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Editorial Office

Acta Dermatovenerologica Croatica

Department of Dermatology and Venerology

Zagreb University Hospital Center

Šalata 4, 10000 Zagreb, Croatia

Phone/Fax: +385-1-4920 014

E-mail: *jasna.lipozencic@zg.tel.hr*

Business correspondence

Medicinska naklada, Vlaška 69, 10000 Zagreb, Croatia; *www.medicinska.naklada.hr*

Aims and Scope

Acta Dermatovenerologica Croatica (ADC) aims to provide dermatologists with up-to date information on all aspects of the diagnosis and management of skin and venereal diseases. Accepted articles regularly include original scientific articles, short scientific communications, clinical articles, case reports, reviews, reports, news and correspondence. ADC is guided by a distinguished, international editorial board and encourages approach to continuing medical education for dermatovenerologists.

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E-mail: *jasna.lipozencic@zg.tel.hr* .

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The First Decade of Croatian Dermatovenerological Society of Croatian Medical Association

Ten years ago, we founded the journal *Acta Dermatovenerologica Croatica* (*ADC*) and Croatian Dermatovenerological Society (CDS). It was the result of our decades-long desires, efforts, and above all, love we shared for our field of expertise, dermatovenerology. Time has passed quickly and this year, we celebrate the 10th anniversary of both the Journal and the Society. On that occasion, let us take a brief look back at the history of both.

A milestone in the development of dermatovenerology in Croatia was the foundation of the Dermatovenerological Section of the Croatian Medical Association (CMA) at the Sisters of Mercy University Hospital in Zagreb, on November 22, 1920. Aleksandar Blašković was the first president of Dermatovenerological Section, and the first secretary was Kamilo Farkaš. The Section was active from the very beginning, and by 1928, it had already organized 20 meetings. In the 1929-1940 period, the Section members met as many as 109 times. It was also the period when the idea of starting a journal of Dermatovenerological Section first appeared. In 1929, Franjo Kogoj (1894-1983) was elected new president, and Srećko Bošnjaković (1900-1947) took the position of the secretary.

The first Congress of dermatovenerologists was organized in Split in 1930, and the next one in Zagreb in 1933. In 1940, the Section changed its name into Croatian Dermatovenerological Society. Kogoj resigned from the position of president in November 1941 and Janko Božić took over. Vladimir Abramović was the secretary during 1941/2-1944 period. After the Second World War, the activity of the Society was enlivened again and Franjo Kogoj (1945-1963) accepted the position of Society's president once again, whereas Dušan Jakac acted as the secretary. The new era of the Society was also marked by organization of various symposia and congresses. From 1965 to 1970, Šime Čajkovac was the president of the Society, and Zorislav Žmegač was the secretary. The first scientific meeting of dermatovenerologists in the postwar period took place in Zagreb on November 23-26, 1950, and was attended by colleagues from all Republics of ex Federal Republic of Yugoslavia. The Croatian Section of Dermatovenerologists of the Croatian Medical Association, which had three branches – Zagreb, Rijeka, and Split – was a member of the Association of Dermatovenerologists of Yugoslavia. Academician Franjo Kogoj organized the second postwar Congress in Zagreb in 1966, whereas Prof. Dušan Jakac, Congress president, organized the next one that took place in Rijeka/Opatija in 1973. Another important event took place in 1974: the journal *Acta Dermatovenerologica Iugoslavica* was launched, for which much credit goes to Prof. Janez Fettich and Prof. Aleksej Kansky from Ljubljana. Croatian dermatovenerologists participated in the foundation of *Acta Dermatovenerologica Iugoslavica* and had published many of their research and professional articles in that journal until 1992.

The Homeland War, which started in 1991 on the territory of Croatia, led to deep political changes and Croatia became an independent state. The Croatian Medical Association resigned from the Yugoslav Medical Association and continued to function as an independent institution. The Croatian Dermatological Society (CDS) was founded again on the initiative of Prof. Ivan Dobrić. It happened on May 29, 1992 at the Department of Dermatovenerology, Zagreb University Hospital Center, and Prof.

