



Analytica Conference 96

- Analytische Methoden
und Anwendungen
- Biochemische Analytik
- Medizinische
Laboratoriumsdiagnostik

Veranstalter in Zusammenarbeit mit der
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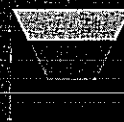
Gesellschaft
Deutscher Chemiker

Gesellschaft für Biochemie
und Molekularbiologie

Institut für Klinische Chemie,
Universität München

ABSTRACTS

23.-26. April 1996
München 



P144

R. Kiehl, Furth

IgE-Regulation, Proliferation and Development of Aids: G. Interferon, Interleukins, Reactive Oxygen Species and Total IgE as Monitoring/Response Tools for Therapy

Toxic mercury or reactive oxygen species (ROS) seem to be not responsible for changes in the IgE-levels of atopic eczema (AE) patients but for activation of metalloproteases and associated glucocorticoid sensitive inflammations of the skin. ROS may be obtained by prolonged exposure of skin cells to sunlight and also responsible for development of skin carcinomas. Metalloproteases degrade GIFN. Especially the course of capillary leucocytes collagenase (and gelatinase) activity out of the skin is opposite to GIFN concentrations and in correlation with the lactoferrin activity from the same lesion. Skin Prick-testings and skin Epicutaneous-testings do not match either with the total/specific IgE-measurements. It is concluded, that the adaption of cells to stress conditions includes the GIFN and Il-4 controlled synthesis of IgE antibodies by B-cells. Environmental pollutants, including formic aldehyde, sulfite/SO₂, isocyanates and anhydrides, reacting irreversibly with the involved essential dithiol/disulfide redox state (and a coupled unknown membrane bound factor: possibly a FeS-protein but not glutathione) or CO, by binding to the NADPH oxidase, are shifting the redox state to the reduced form with enhanced probability for IgE synthesis (low for O₂⁻) and development of AE or hyper-IgE syndrome. The oxidized form ist not able to synthesize IgE but O₂⁻ and the risk for mitogen stimulated proliferations, buildup of leukemia, carcinomas and CGD is extremely high. The first expression of, for instance, food- or inhalative allergen specific IgE and the allergical triggering of AE may purely be incidental and relate to autoimmune diseases. The pathogenesis of AE and concomitantly of leukemia relates to the development of AIDS. All factors influencing mitochondrial energy formation, are influencing IgE and O₂⁻-level. A pharmacological treatment of HIV-infection by nucleotide analogs should take care of this fact.

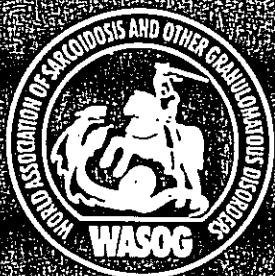
Literatur: Kiehl, R. (1994) Int Alk-Ciba Corn J Symp, Benzheim, Abstr book; Int Conf on New-Appl of Emerg Mol Diagn for Inf Dis, London, Abstr book, P11 and (1995) Ammino Acids 9 (1), 20; WASOG and BSACI J meeting, London, Proc p.54, P119, BIOSpektrum, AV, Hd, in press and J.Mol.Med., submitted.

P145

B. H. Klein, J.W. D.
N-Nitro-L-arginin ur
Nabelschnurblut mit

Stickstoffmonox
des L-Arginins
dauer - mit Fur
eine Rolle spie
methylester, si
diese Inhibitore
ob bei normal
unterschiedlich
Die beiden Arg
lonenaustausch
quantitativ/bes
Es werden die
einzelner chron

- /1/ Kurt Krej
- Naunyn-S
- /2/ Mohamm
- Br. J. Ph



**WORLD ASSOCIATION OF SARCOIDOSIS AND
OTHER GRANULOMATOUS DISORDERS
and
BRITISH SOCIETY FOR ALLERGY AND
CLINICAL IMMUNOLOGY**

