEW ASPECTS. Demonstration & Discussion*

Moderators:

Dr. rer. medic. Peter Lüth,

Dipl. Ing. Cristian Scutaru

Institute of Occupational Medicine of Freie Universität & Humboldt-Universität zu Berlin, Germany.

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ABSTR ACTS¹

THE IMPACT OF ENVIRONMENTAL POLLUTION ON THE RESPIRATORY SYSTEM

Chairpersons:

Prof. Dr. med. Gustav Schäcke

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AN EXPERIENCED OCCUPATIONAL HEALTH SURVEY FOR THE AIRWAY SYSTEM – THE ESSENTIAL BASIS TO PREVENT OCCUPATIONAL DISEASES OF THE RESPIRATORY TRACT

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Objective. The primary target of health promotion at the workplace is to reduce occupationally caused health impairments and even occupational diseases. Around 30 years ago in Germany The Industrial Injuries Insurance Institutes (*Gewerbliche Berufsgenossenschaften*) started together with occupational health scientists and company physicians to organise a standardised examination programme. While the structure of the programme should be uniform the examination procedure is oriented by the different stress factors given by the working material (e.g. asbestos, lead etc.) or by the working procedure itself (e.g. workplaces in compressed air, cold workplaces). While the airway system is the main entrance for a great number of hazardous compounds at the work place a good health survey has agreed meaning for health prevention.

Method. Different working groups prepared several guidelines for specified stress factor.

Results. Each of the guidelines has the same structure:

1. Range of application,
2. Procedure of examination,
3. First examination, 3.1 General examination, 3.2 Special examination,
4. Control examination, 4.1. Examination interval, 4.2 General examination, 4.3 Special examination
5. Follow up examination,
6. Additional instructions, 6.1 Physical / chemical properties, 6.2 Occurrence and sources of danger, 6.3 Incorporation, 6.4 Pathophysiology, 6.5 Clinical syndrome, 6.6 Legal basis, 6.7 Analytical procedure, 6.8 Comments, 6.9 Bibliography.

Actually from the total of 47 guidelines for hazardous compounds and special workplaces certain groups refer to the airway system: Dust (n=3), metals & metalloids (9), gases, solvents, acids (17), fumes & organic dusts (2), airway obstruction (1), cancer (3), climate (3).

Physicians, who want to execute those preventive occupational health examinations, must have an excellent knowledge in occupational medicine.

Conclusion. The result of such a standardized occupational health survey became evident by a reduction of occupational diseases, a better health protection at the workplace and a reduction of insurance premium for the employer.

¹ Abstracts have been accepted for Oral Presentation Sessions and Poster Discussions. Authors are responsible for the spelling and syntax that appears in their abstracts.

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PARTICULAR ASPECTS OF THE ORGANISM'S RESPONSE TO ASBESTOS EXPOSURE

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Introduction. Asbestos is a complete non-genotoxic carcinogen, which could induce chromosomal mutations accompanied by mitotic abnormalities. Oncogenic initiation is made by free radicals released from asbestos fibres. By a similar mechanism act also PAHs from cigarette smoke, the incidence of asbestos-induced cancers being 10 times greater in smokers than in non-smokers. That is why we studied the possible potentiation by smoking habit of some subcellular processes asbestos-induced.

Material and methods. We investigated a group of 44 workers from asbestos industry by a cross-sectional study compared to a control-matched group of public office workers. Asbestos exposure was evaluated by fibre counts in the workplace air. Blood superoxide dismutase (SOD) activity was assessed with commercial kit supplied by Randox Laboratories Ltd (Antrim, UK). Serum lipoperoxides were assayed by thiobarbituric method (Fontaine N., Valli V.E.O., 1977). Informations about smoking habit were collected by a questionnaire and statistic analysis was performed by t Student test.

Results. During the last 13 years, occupational exposure levels decreased from 2-3 fibres/cm³ to 0.1 fibres/cm³ (respirable ratio), taking into account that the MAC since 2002 is 0.3 fibers/cm³.

Blood SOD activity was increased in exposed workers (286,1±90,7 U/ml) compared to controls (203.5±47.7 U/ml), the difference between the two means being significantly statistic (t=5.28; p<0.001).

SOD activity in exposed workers significantly correlated with the length of smoking habit (r=0.4065; p<0.01) and also with the number of cigarette/day (r=0.85; p<0.01). No correlation was found between the length of service in asbestos industry and SOD activity.

Serum lipoperoxides were statistically higher in exposed group (4.0±1.76 mmol/l) than in control one (3.25±0.79 mmol/ml) (t=2.55; p<0.05). This marker was not influenced by smoking habit but directly correlated with the length of asbestos exposure (t=0.32; p<0.05).

Conclusions. 1. Asbestos exposure could induce the rise of SOD activity in blood and smoking habit could potentiate this enhancement. 2. Serum lipoperoxide varied directly with exposure duration but not depending on smoking habit. 3. The good correlation between the two lipid peroxidation markers suggests a common ethiology of their enhancement. This fact is another proof of the harmful effect of smoking upon carcinogen agent's exposure. 4. Our results represent additional arguments against smoking habit in occupational exposure to carcinogens.

EVALUATION OF CHRONIC RESPIRATORY SYSTEM EFFECTS IN OCCUPATIONAL CUMULATIVE EXPOSURE TO HEAVY METALS

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Aim. The study aimed to detect chronic respiratory effects in workers occupational exposed to heavy metals.

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Materials and method. There have been investigated by physical examination, otolaryngology-examination, respiratory functional tests, individual questionnaire, as well as toxicological measurements, 98 subjects from three different plants of plating industry (mean length of exposure of 18.7 ± 6.9 years) and 49 matched controls.

Results. We found a high prevalence of chronic effects on upper respiratory system: 55.0% in group I, (4.1% cases with perforation of nasal septum), 73.9% in group II and 84.6% in group III. We have diagnosed pulmonary emphysema in 48.6% subjects from group I (31.8% smokers), in 56.5% from group II (21.7% smokers) and 6/13 subjects from group III (non-smokers); asthma (group III), laryngian non-kerating epidermoid carcinoma and nasal reverse type papiloma-one case each. Functional respiratory tests showed mild distal obstructive syndrome (at 77% in group I; 20.1% in group II; 1/13 in group III), obstructive syndrome (in 15.4% in group I; 4.3% at group II; 2/13 in group III) and restrictive syndrome (at 7.7% in group I).

Conclusion. Occupational exposure to heavy metals can cause chronic respiratory and malignant effects. Heavy metal concentrations in working area revealed slight increases above MAC values, but with an increased index of cumulative exposure in two of exposed groups. The study draws the attention to the existing associated and malignant respiratory effects with negative consequences in the health status of workers.

ASSESSMENT OF RESPIRATORY SYSTEM IMPLICATION IN OCCUPATIONAL EXPOSURE TO ORGANIC DUST (WOOD, JUTE) AND TO A CUMULATIVE EXPOSURE TO SOLVENTS AND WOOD DUST, BY CLINICAL SCORES

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Aim. Highlighting the utility of scores and index in assessment of respiratory system implication in occupational exposure to organic dust (wood, jute) and to a cumulative exposure to wood dust and solvents.

Materials and method. Two groups of exposed workers were selected from furniture factory: 37 workers with wood dust (group I); 35 workers with solvents and wood dust (group II). 55 workers with jute dust (group III) were selected from a textile factory. The control group consisted of 82 office workers. Scores and index were calculated for clinical item concerning the respiratory system. Correction coefficients were applied.

Results. Index is presented below: difficulties in respiration (group I = 92.4; group II = 51.66; group III = 78; controls = 27.04); coughing (group I = 12.98; group II = 6.44; group III = 13.02; controls = 5.27); expectoration (group I = 11.25; group II = 8; group III = 12; controls = 3); pulmonary auscultation (group I = 23.6; group II = 22.8; group III = 78.8; controls = 1.08); respiratory frequency (group I = 21.16; group II = 4.62; group III = 36.75; controls = 13.2).

Discussions. Difficulties in respiration are marked at workers exposed to wood and jute dust. Coughing is marked at workers exposed to jute dust. Expectoration is pointed by index both at workers exposed to wood and jute dust. Index show a great auscultation manifestations in workers exposed to jute dust. Respiratory frequency is increased in workers exposed to jute dust followed by those exposed to wood dust.

Conclusions. Scores and index are very useful in a global assessment of health status. The assessment of respiratory system is just a part of it.

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SPIROMETRIC ASSESSMENT OF BRONCHIAL MOTILITY AT WORKERS EXPOSED TO ORGANIC DUST (JUTE)

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Aim. Spirometric evaluation of the bronchial motility in workers exposed to organic dust (jute).

Material and methods. A group consisting of 55 workers: aged = 37.5 (26÷49) years, work length = 12.63 (1÷27) years, exposed to organic dust (jute) above MACs and a control group of 82 subjects have been examined. Spirometry was performed by means of Flowscreen.