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Vladimir Čajkovac was elected president of the temporary CDS Managing Board. At another meeting on July 10, 1992, the regular CDS board was elected according to the Croatian Medical Association Statute for Founding Medical Society, and Prof. Vladimir Čajkovac was confirmed as president. Members of the Board came from each of the four CDS branches – Zagreb, Rijeka, Split, and Osijek. During the presidency of Prof. Vladimir Čajkovac (1991-1999), and Jasna Lesić as the secretary, the CDS Zagreb branch awarded Prof. Ruzicka and Prof. Plewig (Germany).

The past 10 years of the Croatian Dermatovenerological Society of Croatian Medical Association have been characterized by its strong independent activity. The first Congress of Croatian dermatovenerologists with international participation (17 countries), organized by Prof. Vladimir Čajkovac, was held in Zagreb, May 15-17, 1998. On November 12, 1999 Prof. Jasna Lipozenčić became elected CDS president and Mirna Šitum the secretary. During the presidency of Jasna Lipozenčić, the Society changed its name into Croatian Dermatovenerological Society, and five Symposia and two Congresses with international participation were organized, as well as four Continuous Medical Education Courses. The second Congress of Croatian dermatovenerologists, "New Highlights in Dermatovenerology", with international participation of 17 countries, was held in Opatija, May 16-19, 2002.

Dermatohistorical sessions are regular part of Croatian Dermatovenerological Society meetings. Our colleagues from abroad have been supporting the activities of Croatian Dermatovenerological Society, contributing to its development and improvement. In 2001 and 2002, the Society awarded Prof. Ring from Munich, and Prof. Holubar from Vienna for special contributions.

Croatian Dermatovenerological Society had an important and far-reaching influence on the development of dermatovenerology in Croatia. Its members put a lot of effort and enthusiasm into their activities and work, and some, like Franjo Kogoj, became even internationally recognized. Academician Franjo Kogoj was one of the most prominent members of the Society and twice its president. Many Croatian dermatovenerologists were eager to continue his work not only at their departments of dermatovenerology in Zagreb, Rijeka, and Split, but also in the Society. The Croatian Dermatovenerological Society still has four branches (Split, Rijeka, Zagreb, and Osijek); its 180 members actively participate in Congresses on national and international level. Presidents of four CDS branches together with the Organizing and Scientific Congress Board are in charge of organization of the next international dermatovenerological congress, "Topical Procedures, Innovations and Mistreatments", which will be held in Plitvice/Croatia, May 29-31, 2003. Another event that CDS is organizing is the Symposium on "Current State on Psoriasis and Naphtalanotherapy", which will take place in Ivanić Grad, Croatia, on September 19, 2003.

New elections for CDS Board of the Croatian Dermatovenerological Society (2003-2007), scheduled for November 21-22, 2003, will take place in Zagreb during the Continuing Medical Education Course titled "Sexually Transmitted Diseases and Infections". I hope the Society will stay as active as it has been all this time, to remain the part of the European Academy of Dermatovenerologists, International League of Dermatology, and International Society of Dermatology.

Ten Years of *Acta Dermatovenerologica Croatica*

The idea of launching an official Journal of Croatian Dermatovenerological Society (CDS) was first born in 1930's, but had to wait almost 60 years to be realized. It eventually happened at Assembly of Delegates of the International League of Dermatologic Society in New York, June 15, 1992 (Croatian delegates were Prof. Dobrić and Prof. Gligora). The same year, on May 29, the Croatian Dermatological Society (CDS) was founded. At that meeting, Prof. Čajkovac and Prof. Dobrić articulated on behalf of their colleagues the need for CDS to have its own official journal. And thus, the process began of founding the official journal of the Society, *Acta Dermatovenerologica Croatica (ADC).* The elected *ADC* Editorial Board concluded the purpose, field of interest, and content of the first *ADC* issue by the end of December 1992. The Journal was to be published in English language with summary in Croatian. The first issue of *ADC* (Vol. 1, No. 1) was published at the beginning of 1993 un-

der the supervision of the following members of Editorial Office: Vladimir Čajkovac, Editor-in-Chief; Ivan Dobrić, Associate Editor-in-Chief (until Vol. 3, No 1-2, when Aleksandra Basta-Juzbašić took over); Dragomir Budimčić, Technical Editor (until Vol. 1, No 4, when Branka Marinović took over until Vol. 4, No 2, and afterwards Mirna Šitum); and Branko Baričević, secretary of *ADC* (until Vol. 4, No 2, when Branka Marinović took over and still obtains the function). Editorial Board consisted of 8 members, and Editorial Council of 8 members. The Editorial Office was located at the Department of Dermatovenerology, Sisters of Mercy University Hospital, Zagreb, until the year 1993, when it moved to University Hospital Center Zagreb, Šalata 4.