JOINT MEETING

15 – 20 October 1995

Kensington Town Hall, London, UK

PROCEEDINGS


Scientific Programme continued

TUESDAY 17 OCTOBER 1995 – continued

PARALLEL D - LOWER FOYER

- | | |
|---------------|--|
| 16:00 – 17:00 | CLINICAL ALLERGY POSTER DISCUSSION – continued |
| P/117 | A Combined Ventilation System/High Efficiency Vacuum Cleaner Approach to Allergen Avoidance in Homes E H Shepherd, J M Frederick, J O Warner and J A Warner University of Southampton, UK |
| P/118 X | Skin Tests and Allergic Symptoms in the First 2 Years of Life of Babies Born to Atopic Parents E A Miles, A C Jones, J A Warner, B M Colwell and J O Warner University of Southampton, UK |
| P/119 | IGE-Regulation, Proliferation and Development of AIDS. Total IGE as Monitoring/Response Tool to Therapy R Kiehl Laboratory and Research for Mol Med/Biology, Furth in Wald, Germany |
| P/120 | Concordance of Specific IGE and SPT Sensitivities to Aeroallergens in Families with Two Generations of Asthma A H Thomson, P Standing, J A Warner, A C Jones and J O Warner University of Southampton, UK |
| P/121 | A Comparison of a Conventional and High Efficiency Vacuum Cleaner in the Homes of Children with House Dust Mite Sensitive Asthma J M Frederick, J Dahil, S Rouhakhsh, J O Warner and J A Warner University of Southampton, UK |
| P/122 | A Clinical Assessment of a Bed Covering System in Atopic Dermatitis (AD) Patients J M Frederick, S Bevin, J A Warner and J O Warner University of Southampton, UK |
| P/123 | Domestic Allergen Exposure in Infancy in South East England O Lynch, J Harris, P Mills, S Moffat, C White, P Cullinan and A J Newman Taylor National Heart and Lung Institute, London, UK |
| P/124 X | Specific Immunotherapy to Parietaria Pollen – Open Study in Patients Monosensitized, with Bronchial Asthma and/or Rhinitis M Morais de Almeida, C Santa Marta, P Leiria Pinto, G Pires, J M Abreu Nogueira and J E Rosado Pinto Hospital Dona Estefania, Lisbon, Portugal |
| P/125 X | Correlation of Total IgE Determinations Obtained by IRMA (with TECAM 8000) and Immulite J M Abreu Nogueira, V Loureiro, M Morais de Almeida and J E Rosado Pinto Hospital Dona Estefania, Lisbon, Portugal |
| P/126 | The Effects of Inhaled Budesonide in Asthmatic Patients Z Arsovski, D Dokic, M Gavrilovski and T Stefanovski Medical Faculty Skopje, Republic of Macedonia |
| P/127 | Specific Intranasal Immunotherapy: Effect on Nasal and Peripheral Eosinophil Counts Eosinophil Cationic Protein and Nasal Provocation Test J Rodrigues, J P Moreira da Silva, L Delgado, M Miranda, L Plácido, L Cunha and M Vaz Azevedo Hospital S Joao, Porto, Portugal |
| P/128 | Nasal Allergen Challenge in Suspected Allergic Skin Prick Test Negative Patients G K Scadding and Y C Darby Royal National Throat, Nose and Ear Hospital, London, UK |


6-820



NEW APPLICATIONS of EMERGING MOLECULAR DIAGNOSTICS for INFECTIOUS DISEASES

June 26-27, 1995
The Regent Hotel
London, England

Please Return to : *Reinhold Kiehl*



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E-mail: chi@world.std.com

Institute of Physico-Chemical Medicine, Ministry of Health

8. M. Yu. Brodsky: Detection and Identification of *Chlamydia Trachomatis*, *Mycoplasma Hominis* and *Ureaplasma Urealiticum* by Amplification of rDNA
(no abstract available at time of print)

Institut Pasteur, Unité d'Immunologie Microbienne

9. Jihong Meng: Interest of PCR for the Diagnosis of Hepatitis E

International Institute of Anthropology

10. G. Lucotte: Detection and Genotyping of Herpes Simplex Virus Types 1 and 2 by Polymerase Chain Reaction

Laboratory and Research for Molecular Medicine/Biology

11. R. Kiehl: IGE-Regulation, Proliferation and Development of AIDS

London School of Hygiene & Tropical Medicine, Department of Clinical Sciences

12. R. McNerney: Using Simple Colorimetric Detection for PCR of Tuberculosis

London School of Hygiene and Tropical Medicine, Department of Medical Parasitology

13. I. S. Adagu: Rapid Detection of Chloroquine Resistance in *Plasmodium Falciparum* Using Whole Blood Sample Blotted on Glass Fibre Membrane
14. Aura Aguirre: Diagnosis of Amoebiasis by Polymerase Chain Reaction-Solution Hybridization Enzyme Linked Immuno-Assay (PCR-SHELA)

Medbioservice Company

15. G. Panasenko: Combination Antisense Approach with Oligonucleotide-Directed DNA Triple Helix Formation
16. G. Panasenko: Identification of HTLV-I by PCR in Patients with Preliminary ELISA-Screening and Investigation These Genomes and Serum

Municipal Health Service of Amsterdam, Department of Public Health

17. G.J.J. Van Doornum: Detection of *Chlamydia Trachomatis* by a Ligase Chain Reaction Based Assay in Samples Collected from Various Sites in STD-Clinic Patients