Results. 46% of workers with jute dust (controls = 15%) needed Ventolin. Statistically significant differences were highlighted in workers exposed to jute dust, concerning the number of Ventolin intake: Monday 2.00 p.m. vs. Friday 6.00 a.m. ($\chi^2 = 6,65$; $p < 0,01$), which confirms the existence of the well-known “Monday syndrome” at organic dust. Considering the level of bronchial contraction, at the end of the workweek, the diminution of MEF25-75 (Maximal Expiratory Flow) values below 75% in workers exposed to jute dust vs. control could be demonstrated by chi test: OR = 3.34, $\chi^2 = 5.74$; $p = 0.01$.

Conclusions. MEF25-75 shows the implication of the distal bronchial segments in occupational exposure to organic dust (jute).

LIFE TIME OF BREATHING FILTERS – DETERMINATION BY SIMULATING BREATHING FLOW PATTERN: STEADY STATE AND SINUSOIDAL FLOW AND INSPIRATORY SAFETY BREATHING CURVES SBCi

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Aim. User of breathing filters must be sure on the efficiency of breathing protection filters. To acquire objective data the service life of a breathing filter can be tested by the aid of the mobile “breathing simulator 'MFP 1.2'” directly at the work place under normal exposure conditions at the work place. This equipment is able to simulate the worker's respiration. The kind of breathing pattern used while checking the filter service life is the essential basis for safety at work. Actually the knowledge of the effect of the inspiration patterns on the filter service life is still insufficient, so that the filter tests are not sure yet.

Method. The studies were carried out by the aid of the mobile “breathing simulator 'MFP 1.2'” and by simulating the steady state and the sinusoidal shape of inspiration flow curve and also breathing patterns in approximation to real-life ventilation– such called Inspiratory Safety Breathing Curves SBCi. These work load specific SBCi were generated under regard of the 95percentile range of the inspiratory flow of the clustered breathing curves which were estimated by an investigation on 55 fire-fighters (age 20 to 30 years; 80% professional and 20% voluntary fire-fighters; occupational experience 2 to 11 years) under simulated typical working conditions in a practical training area. Due to the filter test we selected flow parameters representing the intensity of physical work from 75 to 275 Watt. To determine the service life, the portable apparatus will be connected with a respiratory filter type A2B2-P3

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and coupled to a testing chamber with standardized testing air (temperature $20\pm 1^{\circ}\text{C}$, humidity $70\pm 2\%$ rel.). At each work load level we determined the breakthrough time of the filter by various solvents with a boiling point ranging from 40°C (dichloromethane) up to 110°C (toluene). The airborne concentration of each solvent was changed stepwise from 100 to 1000 ppm. During the breathing simulation, air samples are taken at regular time intervals from behind the connected filter and analysed by an portable FID-detector. Through the results of the analysis and the already detected time of penetration the filter service life was determined.

Results. The apparatus 'MFP 1.2' is able to simulate human breathing characteristics relevant for the respiratory filter. The extreme quickly regulating unit of this apparatus guarantees a high precision of breathing simulation.

We can observe a large difference between the steady state and sinusoidal and SBCi air flow characteristics. Concerning to the maximal air velocity at each work load level we established a significantly difference between the simulation of SBCi and the steady state and sinusoidal flow curves. At the load of 125 Watt we observed a mean inspiratory breathing velocity of 105,26 l/min, for the resulting sinusoidal flow curves were registered a maximal air velocity of 330 l/min and for the SBCi a maximal value of 450 l/min. Under heavy work the maximal inspiratory air velocity of the SBCi is around 10.400 ml/sec. To get a clear idea of the service life at all work load conditions the testing air chamber must generate approximately 200 l/min of standardized testing air.

Conclusion. The obtained results are a reliable base to simulate the worker's breathing and to check the filter service life. This method reduces the risk for the worker and improves the safety of breathing simulation in practice.

THE RISK ASSESSMENT IN OCCUPATIONAL EXPOSURE TO ASBESTOS DUSTS THROUGH SPUTUM CYTOLOGIC EXAMINATION

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Aim. The paper illustrates the possibility of revealing occupational exposures to asbestos dusts through sputum cytological examination by evidentiating the presence of asbestos bodies and fibres in the sputum samples and also by enhancing possible pretumoral changes in specific groups of workers.

Materials and method. We performed the cytological examination of fresh sputum samples from a group of workers occupationally exposed to asbestos dusts and the results were classified accordingly to Babes- Papanicolau system.

Results and discussion. The results of the classification were: 38% 1st class cytology, 47% 2nd class cytology, 14% 3rd class cytology. We found asbestos bodies in 72% of the subjects. The sputum cytological examination can be therefore considered as a useful method in pointing out the presence of asbestos bodies in the lung tissue as a specific marker for chronically asbestos exposure, and also in detecting suspect changes of bronchopulmonary epithelium.

Conclusion. The sputum cytology screening represents a practical, noninvasive and inexpensive approach to the diagnosis and study of asbestos exposure. That is why cytological sputum diagnosis must be engaged much more frequently in the high risk groups so that the prognostically more favourable stages of preneoplasm and carcinoma *in - situ* can be detected and possibly treated curatively.

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CERTAIN ASPECTS OF THE EXPOSURE TO ASBESTOS ON MOLDOVA TERRITORY

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Aim. Considering the implications of asbestos on health status, the aim of this paper is to diminish its level in different work places in Moldova. The present study is part of a project developed in 2003 - 2006 on regional and national level, in order to support Romania's integration in the specific European legislative system:

- Directive 83/477/EEC on 18.09.2003

- Council Directive 91/382/EEC for the modification and completion of the first Directive

Materials and method. We sampled asbestos fibres (Chrysotile) from 12 work places (asbestos boards producing stations, asbestos boards storehouses, reparation-maintenance workrooms). The samples were taken from the respirable zone and the general zone. The method used to detect asbestos fibres was Phase Contrast Microscopy (PCM) – NIOSH 7400.

Results. The levels of the asbestos fibres were higher than the occupational exposure limits (0.3 fibres/cc), depending on many factors: the concentrations of asbestos in the construction materials, the materials hardness, the ventilation, the technologic operation.

Conclusion. The paper presents legislative issues and recommendations concerning asbestos use and its replacement with non-noxious materials.

RETROSPECTIVE ASSESSMENT REGARDING THE MONITORING OF RESPIRATORY HEALTH STATUS OF WORKERS OCCUPATIONALLY EXPOSED TO A MIXTURE OF ORGANIC SOLVENTS

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Aim. Authors aimed to carry out a retrospective study concerning the respiratory health status of workers exposed to a mixture of organic solvents (OS), based on periodic medical control data.

Methods. The retrospective study was carried out during 1992 - 2001 by checking the medical primary data that exist at the medical service of a wood-processing factory. The workers were from Wood painter and Staining units.

Results. The quantitative characterization of occupational health hazards was made by analysing the results of instantaneous measurements in different workplaces of the two units, carried out yearly, in spring and autumn. The OS concentrations were above the TLV.

Generally, the clinical examination was carried out, yearly. Not all workers had made laboratory and exploring tests every year. Clinical examination had shown a polymorphous morbidity; each worker had more than one disease. The most frequent diseases were: respiratory affections, astheno-vegetative syndrome, genital diseases, digestive affections etc. The upper airways chronic irritative syndrome was the most frequent, having prevalence between 10.3% and 20.3%. The number of the smokers was small and the Brinckman-Coates index had "small and medium" values in 80% of smoker subjects. The prevalence of respiratory diseases was greater in Wood painter unit.

Conclusions. 1. The respiratory diseases had a high frequency every year. 2. In Wood painter unit, the presence of OS in association with ammonia increased the risk of the respiratory diseases. 3. There is more need for technique-organizing measures in order to decrease the occupational exposure to respiratory irritants.

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THE RISK ASSESSMENT IN A COTTON MILL

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Aim. To assess the health risk, a cross sectional survey in two mills was carried out. The goal was to control foreseeable workplace hazards through a systematic identification and evaluation process.

Methods. The four steps for risk assessment were accomplished: hazards identification, the level exposure study, the relation dose – response and risk characterization. Environmental samples included: total dust, bacteria, fungi and endotoxin levels. The exposure was estimated for each workplace. The study used a standardised respiratory questionnaire. Pulmonary function tests were performed before and after the Monday and Friday workshift to measure across shift and weekly changes of the ventilatory function. Student test and chi square test using Epi Info 6.0 and Ms Excel programs statistically analysed all the data.

Results. Total dust concentration over passed the TLV at all workplaces. Low endotoxin levels were found. Respiratory symptoms such as persistent cough, dyspnea, chest tightness were aggravated ($p < 0.05$) among cotton workers. The decrease during the shift of FEV (Δ FEV1) was significantly greater ($p < 0.05$) on Monday than on Friday.

We observed a significant decrease in FEV1 and FEF25-75% in labours that had been exposed more of 15 years. The association between exposure levels and across shift decrement in FEV1 was not significant in both two mills.