The first issue (Vol. 1, No 1, 1993) consisted of the Letter of the Editor-in-Chief Prof. Čajkovac; Letter of the Associate Editor-in-Chief Prof. Ivan Dobrić; three original scientific articles; two professional articles, or case reports; one review; two reports; announcements; and instructions to authors. It was a very good issue to begin with. Publisher of *ADC* for the last 10 years has been Grafoplast (1993-2003). From 2003, the *ADC* will be published by "Medicinska naklada" in Zagreb.

The deepest gratitude is owed to the contributors Prof. Čajkovac and Prof. Dobrić, members of the Editorial Board, who succeeded in giving us such a quality pilot issue of 41 pages.

The *ADC* had been published in English language with summary in Croatian until Vol. 8, No 1, 2000, when it was decided not to include the summaries in Croatian anymore. Since 2000 (Vol. 8, No 1), the Editor-in-Chief has been Prof. Jasna Lipozenčić, and Honorary Editor-in-Chief has been Prof. Vladimir Čajkovac. In 2000, the *ADC* changed its front page, table of content page, and technical image, and started bringing information on the CDS activities and announcements of Symposia, Congresses, and Courses of interest to its audience.

The first issue in 1998 (Vol. 6, No 1) brought the Final Program and Abstract book of the *First Croatian Congress of Dermatovenerologists* with International participation Zagreb, which was held on May 15-17, 1998. Next year (Vol. 7, No 1, 1999), Program and abstracts of Symposium *New Trends in Immunodermatology* were published, as well as abstracts of Symposium of *Dermatologic Oncology Past, Present, Future: Epidermal tumors* (Vol. 7, No 3, 1999) that was held in Zagreb, on September 17, 1999. Program and Abstract book of *5th Alpe-Adria-Danube Society of Sexually Transmitted Diseases Workshop* with Annual Meeting of the Croatian Dermatological Society, Opatija, October 29-31, 1999, was printed in No 4, Vol. 7, 1999. Abstracts of the Continuous education *Symposium on Nevi and Malignant melanoma*, Zagreb, November 12, 1999, were printed in No 1, Vol. 8, 2000. Issue dedicated to the *International Symposium on Pediatric Dermatovenerology,* which took place in Zagreb, September 15-16, 2000, was printed in No 3, Vol. 8, 2000. Program and Book of abstracts of International Symposium *The Current Trends in Dermatomycology*, Dubrovnik, June 16-17, 2000, were printed in No 2, Vol. 8, 2000. Program and abstracts of *International Congress on Skin Changes and the Face* and Regional Symposium of the International Academy of Cosmetic Dermatology: *Faces Old and New* were published in No 3, Vol. 9, 2001. The program and abstracts of the Second congress of CDS with international participation, *New Highlights in Dermatovenerology,* Opatija, May 16-19, 2002 were published in No 2, Vol. 10, 2002. Only the program and lectures *in extenso* from Continuous Medical Education Course "Cutaneous Lymphoma", Zagreb, March 16, 2001 were printed in a separate Book. At that time, the principal aim of the Journal was to provide the members of the CDS with professional articles, reviews, and original articles of interest to practitioners. However, we soon came under pressure to adjust the Journal's content profile so as to make it acceptable for inclusion in indexing databases, such as *Excerpta Medica* (EM). In 1994, the *ADC* was included in *EM* database. During the last ten years, the *ADC* has been published quarterly, with only Vol. 3 (No 1-2) and Vol. 4 (No 3-4) bringing double issues due to financial reasons. There have been 280 manuscripts accepted for publication in *ADC*, whereas 35 were rejected (today's rejection rate is 20%). In volumes that contained Congress abstracts, the mean number of papers was 25, whereas the number of abstracts was much larger (80 abstracts on average) (Vol. 6, No 1, 1998; and Vol. 10, No 2, 2002).