IGE-REGULATION, PROLIFERATION AND DEVELOPMENT OF AIDS

R. Kiehl

Laboratory and research for Mol. Medicine/Biology,
93437 Furth, Germany

An "in vivo" test system on blood of atopic eczema patients has been developed which leads to following regulatory scheme for IgE-synthesis, proliferation and development of AIDS: A dithiol/disulfide interchange mechanism is involved in IgE-synthesis. The associated redox state is sensitive to Hg^{2+} , Diamide, γ -IFN and Il-4. Il-4 reacts antagonistically to γ -IFN in blood samples and cell cultures, although to opposite directions. Elements involved in the signal transduction pathway from γ -IFN or Il-4 to IgE were concluded to be the cytokine receptors, (a) cytosolic G protein (s), NADPH oxidase, a yet unknown electron transfer factor (etf), redox factor (ref), nuclear transcription factors and endonuclease. These elements are presumed to build up an electron transfer chain, NADPH to DNA (IgE), which is coupled to ongoing mitochondrial energy formation. The involved reduced ref, stimulating DNA-binding, carries an essential sulfhydryl group, whereas the oxidized state, responsible for catalytic endonuclease activity, carries a catalytic disulfide: γ -IFN transduces redox signals during short time intervals (blood samples) whereas during longer intervals (e.g. cell cultures) the involved oxidized redox factor determines translational activities. The involvement of Mg^{2+} -or Ca^{2+} -sensitive serine residues in the signal transduction to IgE synthesis is suggested by APMSF/EDTA-titrations. An important role in modulating IgE concentrations play kinases, esp. protein kinase C. Toxic mercury or reactive oxygen species seem to be not responsible for the changes in patients IgE-levels but for activation of metalloproteases and associated glucocorticoid sensitive inflammations. Metalloproteases degrade γ -IFN. Especially the course of leucocytes collagenase activity is opposite to γ -IFN concentration. The adaption of cells to stress conditions includes the γ -IFN and Il-4 controlled synthesis of IgE antibodies. Environmental pollutants, including formic aldehyde, sulfite/ SO_2 , isocyanates and anhydrides, reacting irreversibly with the involved essential dithiol/disulfide redox state or CO, by binding to the NADPH oxidase, are shifting the redox state to the reduced form with enhanced probability for IgE synthesis (low for O_2^-). The oxidized form is not able to synthesize IgE but O_2^- and the risk for mitogen stimulated proliferations is extremely high. In addition, weakening of the immune system by dermal and intestinal dysbiosis (*C. albicans*), food (carbohydrate) as well as psychogenic stress (norepinephrine) leads in enhanced development of IgE antibodies. The total (unspecific plus specific) IgE concentrations were normally 10^2 to 10^3 times higher than the measured specific ones. The first expression of, for instance, food- or inhalative allergen specific IgE may then purely be incidental and relate to autoimmune diseases. The pathogenesis of atopic eczema and of leukemia (proliferation) relates to development of AIDS.

Our system is able to be used for detection of almost every blood parameter. This fact is most important for research on AIDS-patients. Pharmacologists were able to do "in vivo" experiments without the use of experimental animals.

References:

Kiehl, R (1994) 13. Vortragstagung der Fachgruppe Biochemie in der GDCh, Abstr. P 2.6; Analytica Conference, Abstr. p.195-196; Biol. Chem. H.-S. 375, S. 61; BIOTEC 94 and Int. Alk-Ciba Corning Joint Symp.

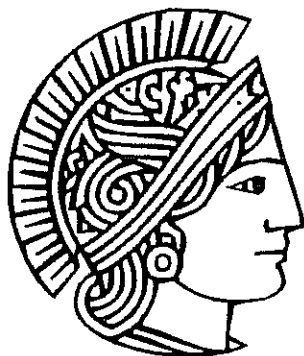


**Gesellschaft
Deutscher Chemiker**

**Fachgruppe
Biochemie**

13. Vortragstagung

**Molekulare Mechanismen
der Signaltransduktion**



**Institut für Biochemie
im Fachbereich Chemie der
Technischen Hochschule
Darmstadt**

**Darmstadt
16. - 18. März 1994**

Termin: Donnerstag, 16.00 - 17.30 h

.Paul Wrede, Gisbert Schnelder, Felix Pahl, Tilman Todt und Sylvia Röhik

ZUSAMMENFASSUNG

Thema:
(in Großbuch-
staben)

IGE-REGULATION BY DITHIOL/ DISULFIDE INTERCHANGE: IN "VIVO"
STUDY ON BLOOD OF ATOPIC ECZEMA PATIENTS SUPERIOR TO CELL
CULTURE SYSTEMS

Autor(en):
(Vortragende
unterstreichen)

R. Kiehl

Institut bzw.
Firma und Ort:

Research Department, Spezialklinik Neukirchen, 93453 Neukirchen, FRG

Zusammen-
fassung

A dithiol/ disulfide interchange mechanism is involved in IgE-synthesis. The associated redox state is sensitive to Hg^{2+} , Diamide, γ -IFN and IL-4. IL-4 reacts antagonistically to γ -IFN in blood samples and cell cultures, although to opposite directions. Elements involved in the signal transduction pathway from γ -IFN or IL-4 to IgE are their receptors, (a) cytosolic G protein(s), NADPH oxidase, a yet unknown electron transfer factor (etf), redox factor (ref), nuclear transcription factors and endonuclease. This electron transfer chain, NADPH to IgE, is coupled to ongoing mitochondrial energy formation. The involved reduced ref, stimulating DNA-binding, carries an essential sulfhydryl group, whereas the oxidized state, responsible for catalytic endonuclease activity, carries a catalytic disulfide: in analogy to the mitochondrial transport and ATP synthesis, where activated disulfides were performing phosphoryl transfer or transport activities. The involvement of Mg^{2+} - or Ca^{2+} -sensitive serine residues in the signal transduction to IgE synthesis is suggested by APMSF/ EDTA-titrations. An important role in modulating IgE concentrations play kinases, esp. protein kinase C. Toxic mercury or reactive oxygen species seem to be not responsible for the changes in patients IgE-levels but for activation of metalloproteases and associated glucocorticoid sensitive inflammations. Metalloproteases degrade γ -IFN. Especially the course of leucocytes collagenase activity is opposite to γ -IFN concentration. Environmental pollutants, including formic aldehyde, sulfite/ SO_2 , isocyanates and anhydrides, reacting irreversibly with the involved essential dithiol/disulfide redox state or CO, by binding to the NADPH oxidase, are shifting the redox state to the reduced form with enhanced probability for IgE synthesis. In addition, weakening of the immune system by dermal and intestinal dysbiosis (*C.albicans*), food (carbohydrate) as well as psychogenic stress (norepinephrine) leads in enhanced development of IgE antibodies. The first expression of, for instance, food- or inhalative allergen specific IgE may purely be incidental and relate to autoimmune diseases. The described pathogenesis of atopic eczema should be compared with development of cancer or AIDS.

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Petersenstr. 22, 64287 Darmstadt,
Tel. 06151 - 163657 - Fax 06151 - 165399 u. 166768

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EQUIPMENT

BIOTEC 94

Aug 94

FORUM FÜR BIOTECHNOLOGIE
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Donnerstag, 17.11.1994

Thema der Vorträge
und Poster:

**Anwendung neuer diagnostischer
Methoden in Forschung und Praxis**

In den vergangenen 10 Jahren hat die Entwicklung diagnostischer Verfahren zum Nachweis von Krankheiten, besonders aber von Infektionskrankheiten, einen großen Fortschritt zu verzeichnen. Diese Entwicklung hat viele wissenschaftliche Teilbereiche erfaßt und stützt sich vor allem auf den schnellen technischen Fortschritt in der Computertechnologie, die zu einer eminenten Verbesserung von Instrumenten und Geräten geführt hat und die heute geprägt wird durch die Verfügbarkeit einer hochspezialisierten Software.

Gegenwärtig beobachtet man daher, daß die mit menschlicher Arbeit stets verbundenen Unzulänglichkeiten bei der Durchführung diagnostischer oder analytischer Aufgaben mehr und mehr durch den Einsatz eines höchst "intelligenten Equipments" kompensiert und damit von Geräten übernommen wird, die Genauigkeit und hohe Effektivität auszeichnet.

Parallel dazu hat die kontinuierliche Entwicklung in der molekularen Biologie und Genetik zur Verfügbarkeit innovativer Methoden und Techniken geführt, die sowohl den Bereich der Forschung, wie den der Routineapplikation revolutionieren. In diesem Zusammenhang werden auf der BIOTEC'94 aktuelle Themen vorgestellt, die sich mit den derzeitigen Problemen des Nachweises von Krankheitserregern oder innovativen analytischen Techniken befassen, für die es bisher noch keine praktische Anwendung gibt. Die Beiträge werden einerseits den Einsatz der PCR-Technik auf verschiedenen Gebieten vorstellen und sich ferner mit neueren Entwicklungen auf dem Gebiet der Fourier Transform Infrarot Spektroskopie und ihrem zukünftigen Trend befassen.

Tagungsleiter: Prof. Dr. F. J. Fehrenbach, Berlin,
Prof. Dr. U. Hadding, Düsseldorf
in Zusammenarbeit mit der Deutschen Gesellschaft
für Hygiene und Mikrobiologie, Abt. für diagnostische
Methoden

Vorträge

9.00 - 12.50 Uhr

P.D. Dr. D. Naumann, Berlin
**Infrarot Spektroskopie und Infrarot Mikroskope -
neue diagnostische Möglichkeiten für die
mikrobiologische Analyse**

Dr. H. Fabian, Winnipeg (Kanada)
**Anwendung der Fourier Transform Infrarot Spektro-
skopie in der Neurobiologie und Krebsforschung**

Dr. E. Schreier, Berlin
Diagnostik und Epidemiologie der Hepatitis C

Dr. A. Rolfs, Rostock
Bedeutung der PCR für die Welt des Mikrobiologen

Dr. P. Lens, Tiernhout (Belgien)
**Qualitativer und quantitativer Nachweis von HIV-
RNA durch NASBA**

Dr. R. Wallich, Heidelberg
Identifizierung von *Borrelia burgdorferi* mittels PCR

Dr. E. Böttger, Hannover
PCR-Diagnostik von Mykobakterien

12.50 - 13.50 Uhr "Round-table"-Diskussion

14.00 - 17.00 Uhr Posterpräsentationen

14.00 - 18.00 Uhr Technologieforum
**Forschungs- und Entwicklungsstandort Deutschland
(Programm-Nr. 406)**