The prevalence of byssinosis was between 16.94% and 21.21%.

Conclusions. Our study showed the importance of risk assessment in organic dust occupational exposure. The quality of textile dust (e.g. type of vegetable fibres, bacterial contamination) was more important in comparison with its concentration. Respiratory disorders and ventilatory test evolution were important tools for risk characterization. Byssinosis risk was important, even we diagnosed this disease especially in its first level of evolution. We also can conclude that preventive measures should include clinical and functional examinations conducted more carefully and frequently in subjects having a long period of exposure. Another important step was the risk communication in all involved partners (employees, employers, general public, and authorities).

THE RESPIRATORY HEALTH OF THE MAN MADE MINERAL FIBRES MANUFACTURING WORKERS

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Objective. To reveal the possible risk for respiratory health status of the man made mineral fibres (MMMF) occupational exposure.

Materials and methods. A cross-sectional study was performed in a MMMF manufacture. The exposed group, 40 subjects: mean age 36.03 ± 6.00 years, mean length of service 15.48 ± 6.69 years, was comparable with control.

Results. Man made mineral fibres mean concentration in the work place air varies between $0.33-0.81$ fb/cm³. Health status assessment comprised detailed occupational anamnesis, clinical examination and pulmonary functional tests. Data analysis revealed a polymorphous morbidity of the exposed group. About 67% of the workers presented irritative and catarrhal

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anomalies of the upper airways with different clinical aspects. These are more severe in the first ten years of activity. The prevalence of the respiratory symptoms was higher among exposed subjects ($p \leq 0.05$). The pulmonary functional tests showed a distal obstructive syndrome in 17,5% of the exposed workers compared to the control group ($p \leq 0.005$) and 25% of the exposed had Small Airways Disease ($p \leq 0.05$). A significant correlation between symptoms, airways diseases and pulmonary functional tests values was found at the exposed group.

Conclusion. Clinical symptoms and pulmonary functional tests may reveal the possible risk for respiratory health status of MMMF occupational exposure, with possible further implications in the structure and severity of chronic invalidating morbidity.

FUNCTIONAL RESPIRATORY CHANGES IN OCCUPATIONAL EXPOSURE TO ISOCYANATES

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Objectives. The evaluation of respiratory symptoms and of ventilatory changes before and after occupational isocyanates exposure.

Methods. The technological process and the working conditions in a poliurethanes small department using polyesters, methylene diphenyl diisocyanates and polyol (melting and moulding and then demoulding forms) were studied and 11 subjects (9 men and 2 female with mean age: 48.21 ± 3.71 years and average exposure: 17.41 ± 4.21 years) were studied. The clinical examination identified nasal symptoms: obstructive chronic rhinitis (1 case), dyspnoea and dry cough (1 case), irritative pharyngitis (2 cases), but not even a case with bronchial asthma. The functional ventilatory tests (SuperSpiroCD-2000) were measured in the first and the last day of working week, before and after the polyurethanes pieces making, respectively.

Results and conclusions. The comparatively ventilatory parameters (FEV_1 , FEF_{50-75} of CV and FEV_1/CV , MEF_{25-75} (flow volume graph) indicated a decrease between 3-20% (7 subjects) after one week exposure (Friday) without clinical symptoms. Similarly decreasing (5 subjects) of the parameters (especially FEV_1) was found at the control group (11 workers with no isocyanates exposure). The pulmonary function tests may reveal impaired respiratory function, even no symptoms are present. The diagnosis of respiratory effects (occupational asthma) requires: establishing the presence of specific antibodies of the suspected diisocyanate, the respiratory symptomatology and the positive challenge tests.

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PESTICIDES

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GAMMA-HEXACHLOROCYCLOHEXANE – AN ENVIRONMENTAL HAZARD

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Introduction. HCH is an aromatic hydrocarbon. Technical HCH contains gamma-HCH in a concentration of 8-15%. In Germany the gamma isomer is named lindane, for medical purpose Jacutin, Kwell, Quellada, for technical use Streunex, Biltex, Hexachlor. Lindane is a polytoxic poison for insects, which kills sucking and biting insects as a contact-, food- and respiration poison. It is used as pesticide against insects in the earth and on plants and as shelter for wood, leather, clothes, carpets and other floor covering. The exposure to pure gamma-HCH may be given by contaminated textile, leather and carpet as well as by the substances itself at the working place. The environmental exposure may be given by medical treatments such as are delousing, killing damaging insects or contact with tools or materials, which are prepared against damaging insects.

Aim. The aim of our investigation was the accumulation of gamma-HCH in different tissues in animals.

Materials and methods. 4 mini pigs, weight of 8 kg, were tested. There was no other exposure to any other chemical hazards in the environment. Over a period of 10 days they got a daily amount of 15 ml of Jacutin per os with a dose of 450 mg gamma-HCH (Jacutin/Hermal). After ten days the animals were killed, samples of different tissues were taken and investigated by GC (gas chromatography).

Results. We observed an increased gamma-HCH concentration in fatty tissue, but low concentrations in muscle, heart and kidney tissue. The concentration in the central nervous system was found little higher than in muscle tissue.

Discussion. In persons working with producing lindane, the maximum concentration reached 188µg/l gamma-HCH in blood serum, for non exposed persons the maximum concentration is 3µg/l. Actually there is no study with representative data on the enrichment of gamma BHC in different tissues except the enrichment of Gamma-BHC in sea food.

Before this background the meaning of gamma-CHC to cause occupation related diseases has to be scrutinized again.

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**GAMMA-HEXACHLOROCYCLOHEXANE-CHANGES IN SERUM
CONCENTRATION BY MEDICAL TREATMENT OF PARASITOSIS**

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Introduction. HCH is an aromatic hydrocarbon. Technical HCH contains a gamma-HCH concentration of 8-15%. In Germany the gamma isomer is named lindane, for medical purpose Jacutin, Kwell, Quellada, for technical use Streunex, Biltex, Hexachlor e.g. As a polytoxic poison lindane is used as a pesticide to shelter wood, leather, clothes, carpets and other floor covering. Exposure to pure gamma-HCH may be in the production of textile, leather and carpet as well as at working place where this compound is handled. The environmental exposure may be given by the application in medical treatments such as are delousing, killing damaging insects or contact with tools or materials, which are prepared against damaging insects. About 90% of the incorporated lindane is carried by food. The dermal resorption is important in commerce as well as in the medical area; it is estimated at around 10%. The biological half-life of gamma-HCH is estimated at 8 days.

Aim. The aim of our investigation was to clear the dermal resorption of gamma-HCH compared to the lindane concentration in human blood serum after a cutaneous application of lindane for medical treatment.

Materials and methods. Six persons (4 male, 2 female; weight between 68 and 82 kg; age between 19 and 48 years) were tested. There was no other exposure to any other professional or environmental hazards. The persons had an infestation with mites at the skin over the spine. At each of the persons we marked a 40 x 40 cm skin area over the spine beginning at the base of the neck; on this area on three following days 200 ml in three similar fractions with a dose of 600 mg gamma HCH (Jacutin/Hermal) each were applied. Before and after 2, 3, 4, 7, and 12 days of the application blood samples were taken from the test persons for measuring the gamma HCH concentration.

Results. Before the application the concentration of lindane in serum was below the detection limit in all patients. From the day of application to the third following day the concentration increased slowly; afterwards up to the fifth day the concentration increased to concentrations between 27 and 54 microgrammes/l. After the day 4 to 5 to the day 6 to 7 the concentration decreased rapidly to ranges between 1.0 and 11.2 microgrammes/l. The detection limit was reached after 12 days.

Discussion. In persons working in the lindane production, a maximum gamma-HCH concentration of 188µg/l in blood serum was reached; for non - exposed persons 3 µg/l are taken as the maximum concentration. The mean range is 14 to 188 µg/l. Blood serum concentrations in children treated with gamma HCH because of ektoparasites, showed a maximum of 0.048µg/ml lindane, that means 48 µg/l six hours after the application of 76-239 mg lindane. The only investigation, which shows a relation between clinical symptoms and blood serum concentration, was made in 1988 in forestry workers, who showed gamma HCH concentrations of 123 and 75 nmol/l. In cases of an exposure to lindane the question for an occupational disease has still to be discussed very carefully.

A POSSIBLE RELIABLE TEST TO ASSESS THE EFFICACY OF OXIME THERAPY IN ORGANOPHOSPHATE POISONING

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Aim. In a previous study we set up a method to determine the reactivating potential of organophosphate-inhibited serum BuChE activity, by incubating it with Toxogonin. We intended to apply this method in a monitoring study of poisoned patients, in order to evaluate the right moment of stopping oxime therapy.

Materials and methods. In 5 organophosphate-poisoned patients we determined daily serum inhibited-BuChE activity and also the activity of the reactivated enzyme by Toxogonin test.