The *ADC* is a peer-reviewed journal, with a reviewer pool consisting of 148 reviewers, experts in different medical specialties of whom 50% are from

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abroad (England, Germany, USA, Japan, Austria, and Italy).

The *ADC* has published manuscripts by authors from England, Germany, Czech Republic, Poland, Hungary, USA, Japan, Brazil, Austria, and Spain. The mean number of papers published per year is 30-35.

Over the years, Editorial Board has grown from 8 to 11 members from abroad.

In 2000, we applied for inclusion in Index Medicus/MEDLINE, the indexing database of National Institute of Health, Bethesda, USA. Out of 22,000 journals that the National Institute of Health receives every year, MEDLINE includes only 4,000, and the *ADC* (graded 3,9) became one of them. The inclusion of *ADC* in MEDLINE in the beginning of 2001 gave us the opportunity to become recognized in the world and it extremely increased our visibility; since then, we have had many requirements for additional offprints of *ADC* articles. Since 2001, we have also been preparing the publication of *ADC* in XLM tagged electronic format (S. Frketić), while plans for the *ADC* web-site are well under way.

In the last two years, there have been novel columns introduced in the regular content of the Journal: *Marko Polo* (S. Fatović-Ferenčić from Vol. 9, No 4, 2001, onward), *Letter to the Editor*, and *News* (beginning with Vol. 10, No 1, 2002). In times when medicine/dermatology is deemed as going in direction of dehumanization, we chose to enrich the content of the journal with texts that mirror personal counterpart in evidence-based papers. Historical articles, for example, are invited to enliven and reveal our historical roots: *Marko Polo* column is intended to be reflective prose itinerary, whereas *Letters to the Editor* has been introduced to get a feedback on papers published in *ADC* or elsewhere. The purpose of *ADC News* is to inform the readers on all CDS activities and professional events in the country and abroad.

Editing these three columns, the *ADC* News, Letter to the Editors, and Marko Polo since 2001 has been a challenge, but I believe we now have a periodical that has successfully grown in stature and scope to meet the member's needs. That being said, let me invite all of you who would be willing to participate actively in the preparation of *ADC* on daily basis to join us. All interested are kindly asked to contact the Editorial Board *(jasna.lipozencic@zg.tel.hr).*

The principal aim of the Journal was to provide the members of CDS with a balance of editorials, reviews, and original articles of interest to practitioners. Over the decade, we have had the privilege of receiving a vast amount of research reviews not only from Europe, but also from all over the world. We hope we have encouraged our authors, especially those inexperienced and aspiring, to publish their work and share their knowledge and experience with the audience worldwide.

It has been a privilege for me to be the Editor-in-Chief of the *ADC* for the past four years, and to see it become a firmly established periodical. This would not have been possible without the members of the *ADC* Editorial Board and secretary Branka Marinović. Without the editor founders in 1993, their dedication, professionalism, and hard work of all of us in the past 10 years, the *ADC* would not be the publication that it is today. However, a lot of credit goes to our reviewers as well, whose sharp criticism and useful advice helped our authors to further improve their articles. It takes a lot of time to review an article and many or our reviewers have spared their valuable time to do it thoroughly and professionally. Also, there is Mrs. Gordana Dučkić, who joined the Editorial staff in 2002 and whose task, among other things, is to make sure that our referees and editors maintain the deadlines. Furthermore, beginning this year, Aleksandra Mišak is the new language editor and Marko Kljaković-Gašpić in charge of the layout and makeup of the Journal.

On behalf of the Editorial Board of *ADC* and myself, I wish further success to our Journal and thank all our Editorial members, authors, referees, and publisher for their efforts and help in making the *ADC* a recognizable periodical in the field of dermatovenerology.

Jasna Lipozenčić
ADC Editor-in-Chief

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Na pitanja slijedi smjesta pismeni odgovor, ako se za poštarinu priloži 1 do 2 Din.