Kurzkurse

14.30 - 17.30 Uhr

Moderatorin: Dr. Martina Blefeld, Düsseldorf
Neue Verfahren in der molekularen Diagnostik

Dr. C. Wolff, Bad Oeynhausen
**Multiplex PCR-Assay - ein Ansatz für transfusions-
relevante Viren und Plasmodium falciparum**

Dr. Rolf Kaiser, Bonn
**HIV, über molekularbiologische Forschung zur
Diagnostik**

Dr. Barbara Dockhorn Dvorniczak, Münster
**Molekularpathologie - Ergänzung zu klinischen
Pathologie. Neue Perspektiven?**

Dr. Hans-Joachim Grundmann, Freiburg
Neue Methoden zur Bakterientypisierung

Dr. Anke Hinney, Düsseldorf
**Molekulargenetische Methoden zur Knochenmarks-
Fremdspenderauswahl. Heute schon Routine?**

Dr. Harald Funke, Münster
Sequencing of candidate genes

Prof. Dr. med. F. J. Fehrenbach
Leiter der Abteilung für Mikrobiologie
Robert Koch-Institut

Nordufer 20
D-13353 Berlin
Tel.: (030) 4547-2250
Fax: (030) 4547-2608

Herrn
Dr. R. Kiehl
Spezialklinik Neukirchen
Krankenhausstraße 9
93453 Neukirchen b. Hl. Blut

Ihre Zeichen und Nachricht vom
23.08.1994

Gesch.-Z.: Bitte bei Antwort angeben
Fe/S.

Telefon: (030) 4547-
2250/2466

Berlin
23.08.1994

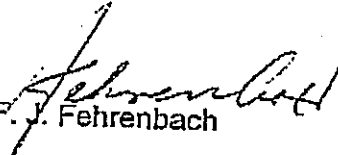
Sehr geehrter Herr Kollege Kiehl,

hiermit bestätigen wir Ihnen, daß Ihr Poster "In vivo study in blood and cell cultures"
zur Präsentation am

Donnerstag, dem 17.11.1994

(und nicht wie telefonisch fälschlicherweise mitgeteilt am Samstag, dem 19.11.94) in der
Zeit zwischen 14.00 und 17.00 Uhr vorgesehen ist.

Mit den besten kollegialen Grüßen und Empfehlungen


Prof. F. J. Fehrenbach

IN "VIVO" STUDY ON BLOOD OF HUMANS RELIABLE FOR PHARMACOLOGISTS
AND OTHER APPLICANTS: SPARE OF ANIMALS AND CELL CULTURES

Reinhold Kiehl

Research Department, Spezialklinik Neukirchen, 93453 Neukirchen, FRG

The "in vivo" assay system we used to explore the IgE regulation in atopic eczema patients proved to be very powerful. IgE regulation is supported by a dithiol/disulfide interchange mechanism. The associated dithiol/ disulfide redox state is sensitive to Hg^{2+} , Diamide, γ -IFN and IL-4. IL-4 reacts antagonistically to γ -IFN in blood samples and in cell cultures, although to opposite directions. γ -IFN transduces redox signals during short time intervals (blood samples) whereas during longer intervals (e.g. cell cultures) the involved oxidized redox factor determines translational activities. The developed system is able to be used for detection of almost every blood parameter. The system is fast and to compare with "life" conditions, by this way cell culture systems with artificial "in vitro" conditions are to spare. This fact is most important for research on AIDS-patients. Pharmacologists were able to do "in vivo" experiments without the use of experimental animals.

R. Kiehl (1994) 13. Vortragstagung Fachgruppe Biochemie GDCh, 03/16th to 18th, Darmstadt, Abstract P 2.6; Analytica Conference, 04/19th to 21st, München, Abstract-book p.195 - 196; J. of Immunology, subm. and Meeting of the Gesellschaft für Biologische Chemie, 09/19th to 21st, Würzburg.

SUPPLEMENT

Number 12
Volume 47
1992

Abstracts
XVth Congress of the
European Academy of
Allergology and
Clinical Immunology
Paris, France, 10-15 May 1992

Editor:
Jean Bousquet

Munksgaard, Copenhagen

EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

ALLERGY

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| Satellite-Symposium author index | 354 |

This special supplement of *Allergy* contains abstracts of the scientific papers to be presented at the 1992 Triennial Congress of the European Academy of Allergology and Clinical Immunology. The abstracts are classified by topic and appear from Monday May 11 through Thursday May 14 and are identified as:

FC: Free Communication
PS : Poster Session Discussion
PP : Poster Presentation

To assist in planning a personal schedule at the congress, the time and place of each presentation is also provided.

THE ALLERGY INFORMATION SYSTEM: A COMPUTER-BASED EDUCATIONAL PROGRAM FOR ALLERGISTS AND GENERAL PRACTITIONER.