Results. The reactivating degree - (Reactivated enzyme activity-Inhibited enzyme activity) \times 100/ Reactivated enzyme activity - in the first day of poisoning varied between 54-91 %. The moment of cessation varied from one case to another, lasting quite to the 10th day of intoxication, in a case where percutaneous organophosphate absorption was continuing, due to incorrect decontamination of hair and skin.

Conclusion. In each case, our test indicated the necessity of applying oxime therapy, because the enzyme was reactivable and we appreciated that oxime infusion could stop when serum BuChE activity in Toxogonin test is no more reactivable, or the reactivating degree is less than 16 %. Our test is useful in monitoring organophosphate poisoned patients and also for assessing the efficacy of the therapy.

CELLULOSIC POLYSACCHARIDES IN ORGANOPHOSPHATE SUBSTANCES POISONING

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Background. In previous experiments we proved that Keltrol, a cellulosic polysaccharide, is able to bind organophosphate compounds preventing their absorption in case of poisoning. We also proved that, in rats, organophosphates absorption takes place in the first 1/3 of the bowel. But no references exist on intradigestive organophosphates pharmacokinetic and on the hypothetical good influence upon it, of the other members of cellulosic polysaccharides group: Gelan, Chitosan.

Purpose. To imagine an experimental model useful to analyse organophosphate intoxication in terms of intradigestive pharmacokinetic and polysaccharides neutralising therapy.

Material and methods. Intra gastric inoculation of trichlorfon 200 mg/kg, alone (T) and together with Keltrol (K), Gelan (G) and respectively Chitosan (Ch) 0.5 g/rat to Wistar male rats, was followed by gas-chromatographic determination of trichlorfon in the digestive content (separately from three compartments: I – preabsorptive stomach; II – absorptive 1/3 bowel; III – postabsorptive-the rest of bowel; at 1, 4 and 12 hours after inoculation).

Results. (in ppm) T: (1h: I=0.226, II=0.070; III=0.068; 4h: I=0.074, II=0.068; III=0.070; 12h: I=0.076, II=0.024; III=0.044); T+K: (1h: I=0.046, II=0.030; III=0.038; 4h: I=0.056, II=0.070; III=0.055; 12h: I=0.230, II=0.035; III=0.046); T+G: (1h: I=0.378, II=0.124; III=0.058; 4h:

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I=0.055, II=0.046; III=0.094; 12h: I=0.069, II=0.020; III=0.083); T+Ch: (1h: I=0.062, II=0.194; III=0.054; 4h: I=0.128, II=0.049; III=0.172; 12h: I=0.064, II=0.041; III=0.040).

Conclusions. In starved rats, at 1h from intoxication only small amounts of organophosphate substances (0.7 %) could be found in the digestive tract, and this amount has reduced to 30 % at 4h and remained unchanged until 12h. All tested polysaccharides proved to bind organophosphates, releasing them, under enzymatic action, after various time intervals.

SERUM IMMUNOASSAY FOR ATRAZINE: VALIDATION AND EXPOSURE ASSESSMENT

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Aim. A previously described monoclonal antibody based competitive enzyme-linked immunosorbent assay (ELISA) was validated for determination of atrazine in human serum. This simplified approach minimizes the effects of nonspecific interfering substances in serum and eliminates the need for sample extraction and clean - up.

Method. A total of 16 rat serum samples were initially tested by ELISA and by high-performance liquid chromatography (HPLC) to assess whether the ELISA could be considered a reliable technique for the quantification of atrazine in serum. Twenty manufacturing workers (12 men), 30 – 46 years old, exposed 16.45 ± 4.44 years to atrazine, were studied to validate the ELISA for risk assessment studies.

Results. A correlation coefficient of $r = 0.95$ ($p < 0.001$) demonstrated that the results using the ELISA and the HPLC method were comparable. The recoveries, calculated as the percentage of concentration in spiked human serum divided by that of the original sample, were within a range of 78 – 112 %. The limit of detection was 100 ng/L and the coefficients of variation less than 12 %. The estimation of uncertainty based on accuracy (trueness and precision) is described.

Conclusion. Based on these results it is suggested that this quantitative, sensitive and reproducible immunoassay could be of interest for biological samples monitoring in exposure assessment studies.

EXPERIMENTAL STUDY ON EMBRYOTOXIC-TERATOGENIC POTENTIAL OF 2,4- DICHLOROPHENOXYACETIC ACID

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Aim. This study is part of a complex research program, aimed to identify and point out certain toxicological characteristics of 2,4- dichlorophenoxyacetic acid, a pesticide (“phenoxy” type herbicide) still frequently used in agriculture.

Material and method. In order to assess the embryo-toxic and teratogenic potential of 2,4- D, we performed our experiment on pregnant females of Wistar albino rats; the substance was administered daily, in food, in two different doses (100 mg/kg and 200 mg/kg, respectively) during the whole gestation period. The exposed groups were matched with two control groups untreated and solvent group (sunflower oil), respectively. After sacrificing the animals (in the

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28th gestation day) the uterus content was evaluated, in order to establish the fertility and prolificity indicators.

Results. The tested substance (both doses) didn't cause maternal death; the small dose (100 mg/kg) caused no changes of fertility and prolificity indicators. The big dose (200 mg/kg) correlates with a decreased rate of alive foetuses on gestant female, and a big rate of resorbitions (precocious resorbitions especially). Both doses affected the offspring quality, causing decreased foetal body weight for both sexes of the embryos.

Conclusions. In this preliminary stage of the study, the results enhance the noxious effect of 2,4- D on reproduction; we assume that it is necessary to continue and extend investigations with different doses and administration pathways.

HEMATOLOGICAL ISSUES IN OCCUPATIONAL EXPOSURE TO TRIAZINIC HERBICIDES

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Aim. To assess the potential adverse effects upon the haematopoietic system in occupational exposure to atrazin in the synthesis industry and to identify appropriate prophylactic measures.

Methods. Cross-sectional study followed by a 3 years cohort study on 149 workers occupationally exposed to atrazine versus 143 matched controls.

Exposure evaluation comprised GC measurements of atrazine in workplaces air and HPLC assessment of atrazine urinary levels. Occupational anamnesis, clinical, endocrinological, haematological as well as biotoxicological investigations have been done.

Results. Exposure evaluation revealed, in the workplaces air, atrazine levels of 1.1 – 12.4 mg/mc, usually correlated with urinary levels of atrazine: 10-27mg/l.

Examination of the health status revealed allergological, endocrinological and haematological changes (the latter prevailed). Careful haematological investigations revealed qualitative and quantitative changes of white and red blood cells at 28.2% of the exposed vs. 8.4% of controls (Yates'chi square: 17.68, p:0.00003, OR=4.29, 95% CI:2.15-8.55). In exposed lot, haematological findings mainly consisted in major atypical lymphocyte changes (hairy lymphocytes, hand-mirror lymphocytes, bilobate, trilobate vacuolar lymphocytes, activated lymphocytes) and were found at 12.08% of the exposed vs. 0% in controls (Yates'chi square: 13.72, p:0.0002, OR=19.51, 95% CI:2.57-148.21) and were significantly correlated with exposure levels and length of service. Other haematological findings in exposed lot consisted in red blood cells (RBC) changes (hypochromia, anisocytosis, decreases in haemoglobin as well in RBC number) in 20.1% vs. 8.4% in controls (Yates'chi square: 6.00, p:0.014, OR=2.54, 95% CI:1.24-5.20).

After three years of exposure to increasing doses, the haematological investigation revealed the following aspects: 1. the increase of the exposed subjects with major atypical lymphocyte changes (from 42.8% to 61.9%, significant t test: p=0.042); 2. the increase of the frequency of these changes in the same subjects (quantitative aspect), and 3. the increase of the number of such changes associated in the same subjects (qualitative aspect). It is also to be mentioned that we have found thrombocytopenia as well as, in the bone-marrow, a large number of megakaryocytes and other young bone-marrow cells with atypical morphology.

Conclusions. Occupational exposure to atrazine seems to be able to induce a state of altered reactivity at the haematopoietic system level, which could be consistent with medullar

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dysplastic syndromes, even at exposure levels comparable with some TLV. Further reconsideration of exposure standards seems to be a suitable prophylactic way.

CHANGES OF LIPID METABOLISM IN OCCUPATIONAL CHRONIC EXPOSURE TO ATRAZINE

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Aim. To emphasize the lipid metabolism changes of employees implied in technical atrazine formulating and bagging processes.

Material and method. We investigated 20 subjects (12 men) with a mean age of 35.4 ± 4.1 years, a mean exposure period to atrazine of 16.4 ± 4.3 years and a control group also, matched with the exposed one by age, sex and socio-economical features, in order to establish whether the eventual pathology is occupationally conditioned or facilitated. The complex investigations system we performed includes also lipid metabolism markers (cholesterol, total lipids, triglycerides and lipoprotein fractions) and endocrinological parameters (T3 and T4). Exposure risk has also been assessed through seric atrazine immunoenzymatic technique.