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Dušan Jakac: The Life in Dermatovenerolgy

Stella Fatović-Ferenčić, Jasna Lipozenčić

Correspodending author:

Stella Fatović-Ferenčić, MD, PhD

Assistant Professor

Croatian Academy of Sciences and Arts

Institute for the History and Philosophy of Sciences

Division for the History of Medical Sciences

Zagreb, Croatia

stella@hazu.hr

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SUMMARY This is a story of Dušan Jakac, one of the most prominent Croatian dermatovenerologists. Born in 1906, he is also our oldest dermatovenerologist and certainly among the oldest in Europe. His life and experience constitute a treasure of information on dermatovenerology in the region, which motivated us to ask him for an interview. In his life, Jakac experienced the time when Europe saw its unrest and witnessed the shift of dreadful epidemics such as Spanish flue, syphilis, and recently AIDS. He has observed different diagnostic approaches, their benefits and failures, and practiced various therapeutic approaches, never forgetting to take care of their side effects. Jakac's career illustrates the medical and cultural times in a striking way. We met him at his apartment in Zagreb, where he lives now and where he answered promptly and enthusiastically all our queries. Thanking him warmly, we can truly state that talking to Dušan Jakac was a unique experience for both the historian of medicine and the dermatovenerologist.

Written sources, pictorial documentation and other materials give us the possibility to learn about past periods. However, using such methods many elements remain neglected, for example, personal views, institutional relationships, cultural or historical settings, individual perspectives, etc. For this reason, interview is the optimal choice to complement historical data or often limited written sources. It is a rare chance to meet people who have dedicated their lives to their profession and who have lived long enough to be able to turn back and reassess all what was their daily practice. Thus, it is a great advantage to have the possibility to share with them these experiences and personal understanding of the past periods.

Meeting Dušan Jakac, talking to him, learning from his life's experience have provided us with an excellent opportunity to look into a long period of time in which dermatolovenerology in Croatia was strongly developing. This text is therefore our contribution to the efforts at re-enacting the perspectives and thoughts, thereby to illustrate the profile of an extremely modest, nonetheless amazing dermatovenerologist of ours.

Dušan Jakac was born in Veli Mlun near Buzet, today's central Istria, on June 3, 1906. This was exactly a hundred years after Alibert had published his Atlas *Description des Maladies de la Peau* and the same year when Fritz Schaudinn (1871-1906), the discoverer of *Treponema pallidum* died. In the

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same year, the Croato–Serbian coalition was created, which remained in power until the fall of the Habsburg Monarchy. When Jakac entered the six-year elementary school in Buzet, Istria was on its way to improving its political as well as economic situation, and it was one of the brightest periods of its history. Vineyards, olive and fruit groves were cultivated; the export of salt was rising, particularly with the inland parts of the Austro-Hungarian Monarchy. The economic progress expanded largely through three important harbors of Rijeka, Pula and Trieste. Great attention was paid to education in Istria since the time of bishop Juraj Dobrila and much enthusiasm was put into it (1). As the result of such developments, many schools were opened, with classics high school in Pazin as most prominent of them.

During the ominous year of 1918, when Jakac entered the classics high school in Pazin, several turbulent events directed his life to other places, away from his loving Istria. Also in 1918, the continuity of the Croatian state was interrupted, the Croatian Diet was abolished and parts of the Croatian national territory such as Istrian peninsula, Rijeka, Zadar, and some islands had to be surrendered to Italy. It was also the year when the dreadful pandemic of flu known as Spanish influenza spread and its occurrence in Istria had great impact on the people's lives. The classics high school in Pazin was closed and its students were referred to other places. Jakac hence found himself first in Karlovac and not long thereafter in Zagreb, where he graduated from high school in 1927 (2). It was the period of deprivation of Croatian identity, the period when Stjepan Radić's Croatian Peasant Party was the leader of resistance to Serbian hegemony, and regarding dermatology, the period when Franjo Kogoj was studying in Strasbourg at Lucien Pautrier and described his pustule (3).