K.-Ch. Bergmann (1), L. Kolsi (2), H. Müsken (1), I. Termer (2), B.R. Tigges (2)
(1) Allergy and Asthma Clinic, Bad Lippspringe
(2) Physis Software GmbH, Lünen, FRG

The Allergy Information System (AIS) is an educational software with teaching and practical informations for allergists and general practitioners.

IBM-PC or compatible hardware using MS-DOS (version 3.0) and a minimum of 400 KB free RAM may be used. A microsoft-compatible mouse and a VGA color monitor are recommended for easier use of the 7 MB-program. The menu-supported AIS-software can be used without any pre-existing knowledge of computers.

The program gives informations (text, pictures) on 4 main topics: Basic knowledge of the allergic reactions: regulation of IgE synthesis, cells and mediators, allergens, immediate and late reactions, characterization of allergic diseases. Allergy diagnosis: anamnesis, skin and provocation tests, in vitro-tests. Therapeutic management: allergen avoidance, medicaments, immunotherapy, rehabilitation. Useful informations for the allergic patient: addresses of patient-self organisations, pollen information service and allergy-specific advices which may be printed as personalized letters. The development of AIS was sponsored by UCB Chemie GmbH.

AUTOGENIC TRAINING AND NOREPINEPHRINE LEVELS IN ATOPIC ECZEMA, ALLERGIC ASTHMA AND PSORIASIS.

G. Ionescu, R. Kiehl, J. Müller-Steinwachs
Research Department, Spezialklinik Neukirchen,
8497 Neukirchen, FRG.

Free plasma norepinephrine (NE) levels were measured by means of a standardized HPLC method (Waters, FRG) in 41 adult patients with severe atopic eczema (401 ± 164 pg/ml), in 12 adult patients with allergic asthma (577 ± 208 pg/ml), in 50 adult patients with psoriasis (305 ± 95) and in 18 healthy volunteers (174 ± 55). The circulating NE-levels were significantly higher in the disease subsets ($p < 0.005$), by contrast only slight differences were found in the epinephrine and dopamine concentrations. Neither elevated dopamine- β -hydroxylase activity nor decreased catechol-O-methyl-transferase- and phenylethanolamine-methyltransferase activities were found in patients plasma. We previously concluded that MAO activities are also not responsible for the abnormal NE-levels. However, we cannot rule out the possibility that the elevated transmitter may be released from and/or taken up by the sympathetic via a disturbed regulatory mechanism. Psychogenic stress, biogenic amines, food additives or other environmental agents are possible triggering factors. Autogenic training (AT) prescribed to relieve psychogenic stress significantly lowers NE-concentrations in relaxing patients (194 ± 33 vs 424 ± 114 , $p < 0.001$). However, in contrast to controls, the NE-circulating levels in patients are rising back towards initial values 1/2 hr after AT suggesting an uncontrolled release from the sympathetic. It is concluded that repeated autogenic training positively influences the disturbed sympathetic activity and the abnormal distribution of α - and β -receptors (Acta Dermatovenere Suppl. 92: 19-21, 1980).

A COMPLEX MATRIX FOR THE DIAGNOSIS, THERAPY, AND PATIENT MONITORING IN FOOD ALLERGIES AND INTOLERANCES

NEKAM, Kristof Natl. Inst. of Rheumatology, Dept. Autoimmune Diseases
H-1525 Budapest 114, POB 54. Hungary

The increasing number of patients with diseases finally diagnosed as food allergy/intolerance, the expanding variety of additives in every-day foods, and therefore, the multiplying number of data make imperative the use of computers in this field of allergy, too. In the presentation we introduce one possible version of a complex "questionnaire" including questions for: A/family and patient history, B/clinical symptoms and changes in their activities of the often involved organs, C/dietary effects, and D/therapeutic procedures and patient information. The structure of the matrix is built up with special care of recent observations like the OAS, or possible links between pollinosis+food allergy, or portprandial immunocomplexemia. While constructing the matrix based on observations made on about 100 patients in this field, the baroque complexity was preferred to simplicity, for the sake of full scale data-acquisition.

QUALITY OF LIFE (QoL) AND NON-SPECIFIC BRONCHIAL RESPONSIVENESS IN ADULT ASTHMATICS. G Coccoi, F D'Agostino, M Schiano, A Mattiello. Div. of Pneumology and Allergological Center - "A. Cardarelli" Hospital - Naples - Italy.

In this study a 72-items scale for assessing QoL in adult asthmatics ("Living with Asthma - Questionnaire") has been administered to 35 consecutive subjects (14 males; 16 - 61 years old, mean age 31 yrs; 17 skin positive to one or more allergens) referred by GP because of possible asthma. The questionnaire covers 11 domains of life experience, and has been previously validated. During the routine asthma assessment, a methacholine bronchial challenge (BPT) has been administered to the same subjects. The results of the two tests have been statistically compared. All applied statistical tests have been inconclusive for any correlation between QoL score (both as total score and as single domains score) and BPT results. Therefore bronchial hyper-responsiveness, a pathophysiological condition related to the development of asthma, cannot measure patients' perceived health. An assessment of QoL score will be needed in addition to laboratory tests in evaluating the results of trials on asthma management.