Results and discussion. We found increased values of total cholesterol, triglycerides and total lipids in a statistically significant higher rate for the exposed group compared with the control one ($p < 0.001$). The exposed group's frequency of alterations of the lipoprotein fractions (HDL, VLDL, LDL) does not significantly differ from the control values. The Lp(a) fraction is present at 45% of the exposed subjects (versus 5% of the controls) and correlates positively with the seric level of atrazine ($r = 0.84$; $p < 0.01$). The levels of T3 remained close to the reference values and those for T4 were decreased in 60 % of the exposed subjects.

Conclusions. The high frequency of the lipid metabolism changes in the exposed group can be associated with the presence of atrazine in the work places' air as it is a well-known fact that this triazinic herbicide disturbs the hormonal balance increasing the levels of the above-mentioned markers.

PRELIMINARY DATA CONCERNING TOXICOLOGICAL RESEARCH ON 2,4-DICHLOROPHENOXYACETIC ACID. EXPERIMENTAL STUDIES

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Aim. 2,4-dichlorophenoxyacetic acid (2,4-D) is a herbicide still used in agriculture. The basic mechanism of the metabolic changes induced by 2,4-D remains still unknown. The paper presents a series of experiments - acute, sub-acute and teratogenesis, - performed on Wistar white rats, males and females.

Materials and method. We assessed multiple indicators, as follows: biochemical, biotoxicological, haematological, mutagenic, teratogenic and pathomorphologic ones.

Results. We found certain changes in protein metabolism. The urinary 2,4-D levels demonstrate that it does not cumulate in organism. On the other hand, the changes in peripheral blood suggest the toxic potential of the herbicide. The evaluation of genotoxicity

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showed that 2,4 - D can interact with fusal proteins, thus disturbing the cell division. The teratogenesis experiment evidenced a potential embriotoxic effect depending on the administered dose, and we observed pathomorphologic changes in all investigated organs.

Conclusion. After an integrative interpretation of the results we conclude that the herbicide 2,4 - D has a potential toxic effect, therefore we consider that it is necessary to continue and extend our research by including also the assessment of the protective effect of certain compounds, e.g. amino acids, which could counteract the toxic effects of the compound

POLYCYCLIC AROMATIC HYDROCARBONS

OCCUPATIONAL EXPOSURE TO POLYCYCLIC AROMATIC HYDROCARBONS AND LUNG CANCER RISK

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Aim. Occupational exposure to chemical carcinogens has been associated with high cancer incidence. Polycyclic aromatic hydrocarbons (PAH) and aliphatic hydrocarbons (AH) are included in the group of the substances with increased risk for respiratory tract. Smoking habit is associated with alteration of the bronchial epithelium, reversible a long time period and with changes in the activation of the state of the inflammatory and immune cells by the respiratory tract. Recent studies have been associated the effects of the chemical carcinogens and of the smoking with immune functions. The sensitised leukocytes to the anti-tumour immune factor lose their ability to adherence to glass or plastic surfaces than they are exposed. The aim of this study was to assess the effects of the polycyclic aromatic hydrocarbons and aliphatic hydrocarbons on occupational exposed workers.

Materials and method. We investigated 200 workers, using radiological, cytological and immunological investigations. The cytological screening of the sputum was performed by Papanicolou method. Leukocyte adherence inhibition test (LAI test) was performed for detection of the anti-tumour immune factor in the exposed workers.

Results and discussion. In the investigated group, 24% of the cytological examinations were with moderate and marked atypia; 88 % of the subjects are high smokers. The LAI test disclosed positive responders against the crud tumour extract at the 79% of the subjects with III and IV type of the sputum cytology. All of them are heavy smokers. PHA and AH - exposed workers presented an increased risk for respiratory tract cancer.

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HAZARDOUS COMPOUNDS AND REFERENCE VALUES IN OCCUPATIONAL HEALTH

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Objective. The main target of occupational medicine is to detect occupational health risks as early as possible. For this purpose biological monitoring has continuously been developed. In practice biological monitoring considers mainly clinico-chemical examinations and the broad spectrum of occupational chemical health risks. But the quality of biological monitoring depends essentially by the quality of reference values.

As far as available, reference values depend on a "sound" state.

Only few of them depend on age and/or gender. In most cases background information on differentiated paths of professional and environmental exposure or lifestyle are missing.

The target of our study is to include those different factors for a differentiated approach to reference values to get a better background for the risk assessment of hazardous compounds.

Methods. Within the period from 1994 to 2002 we examined 974 persons (occupational health survey, medical expert opinion, students) with a different occupational, environmental, and social background). From all probationers we recorded by a standardized questionnaire health history, occupational biography including occupational and environmental exposure, state of health.

Samples of blood and urine were taken for a clinico-chemical check up and for the analysis of lead, cadmium, aluminium and selenium. For the statistical evaluation we used SPSS V10.07.

Results. We observed some different values: For lead and Cadmium in blood male persons showed higher values than female and were higher in 1995 than in 2000 (1995: Pb m: 30.3 µg/l, f: 22.8 µg/l; Cd m: 0.5 µg/l, f: 0.4 µg/l; 2000: Pb m: 24.0 µg/l, f: 20.7 µg/l; Cd m: 0.3 µg/l, f: 0.3 µg/l. Smokers showed the same tendency, but on a higher level than non-smokers. Persons with a high consumption of mushrooms had an increased level of Cadmium, while persons from areas with high traffic density showed a higher aluminium concentration than others.

Conclusions. Reference values have to be revised periodically to guaranty a safe assessment of hazardous compounds in occupational and environmental medicine.

INTERNATIONAL RESEARCH PLATFORM *REFMED*- ANALYTICAL

REQUIREMENTS FOR SAFE REFERENCE VALUES AND MODERN METHODS

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Aim. The state of human health depends on various, complex factors from workplace, the environment and the lifestyle. From the etiological point of view and for the health risk

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assessment definite safe reference values are necessary. At present the quantity, the quality and the actuality of the published reference values are insufficient. A capable quality control management must be established and the analytical requirements must be defined.

Method. To improve the situation the actually available reference values were checked in terms of quantity and quality and the analytical requirements were analysed.

Results. Concerning to the few published reference values in the majority of cases we cannot find reliable details about the quality. In regard to the reference values and the trace analysis we have to realise that the analysis is a very complex system of different analytical steps. At all steps we can observe numerous interference factors which can influence on the final result and which are difficult to eliminate. We have to distinguish various pre-analytical factors and analytical factors. In our laboratory approximately 15% of the total working time is used to perform the internal and external quality control. In Germany the external quality control on hazardous compounds in blood and urine has been performed under occupational and environmental health aspects.

Conclusion. The history of the reference values is closely connected to the development of safe analytical and reference methods and to a safe quality assurance management system. This must be taken into account in the new established *Refmed* programme which aims to provide national and European decision makers, occupational and environmental-health professionals, the general public and the media with an up-to-date, easy-to-use database of safe reference values and an source of information to help them make better-informed decisions in prevention, rehabilitation and for the compensation.

SIMPLE COMPUTER BASED ANAMNESIS-TOOL “E-ANAMNESE 2003” FOR GATHERING LARGE DATA AMOUNTS

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Aim. For a reliable differential diagnosis the individual state of health and the exposure from the workplace and the environment must be established on high level of accuracy, precision and completeness. The collection of all necessary data needs time from physician, patient and data transfer process. To minimize the expenditure of human labor and the errors the anamnesis procedure is to be optimized. Target is to find an elementary computer based solution.

Method. For this purpose we analyzed the anamnesis process and the in-house developed questionnaire structure and developed an algorithm. For the programming various programming languages were selected and compared. The main choices were a C++ based language or similar (Visual Basic, Delphi) or an Internet based solution (PHP, Java, Pearl). The necessary ergonomically tools were determined by testing the software by a diverse population (in-house colleague, various people on conventions (Medica 2002 Düsseldorf, ICOH 2003 Brazil, DGAUM 2003 Dresden), people ageing from 22 to 65).

Results. As a common characteristic for the anamnesis process, the physician asks a question and depending on the answer given by the patient, the next question(s) is asked.

The tree structure of the questionnaire is mirrored in the database, which runs in background. C++ was chosen because of the programming possibilities and the specifications the software has to accomplish such as dynamical forms, to read out current question, language independence, speed, and complexity of the questionnaire.

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Simple computer based solution means dynamical-triggered forms. The next questions are shown or not based on the answer the patient previously gave. In this way only relevant questions are asked, avoiding an unnecessary fatigue and allowing large questionnaires. The current questionnaire allows the recording of over 9.000 parameters. A paper & pen questionnaire version would be, in this case, unreasonable. Another main aspect is the ergonomic variances the software. The change font size, font color, question position and even text magnifying is possible. As a result the patient is able to set the parameters for an individual user-optimized surface for answering the questionnaire. The software can be operated by a keyboard and mouse or by touch screen. The program reads out loud the current question.

The software also permits the creation of any other data based dynamic questionnaire. The patient data is saved in a central database. New questions or later corrections can be done any time later by means of an editor. It is also possible to change the question order. The time and the misses of the patient are recorded for each questionnaire page so we can improve the ergonomics of the questions.

Conclusions. We developed new multimedia and multi-language patient questionnaire software "*e-Anamnese 2003*", which records all the parameters from the patient. As a result we have a very efficient, complete and time-cutting anamnesis. The whole process is highly standardized which allows complex statistical analysis on the gathered data.

The software can be used in the medical praxis as a reference values generator and supporting tool in the differential diagnosis.

MAXIMUM ADMITTED VALUE OF CHEMICAL HAZARDS IN THE WORKING ENVIRONMENT AND BIOLOGICAL FLUIDS. CERTITUDES AND CONTROVERSIES IN ROMANIA

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Evaluation of industrial chemical hazards requires a comparison between measured levels for chemicals in the working environment and biological fluids and a set of standards published in each country at variable spells. Specialized organisms from developed countries (ALGIH, NIOSH, OSHA) elaborate these standards with modifications according to up to date research results. From the point of view of their name, these "admitted values" are different for each organization and this creates confusions for the countries, which adopt them. It is accepted that the name Maximum Admitted Concentration (CMA) used in the Romanian standards needs to be discussed and possibility revised.

Considering personal experience as well as speciality literature data, the authors critically estimate the notions of "Levels Without Occupational Exposure", "No Adverse Health Effect Level", "Chemical Effect Level", "Admissible Biological Limit" (term used in Romanian legislation). This paper also remarks the importance of the so-called "grey zone" for Occupational Medicine. Also presented and discussed are the levels of these "limits", as they are sometimes very different with different authors.

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SPECIALS

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BIOTRANSFORMATION AND MULTIDRUG-RESISTANCE TRANSPORTERS (ABCG2) IN HUMAN TUMORS: IMPLICATIONS FOR CANCER CHEMOTHERAPY

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The efficacy of chemotherapy is limited by the intracellular concentration of anticancer drugs in tumour tissue. Drug metabolizing phase I/II isoenzymes and membrane transport proteins (efflux pumps) can significantly alter drug concentration in tumour cells and have therefore great impact on the clinical outcome of patients. Previously, we showed that the cytostatic drug flavopiridol, an inhibitor of cyclin-dependent kinases, is biotransformed by the glucuronosyl-transferase (UGT) isoenzymes 1A1 and 1A9. In human liver cells, flavopiridol is excreted in its glucuronidated form by the multidrug resistance related protein 2 (MRP2), while parent flavopiridol is a substrate for the novel multidrug-resistance (MDR)-transporter ABCG2. Although MRP2 and UGTs have been already identified in the human biliary tract, there are no data about the expression of the novel half transporter, ABCG2, and of sulfotransferases in bile tract tumours. In gallbladder specimens, we found high expression of ABCG2 mRNA and protein. While in epithelial cells in specimens from cholelithiasis patients and in well-differentiated gallbladder tumour cells (histological grade I), ABCG2 is generally located at the luminal plasma membrane in poorly differentiated tumours, ABCG2 is almost exclusively located in the cytosol. This is also seen in high grade cholangiocarcinomas. As ABCG2 has a unique spectrum of cytotoxic substrates and mediates excretion of porphyrins, the clinical consequence of the intracellular localization in poorly differentiated carcinomas of the biliary tract has to be determined.

Using RT-PCR, we also show expression of the drug and hormone-metabolizing sulfotransferase isoenzymes SULT1A1, 1A2, 1A3, 1B1, 1C1, and 2B1, but not 2E1 and 2A1 in human gallbladder samples. This indicates that not only hepatocytes, but also cells in the gallbladder may have an important role in drug biotransformation and excretion. Ongoing studies in our lab show that sulfotransferases are also highly expressed in breast cancer tissue. Sulfation of drugs might be therefore favored over glucuronidation, which have been already shown with estrogen. Therefore, metabolism of flavopiridol is currently studied in breast cancer cell lines using SULT1A1-transfected MCF-7 cells. In summary, our studies on drug metabolism and MDR-transport proteins in the individual tumours should lead to the development of a more selective cancer treatment

COULD FUNCTIONAL CINE MAGNETIC RESONANCE IMAGING BE A USEFUL DIAGNOSTIC METHOD TO DETECT LARGE BOWEL FUNCTION IN OCUPATION RELATED DISEASES?

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Introduction. Constipation can be caused by different pathologies, e.g. focal lesions, following inflammatory diseases as well as systemic pathologies like diabetes or Parkinson's disease. In the list of occupational diseases there are many with gastrointestinal symptoms of the large bowel associated with occupational relevant hazards. Chronic intoxication such as plumb, thallium and different allergens are known for their costive effects. Therefore we mean that the knowledge of large bowel motor function could play an important role for better early diagnosis also in the field of occupational diseases. For this reason we studied the large bowel motility by magnetic resonance imaging (MRI) visualization.

Method. For our examination we used a 1.5T MRI system (SONATA, Siemens, Erlangen, Germany). Two blocks of repeated measurements (in total 40) of the entire abdomen were performed. After the first block of measurements the volunteers drank 180 ml of senna-tea (mild purgative). Images were sorted according to their slice position and viewed in cine mode. The corresponding parameter for measuring bowel motility was the diameter of a bowel segment at a given position on each image (copy / paste mode). Measurement regions were set 5 ± 3 cm adoral of the right colic flexure for the ascending colon, in the medial transverse colon and 5 ± 4 cm aboral of the left colic flexure for the descending colon. Changes of diameter were plotted against time pre and post dose of senna-tea.

Patients. Our pilot study enrolled 10 healthy volunteers (5 male, 5 female) with an age range from 20 to 45 years. None of them showed signs and symptoms of constipation or bowel disorders. They were examined early in the morning (6-7 a.m.) after a starving phase of minimum 8 hours; the overall time of examination varied from 30 to 40 minutes.

Results. Data, which represent diameter of bowel lumen are given as medians and 25%-, 75%-quartiles. The analysis of our examination showed, that in the first block of measurements (without senna-tea) the median of diameter in the determined measured regions in the large bowel counted 3.28 cm (3.18 cm; 3.38 cm) for the ascending colon, 3.04 cm (2.9 cm; 3.09 cm) for the transverse colon and 3.06 cm (2.97 cm; 3.17 cm) for descending colon. The mean deflection in all three regions averaged 0.13 ± 0.1 cm to a given reference line. After the intake of senna-tea the median of bowel diameter increased to 3.43 cm (3.27 cm; 3.63 cm) in the ascending colon, to 3.22 cm (3.1 cm; 3.37 cm) in the transverse colon. The descending colon showed almost no change of luminal diameter, the median of this measurement point counted 2.97 cm (2.8 cm; 3.08 cm). The average deflection of one peristaltic wave gained 0.34 ± 0.8 cm this time.

Conclusion. The use of the study is the description of a MRI protocol, which is designed to assess large bowel motility. It is a non-invasive, radiation-free and for the patient absolutely harmless procedure. It is easy to perform, pain free and not time consuming. We mean, that functional cine MRI is an objective and unified diagnostic technique for examination of large bowel motility, represented by luminal diameter changes and their amplitudes as well as by frequency of these changes. We think that this examination technique may improve the

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diagnosis of large bowel motility disorders, which by now can be only diagnosed by invasive or poor specific x-ray-assessments, e.g. colon transit time. To assess the validity of these methods for occupational medicine further studies will be performed.

THE INFLUENCE OF GASTRITIS TO ABSENTEISM

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Aim. 2% of the inhabitants of Germany suffer from peptic ulcer, 4,000 people die. Different authors report, that about 100% of duodenal ulcer and chronic gastritis are associated with helicobacter pylori. In the annual review of the health insurance companies there were reported in 1995 600,000 cases of disability by gastritis and duodenal and stomach ulcer with 6 million days of disability. We liked to see, whether we can influence the connection between disability and Hp-associated gastritis by eradication of Hp.

Methods. 61 patients were divided into three groups. All persons had to fulfil inclusion and exclusion criteria. Group 1 with 30 patients was treated with amoxicilline, metronidazole and pantoprazol for 10 days, group 2 with 5 persons with azithromycine, metronidazole and pantoprazol for 7 days, group 3 with 26 persons was a control group without treatment. All persons got a endoscopic examination of the upper gastrointestinal tract before and after therapy. In the period of work of two years before the study the disability days were ascertained and compared with the disability days over 1 year after eradication.

Results. After eradication of Hp. the endoscopic results of the gastric mucosa were much better than before. Only in a few cases we observed a minimal gastritis, no ulcer, no erosion. Before eradication the disability frequency was around 27 days in both therapy groups. After eradication of Hp. the successfully treated persons showed a disability for 5.5 days only, while the non-responders showed a disability of 26 days in group 1 and 29 in group 2.