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ALLERGY

EOSINOPHILES AS A CRITERION OF CRAB ALLERGY

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Different clinical manifestations of allergy were observed in crab-processing workers: dermatitis, bronchitis with asthmatoïd component, laringitis (combined form). Total percentage of patients with allergy working on floatating base is 40%.

Diagnosis of crab allergy was varied according to the clinical picture and laboratory results: patients blood was investigated in specific with crab allergen and nonspecific tests.

A marked eosinophilia was observed in patients with crab allergen. Percentage of eosinophiles in patients with allergic bronchitis was $15 \pm 2\%$, allergic dermatitis $7.1 \pm 0.9\%$, laringitis $8 \pm 1.6\%$.

A FAST WAY TO SEPARATE WHITE BLOOD CELLS FOR DETECTION OF CELLULAR COMPONENTS

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The mostly used Percoll or Ficoll leucocyte separation techniques need special laboratory equipment, are not easy to handle and do not supply the actual concentrations of cellular components. We therefore decided to look for an easier alternative way to separate blood leukocytes. We tested 2 different approaches: 1) Separation by erythrocyte lysis and 2) Separation by natural sedimentation. 1: Starting with 2 ml fresh EDTA-blood, lysis for 1 min with 5 ml Immunoprep A (formic acid, 1.2 ml/l and stabilizing agent) from Coulter, FRG, 3 min spin at 1600 rpm/min, 3x washing with PBS-buffer (KPi, 0.01 M, NaCl, 0.15 M, pH 7.2), resuspension and cell counting, Trypan blue vitality test and cAMP determination (RIA with Triton extract). As result emerge 13-24 pmol cAMP/ 10^7 cells, a value similar to that obtained on skin cells (Brit. J. of Derm. 101: 413-419, 1979). The vitality test on these cells is not reliable because of the membran glycolix impairment by formic acid treatment. 2: Starting with 7 ml fresh EDTA-blood, 3 1/2 hrs sedimentation at 20°C, supernatant spin 3 min at 1600 rpm/min, supernatant removed, pellet washed once with PBS, resuspended in 0.5 ml PBS, cell counting, vitality test and cAMP determination. As result emerge 6-9 pmol cAMP/ 10^7 cells, a value too low as compared with the above data. The vitality test shows 98 to 99% intact cells. The conclusion: The first method is fast (15 min) and supplies reliable concentrations of actual cellular components like cAMP, cytokines, prostaglandines, etc. .

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CORRELATION BETWEEN IMMUNE CELLS AND INFLAMMATORY MEDIATORS IN BAL OF PATIENTS WITH ASTHMA.

It is known that the pathogenesis of asthma is due to the production of inflammatory mediators secreted, at least in part, by immune cells present in the BAL. Aim of our study is to correlate the number and the type of immunological cells with the amount of inflammatory molecules in the respiratory fluids.

The results show that the levels of inflammatory mediators (TxB₂; PGF₁α; LTB₄ etc.) in BAL of patients with asthma were significantly higher ($p < 0.05$) than those in BAL from healthy subjects. This increase could be correlated with a migratory of activated macrophages, as observed for neutrophils and eosinophils.

UNIVERSITY OF NAPLES - 1st MEDICAL SCHOOL -
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GRELLA E.; CAMMARATA A.; BIANCO A.; LICCARDO G.;
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Increased generation of inflammatory mediators and cells in BAL and in peripheral blood in patients with asthma: protective effects of nedocromil sodium.

Some evidence suggests that bronchial hyper-reactivity, a main feature of asthma, is caused by airway inflammation - Bronchial inflammatory cells, and the mediators they release, play a central role in the pathophysiology of asthma. We evaluated the level in the BAL and in the blood of more important mediators and cells before and after treatment with nedocromil sodium.

The results showed a decrease of level of ECP, TxB₂, PGF₁α, LTB₄ ($p < 0.01$) in the BAL related to decrease of ICE and eosinophils in the peripheral blood after treatment.

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P2 213

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ATOPIC DERMATITIS: UTILITY OF ALLERGOLOGICAL INVESTIGATION.

Patients with atopic dermatitis according to Hanifin and Rajka criteria and no other associated allergic disease have been investigated by a routine protocol which includes prick test, RAST, exclusion diet and exposition test to the food allergens with the aim to identify the allergens responsible of the cutaneous disease. Test performed were negative in 1% of the affected patients. Our data agree with the literature. However, tests are often expensive and of limited utility, as for RAST, which is reported to about 30% false negatives. Other reactions, such as delayed reactions with involvement of other classes of immunoglobulins (IgG4) or of basophils and lymphocytes as in cell-mediated (Type IV) reactivity, are involved in atopic dermatitis. We think that the actual diagnostic approach is of very limited use and that a new one, better investigating the etiology of atopic dermatitis, should be discussed.