Conclusion. The annual review of the health insurance companies shows, that 66.6% of the disability days are caused by 4 groups of diseases: musculo-skeletal disorders, respiratory diseases, accidents and diseases of the stomach and bowel. Gastrointestinal diseases themselves have a rate of 27.6 disability days per year, most of them in male workers with an age >45 years. Between 1980 and 1995 the rate of disability days by diseases of the upper gastrointestinal tract decreased by 24%. The rate of cases increased with 41%. Eradication of Hp. at workers with Hp-positive gastritis can reduce the rate of disability days to one third. No difference was found between the two different therapies. The disability days caused by gastritis and ulcer are of great economic importance. The cost for eradication of Hp. is about 250 Euro; about 3.5 mrd. Euro is the amount, which is lost for the national income caused by disability days. Strictly eradication of Hp. could be of great interest for health care workers and occupational medicine in industry.

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HEPATIC AND KIDNEY EXTRACELLULAR MATRIX EXPERIMENTAL STUDY IN ACETAMINOPHEN INTOXICATION

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Aim. The aim of this study was to assess the hepatic and kidney extra cellular matrix proteoglycans under toxic doses of acetaminophen (APAP), a mild analgesic and antipyretic agent.

Materials and methods. 20 mice and 30 Wistar rats were treated with toxic doses of APAP, in acute and chronic experiment. Serum analysis, histopathological study and image analysis for liver fibrosis were performed in chronic experimental group. In acute intoxicated mice group, liver and kidney tissue were prepared for light microscopy, electron microscopy and RT-PCR analysis.

Results and discussion. Ultrastructure of proteoglycans reveals convoluted filaments with lateral projections, frequently associated to collagen fibres, cell surface and other matrix components.

Strong positivity was detected in the necrotic area of acutely damaged liver, perisinusoidal space and the portal area. Kidney reveals high amounts of proteoglycans, controle mesangial proliferation and matrix accumulation.

Conclusions. Proteoglycans could create an electrostatic barrier to the transfer of anionic molecules from the sinusoids to the hepatocytes within the subendotelial space; detection of increased positivity of proteoglycans in the perisinusoidal area suggests that cells of this region could be involved in proteoglycans production in normal and damaged liver. Prolonged APAP administration causes progressive and irreversible damage to kidney interstitial matrix.

PSYCHOLOGICAL DIMENSIONS IN STRESS MANAGEMENT – POSSIBILITIES TO ACT FOR OCCUPATIONAL HEALTH IMPROVING

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Aim. To find significant relationships between some individual psychological dimensions and psychosocial stress resistance, aiming at some interventional measures to increase the stress management abilities, for negative effects on health status reduction.

Material and methods. In a group of 271 subjects from a food industry, were investigated: the level of emotionality, activity, length of reactions, learned helplessness, motivational option quickness, intrinsic motivation and individual resistance to psychosocial stress. The data were analysed by multiple regression of stress resistance on psychological dimensions scores.

Results. Psychological dimensions with significant influence on stress resistance:

Psychological dimensions	Regression coefficient	Std. Error	t (263)	p-level
Intercept	2.636	.333	7.905	.000000
Emotionality	-.193	.070	-2.745	.006
Activity	.267	.093	2.882	.004
Motivational option quickness	.338	.115	2.936	.003

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Conclusions. Since the psychosocial stress resistance was significantly related with the level of emotionality, activity and motivational option quickness, it is possible to initiate some psychological interventions focused on emotional level reduction, activity level and motivational option quickness increment, related to symptomatology evaluation before and after intervention.

PULSED MICROWAVES EFFECTS ON PERIPHERAL NERVOUS SYSTEM IN RADAR OCCUPATIONAL EXPOSURE

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Aim. To reveal the possible peripheral nervous systems' (PNS) impairment in long-term, low-level exposure to pulsed microwaves (PMW)

Method. Complex epidemiological design (cross-sectional and cohort retrospective studies followed by three years prospective study). Exposure evaluation included PMW's power density (PD) measurements and ergonomic analysis. Focused on PNS, health status assessment comprised clinical, neurological examinations and electromiogram. Data was processed by STATISTICA and EPIINFO. The exposed were comparable with controls.

Results. PMW had 300-12000 MHz frequencies, 500-2000 Hz pulses repetition frequencies, and 0.5-2 μ s pulse lengths. PD had wide range but, generally, didn't exceed permissible levels. Health status revealed significant decreases of sensory and motor conduction velocities, associated with occupational exposure; RR shows a six time higher risk for sensory or sensory motor polyneuropathy (PNP) after 16 years of exposure than the controls. Prospective study showed oscillations and reversibility of PNP and significant association ($z=2.13$, $p=0.033$) with the annual exposure. The test of associations between PMW's radiometric parameters and PNS conduction velocity was positive for peak PD, and in the case of dosimetric parameters, for last month and last year doses. Pearson "r" and linear regression supported dose-effect relationships. By revealing 85% value, power study (1- β error) support these findings.

Conclusions. An international priority, these results shows, by means of positive causality test, an important but reversible impairment of PNS in PMW occupational exposure. PNP changes dependence of PMW's parameters is a challenging finding and indicates the role of cellular induced fields in neurotransmitters metabolism and in neuro-physiological mechanisms.

PROPOSAL FOR IMPROVING PROTECTION STANDARDS FOR OCCUPATIONAL EXPOSURE TO EXTREMELY LOW FREQUENCY MAGNETIC FIELDS

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In last decade, some important documents concerning exposure standards such as NRPB (1993), CENELEC Prestandard (1995), ICNIRP Guidelines (1998) have been released. These documents are dealing with the entire frequency spectrum of varying electromagnetic fields (0 Hz - 300 GHz).

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In order to achieve the harmonisation of Romanian regulations with EU ones, we have proposed a new Romanian standard in the field of health protection against occupational exposure to electromagnetic fields. The limit values are mainly based on the ones set by ICNIRP guidelines. At the low end of spectrum, additional limits have been introduced, in terms of frequency-dependent values, in order to make a continuous transition between adjacent frequency ranges with discordant specifications for short-time exposures. In this paper the method used to eliminate the discontinuity of short-time exposure levels is presented.

In the case of ICNIRP guidelines, both ceiling and time-weighted average values are provided for static fields, but only ceiling limits are provided for extremely low frequency fields. The absence of ceiling limit values for slowly variable fields leads to a discontinuity of limit value for short-time exposure when the frequency tends to 0 Hz. The new additional limits for short-time exposure to magnetic fields were calculated to fit to the limit values set by ICNIRP for static and extremely low frequency magnetic fields and, also, to provides the continuity of limit values for the entire frequency spectrum.

The proposed method of setting both types of limit values for magnetic fields between 0 and 1 Hz can contribute to achieving exposure standards that have continuity on the entire frequency spectrum. As far as it eliminates discontinuities, it will also help the implementation of regulations by eliminating some uncertainties. Therefore, it could reduce difficulties in checking compliance with standards.

USE OF GAS CHROMATOGRAPHY FOR ASSESSING OCCUPATIONAL EXPOSURE TO SOME ANTINEOPLASTIC AGENTS (CYCLOPHOSPHAMIDE AND IPHOSPHAMIDE)

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Objective. Determination of some specific indices, by a sensitive and selective method, in occupational exposure to cyclophosphamide and iphosphamide was the aim of this study.

Methods. After environmental air is sucked through a filter, the filters are extracted and following the concentration, the antineoplastic agents are derivatized with trifluoroacetic anhydride. A capillary column and the electron capture detector are then used to perform the gas chromatographic analysis. Urine samples were collected at the end of workshift and after extraction, centrifugation and concentration, cyclophosphamide and iphosphamide were derivatized and analysed as mentioned above.

Results. Detection limit of the method is 20 ng/m³ air and 24 ng/l urine respectively. In the investigated working places, cyclophosphamide has been detected at levels of 0-73 ng/m³ air and 0-25 ng/l urine respectively. Iphosphamide was not detected in any of air and urine samples. Air sampling was done during preparation of the drugs.

Conclusions. The described method, completed by other tests, may be useful for risk assessment in relation to occupational exposure to antineoplastic agents during preparation and administration of these drugs. Difficulties occur because there are not threshold limit values for these compounds.

DETERMINATION OF SOME HALOGENATED ALIPHATIC HYDROCARBONS BY HEADSPACE GAS CHROMATOGRAPHIC METHOD

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Objectives. In this study we intend to elaborate a method for the simultaneous determination of some halogenated aliphatic hydrocarbons, trichloroethylene (TRI), tetrachloroethylene (TET) and of the metabolite trichloroacetic acid (TCA) in blood and urine from exposed workers, using a headspace gas chromatographic (HSGC) method.

Method. For the analytical determination we used an Agilent GC 6890 equipped with ECD and a HP-5 column (30 m x 0.32 mm x 0.25 (m). The oven temperature programme was as follows: isothermal at 350 °C for 5 min., then raised at 180 °C/min. to 400 °C for 1.64 min. and finally raised at 1500 °C with 27 °C/min. when held 2,74 min. Automatic headspace sampling was performed using an Automatic Sampler 7683. The injection was performed in splitless mode and the injected headspace gas volume was 50 µl. TCA was determined as chloroform, which is produced by thermal decarboxylation. For simultaneous determination of TRI, TET and TCA 0.5 ml of blood or urine were diluted in 0.5 ml of Na₂SO₄ saturated solution, using standard vials of 2 ml, tightly closed with screw caps. The incubation was performed at 900 °C for 90 min. before HSGC analysis.