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SYMPATHETIC ACTIVITY AND IMMUNE RESPONSE IN ATOPIC ECZEMA

Intact noradrenergic innervation in lymphoid tissue is necessary for normal primary antibody and cell-mediated (delayed hypersensitivity and cytotoxic T-cell) immune response in vivo. This implies that physiological norepinephrine (NE) release and availability may be obligatory for normal T-cell (and possibly B-cell) function. Total IgE and specific IgE in serum, B-cells, CD4- and CD8-T-cells, the CD4/CD8 ratio and natural killer (NK-) cells in peripheral blood as well as NE-levels in EDTA-plasma have been investigated in 31 atopic eczema (AE-) patients (aged 16-53 years) using standard enzyme immuno assays (Pharmacia, FRG, Pasteur, FRG), nephelometric assay (Atlantic Antibodies, USA), flow cytometry (Coulter, FRG) and HPLC (Waters, FRG), respectively. Total IgE varied from 120 to 8100 U/ml and in 92% of the cases specific IgE antibodies were found. CD4- and CD8-T-cells showed no unique pattern, however CD4/CD8 ratio in 33% of the patients exceeded 2.1 - the upper value of the normal range. B-cell counts in 30 of 31 patients were in the normal range. On the other side NK-cell numbers in the atopic group were significantly lowered, when compared to controls (220 ± 80 vs 82 ± 57 , $p < 0.001$). Our earlier report on elevated NE-levels in severe AE could be confirmed in 69% of the present patients (371 ± 169 vs 174 ± 56 , $p < 0.01$), but we could not find a direct relationship between the NE-levels and most of the immunological values described above. However, 72% of the atopic subjects with lowered NK-cells showed significantly elevated NE-concentrations. Autogenic training significantly lowers the NE-concentrations in AE-patients (194 ± 33 vs 424 ± 114 , $p < 0.001$) but the circulating levels are rising back towards initial counts within 1/2 hr after this therapy.

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ATOPIC DERMATITIS: PSYCHOLOGICAL, IMMUNOLOGICAL AND NEUROPHYSIOLOGICAL CHARACTERISTICS.

10 patients (20 females, 10 males, mean age 24 years, range 15-40 years) were studied. All patients were affected by atopic dermatitis of medium-high seriousness and were subjected to allergological investigation by Prick tests and RAST for food, inhalants and pollens. 75% of patients showed a pathological personality picture, with neurotic area alterations and contact difficulty in interpersonal relations; furthermore we noticed an increase of trait anxiety and poor and/or not very structured self-image.

We correlated psychological picture (personality profile, affective state, self-image) to disease seriousness and length and IgE specific presence.

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IS INFANTILE SEBORRHEIC DERMATITIS A MARKER OF ATOPY?

179 patients affected by Infantile Seborrheic Dermatitis (ISD) were re-examined after 5-15 years in order to evaluate the evolution towards recovery, atopy or psoriasis.

The patients were classified in four groups clinically: patients suffering from cradle, from cradle and flexural eczema, from diaper dermatitis and from napkin psoriasis.

By means of questionnaire, dermatological examination and allergological investigation, we were able to subdivide the initial population into three groups:

- 1) recovered patients (65.4%);
- 2) atopic symptomatic patients (25.1%: 14.5% affected by atopic dermatitis, 20.7% by respiratory atopy);
- 3) psoriatic patients (4.5%).

These data suggest that a high percentage of patients diagnosed as having ISD develops an atopic form.

Table 1 Immunological values of atopic eczema patients and controls
 related to norepinephrine levels

| | Controls (n=30) | Atopic eczema (n=31) | | |
|-------------------------|-----------------|----------------------|----------------|------|
| total IgE | 60 ± 40 | 4120 ± 4000 | U/ml | (hs) |
| specific IgE | negative | positive | | (hs) |
| gammaglobulins | 1.3 ± 0.5 | 0.87 ± 0.56 | mg/dl | (NS) |
| B-cells | 305 ± 125 | 320 ± 138 | cells/ μ l | (NS) |
| CD4-helper-cells | 995 ± 295 | 1229 ± 908 | cells/ μ l | (NS) |
| CD8-cytotoxic-cells | 600 ± 230 | 649 ± 500 | cells/ μ l | (NS) |
| CD4/CD8 | 1.63 ± 0.48 | 2.44 ± 1.3 | | (NS) |
| NK-cells | 220 ± 80 | 82 ± 57 | cells/ μ l | (hs) |
| Monocytes (Macrophages) | 5 ± 3 | 9.5 ± 2.5 | % | (hs) |
| Norepinephrine | 174 ± 56 | 371 ± 169 | pg/ml | (hs) |

s = significant, hs = highly significant, NS = not significant

FIG. 1 CIRCULATING NORADRENALINE LEVELS IN ATOPIC ECZEMA PATIENTS AND HEALTHY CONTROLS BEFORE AND AFTER AUTOGENIC TRAINING