Results. The standard curves for TRI, TET and TCA were linear on the used concentration ranges 0.146 – 1.46 µg/ml, 0.162 – 1.625 µg/ml and 0.014 – 0.148 µg/ml respectively. The calibration curves equations were: $y = 704.109 x + 26.56$, correlation coefficient 0.9973, $y = 3756.926 x + 0.830$, correlation coefficient 0.9995 and $y = 42143.568 x - 83.084$, correlation coefficient 0.9975.

The proposed method is rapid and good precision is possible. Sample preparation is simple and the sensitivity is good (0.01 µg/ml). For this reason the proposed method is suitable to estimate occupational exposure to chlorinated solvents in human.

MULTIPLE EXPOSURES IN THE ANTIBIOTICS INDUSTRY AND THEIR POTENTIAL EFFECT ON THE EMPLOYEES' HEALTH STATUS

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Aim. Our study is aimed to investigate the health status of the workers involved in processes of antibiotics research and manufacturing in relation with the workplace conditions and occupational exposures to multiple hazards. The cumulative exposure consists of cutaneous and respiratory intake of chemical hazards and antibiotic products, mainly vapours and dusts.

Materials and methods. A cross-sectional study was performed. It focused on 43 workers (44.2%) women, mean age 44.2±6.4 years and mean exposure period 23.5±7.5 years in the field of antibiotics research and production. We performed different tests concerning the health status impact on working conditions, and many tests containing complex questionnaires about life-style, work-history, clinical and physical examination, respiratory physiologic indicators, electromyography, electro-cardiogram, haematological examination, biochemical and biotoxicological tests.

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Results. The processed data revealed the high prevalence of digestive diseases (59%) and cardiovascular diseases (45%). The lung function evaluation showed respiratory disorders in 23.7% of the subjects. The electro-cardiogram revealed rhythm disturbances and/ or ischaemical changes in 33.3% of the workers. The electromyography distinguished motor-sensitive polyneuropathy in 48.7% of the patients. Biological effect markers showed certain abnormalities, possible induced or potentated by cumulative noxious chemicals in workplaces.

Conclusions. This study showed the multitude and the diversity of the pathological changes in the health status of the studied group of workers. We assume that the occupational exposure might have a main role in the ethiology of these changes.

IMMUNOGLOBULINES SERIC LEVELS EVALUATION IN OCCUPATIONAL EXPOSURES TO ORGANIC DUSTS

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Aim. Assessment of the immunoglobulines (Ig) seric levels in workers exposed to organic dust (wood and jute).

Material and method. A number of 145 individuals – 97 exposed (group I: 47 workers with wood material processing furniture; group II: 50 workers with jute) and 48 controls have been investigated.

The seric levels of IgE (ELISA - immunoassay enzyme multiplied) and of IgG, IgA, IgM (immuno-diffusion Mancini technique-on immune-plates) were determined.

Results. In both types of exposures there are cases with: at least one type of Ig modified (exceeded the reference values) and concomitant changes of at least two type of Ig.

Considering the rate of subjects with increased values we noticed:

GROUP	Ig E %	Ig G %	Ig A %	Ig M %
group I	8.50	25.35	4.25	23.40
group II	36.00	32.00	8.00	14.00
Controls	25.00	37.50	6.25	25.00

Conclusion. Taking into account the statistical significance (chi2 test), the numerous cases with increased values of Ig in controls (general population) is a confounding factor that is a challenge for authors to continue this study with a larger number of subjects.

EMOTIONAL CHARACTERISTICS EVALUATED WITH WAGNER HAND TEST AT WORKERS OCCUPATIONALLY EXPOSED TO VEGETAL DUSTS AND FIBRES

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Aim: The assessment of certain emotional characteristics of subjects occupationally exposed to vegetal (jute) dusts, fibres and microorganisms.

Material and method: The Wagner Hand Test (projective technique based on hierarchical behavioural organizations) was applied to 113 employees in a textile unit using jute imported from Bangladesh. The work place air contains vegetal dusts, fibres and microorganisms (bacteria and fungi).

Results: The investigated group contained socially positive categories (useful social roles: Afection = 33%; Dependence = 7.08%; Communication = 100%) and negative categories (Direction - domination, control = 2.65%; Agression = 36.28%). The subjects presented: 66.37% - Maladjustive scores concerning "difficulty in successfully caring out action tendencies"; 24.78% - Crippled scores, types of inferiority and degrees of incapacitation; 57.52% - Tension, partial suppression and dissipation of energy under stress; 12.39% of the subjects presented Withdrawal scores, abandonment of meaningful, effective life roles; 7.96% - Description, feeble and safe reaction to reality; 4.42 - Failure, organic deterioration, dissociative tendencies. Also, the lack of caution and circumspection represent 15.93%, and 72.56% of the subjects presented pathological scores (15.04% represent mild and more marked psychopathological disturbances).

Conclusions: Agression, Maladjustive, Crippled, Tension, Withdrawal, Pathological scores suggest some consequences of the emotional and physical discomfort; in particular could be a occupational discomfort, considering the workplace conditions characterised by the presence of vegetal (jute) fibres, dusts and microorganisms.

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ROLE OF SULFOTRANSFERASES IN THE BIOTRANSFORMATION OF ENVIRONMENTAL CHEMICALS

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The efficient excretion of toxic environmental chemicals is dependent on their water solubility. Therefore, lipophilic compounds are metabolized by phase I and phase II biotransformation enzymes to more hydrophilic derivatives. While in phase I, a hydroxyl-group is introduced into the molecule, in phase II, either the hydroxylated metabolite or the parent compound is conjugated with e.g. glucuronic acid, glutathione and sulfate.

Members of the cytosolic sulfotransferase (SULT) superfamily promote the sulfation of a huge amount of structurally diverse drugs and xenobiotics, hormones and neurotransmitters.

The reaction is catalyzed by the transfer of the sulpho-moiety from the cofactor 5'-phosphoadenosine-3'-phosphosulphate (PAPS) to the hydroxyl- and/or amino groups of acceptor molecules. The activity of SULTs is of particular interest, as, although it generally leads to a detoxification, and it can also produce more toxic compounds. In the case of detoxification, the resulting sulfate products are stable and more hydrophilic than the parent compounds. Therefore, they are easily excreted. This applies for a number of sulfate-conjugates formed from e.g. nonylphenol, bisphenol A, diethylstilbestrol acting as environmental estrogens. However, other sulpho-conjugates are unstable. Strong electrophiles are formed, which covalently bind to DNA and proteins. In this case, conjugation by SULTs results in metabolic activation and toxification. In fact, the mutagenicity and ultimate carcinogenicity of many xenobiotics after sulfation, e.g. of hydroxyl arylamines and benzyl alcohols, had been established.

In humans, 10 SULT genes have been characterized. The expressed SULT isoenzymes substantially differ in their substrate specificity and tissue distribution. Genetic polymorphisms in different ethnic populations occur to a high degree. A relation between SULT polymorphisms and their functional consequences had been recognized, and the influence of the individual SULT1A1 genotype on susceptibility to colorectal and breast cancer had been established.

Today, the identification of SULT-isoenzymes and expression of individual SULT-isoforms in cell culture systems offers excellent tools to further understand the role of SULTs in the toxification and detoxification of environmental toxins.

BASIC ASPECTS OF COMPREHENSIVE ERGOPHTHALMOLOGY

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Ergophthalmology represents a branch of the area of health management at work and is not only ophthalmology applied in the field of health risks arising from working conditions. Therefore, it is essential to follow some definitions of WHO when it comes to locating the current position of ergophthalmology.

In July 1997, WHO published its „Healthy Work Approach“, which specified the „Global Strategy on Occupational Health for All“. The Healthy Companies Network (HECONet) was the first practical implementation of this concept. In this program four fundamental principles are considered as important:

Health promotion

1. Occupational and environmental health and safety, including the aspects of Public Health
2. Human resources management
3. Sustainable social and environmental development

For reasons of efficiency and costs it is highly recommended to integrate these principles at a practical level. A good example of a holistic approach is GP HESME, the joint program of the European Union and WHO. Here three key factors are considered as important for an effective workplace health promotion:

Interdisciplinary effort involving many different players in the enterprise;

active participation and cooperation among all players;

a comprehensive approach, combining activities that focus on the individual with those that address the design of the working and organizational conditions.

These give a clear picture of the objectives of ergophthalmology: to create visual working environments that are equally conducive to quality of life and performance, to strengthening the individual in order to be able to achieve his/her maximum performance. This entails looking at the system overall, and not only at the individual. It also entails prevention related both to the workplace situation and to the individual behaviour at the workplace and outside it.