Classical education and proficiency in several languages enabled Jakac to choose and enter the Medical School in Padua in 1928, where he completed the first two years. Although remarkably successful in passing exams, he left Padua for political reasons. He continued his medical education first in Ljubljana (fifth semester) and then in Zagreb, where he graduated on January 31, 1934. During 1935, he served one-year internship as a secondary physician in dermatovenerological clinics at the Zagreb County Workers' Insurance Department. In parallel, he volunteered at the Deparment of Dermatovenerology, Zagreb School of Medicine, which had been well established by the time and led by Franjo Kogoj. The Section of Dermatovenerology, established in 1920, had already been very active and its activity was growing with a prominent aim to develop dermatovenerology through professional and scientific efforts of its members (preventing and curing venereal diseases and prostitution). The first congress of dermatovenerologists was organized in Split in 1930, and the next one in Zagreb in 1933 (4). In 1935, when the International Congress of Dermatology presided by Louis Nékám was held in Budapest, and when Gerhard Domagk, a Nobel Prize winner (1895-1964), published his experiments with Prontosil, Jakac was adopted as member of the Croatian Medical Association (CMA) and started his activities at the Section of Dermatovenerology. During the Great Depression and just when the World War II was imminent, he had completed specialization in dermatovenerology (1939) but did not get position at the Department of Dermatovenerology in Zagreb until 1943, when he was appointed assistant (2).

His interest grew slowly towards venerology and occupational dermatoses. To understand why such interests occupied a young dermatovenerologist as Jakac, one should know that he considered it important to be acquainted with the main movements in medicine, embracing a vision of socialization, a line of thinking which related to the public health movement. It aimed to incorporate wider questions such as income, employment, lifestyle, profession, psychosocial economy, etc. Venereal diseases, which kept busy the majority of dermatovenerologists, had already become a popular arena for verification of such concepts, while occupational diseases were on their way to establish a place for themselves. Jakac's paper on the importance of cutaneous diseases at the social insurance level, published in 1938, was therefore definitely up-to-date to the current concepts of social medicine of the early 20^{th}-century Europe. It appeared in No. 11 of Liječnički vjesnik, an issue dedicated exclusively to various dermatologic topics, on the occasion of the 10^{th} anniversary of the Zagreb Department of Dermatology (5). At the same time, it was a period in which Kogoj and his assistant Bošnjaković carried

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out their studies on palmoplantar keratodermias, challenging other investigators abroad. This topic was linked exclusively to the island of Mljet. Ever since, it has been inspiring dermatologists, including Jakac who published a paper on palmoplantar keraodermias in the 1960s (6).

Respected by his colleagues, Jakac was finally offered employment by Kogoj at the Department of Dermatovenerology in Zagreb. However, he chose to go to Rijeka where he was given an opportunity to chair the Braća Sobol General Hospital Department of Dermatovenerology (a decree from the Ministry of Health from September 1946). Albeit, it was not an easy task to accomplish because no department for dermatovenerology had existed there before. Jakac accepted the position with enthusiasm and dedication, and was also close to his beloved Istria again. He pioneered by founding dermatovenerology in Rijeka as an academic discipline despite all adversities of the time. In 1957 he was appointed head of the University Department of Dermatology and chair of the discipline at the newly founded Medical School of Rijeka. During that period he developed his interest in many directions and published papers on photodermatoses, side effects of various therapies, Stevens-Johnson syndrome, importance of vitamins in dermatology, cases of sodoku, thalassotherapy, skin cancer, etc. (2). His interests evidently went in parallel with dermatovenerology developments and new results in immunology.

In 1961 he was appointed associate professor and in 1965 professor of dermatovenerology. Jakac widened his expertise in professional dermatoses at various European medical centers, particularly in Dortmund. He also visited many overseas clinical departments such as New York, Cairo, Tunis, Beirut, etc. As member of the Dermatovenerological Section, Jakac continued participating in various congresses, events and other activities, and was even principal organizer of the congress that took place in Rijeka/Opatija in 1972. The international reputation of Dušan Jakac, the Congress President in Opatija, as well as the fame of Franjo Kogoj, who was honorary president, contributed undoubtedly to the attendance by reputable dermatovenerologists from 11 countries (4).

During the 1959-1965 period, Jakac was vice-dean, dean and then vice-dean again of the Medical School in Rijeka. He was member of the editorial boards of several Croatian journals such as *Arhiv za higijenu rada i toksikologiju* and *Medicina*. He presided the CMA Section of Dermatovenerology in 1981-1983, and Association of Dermatovenerologists of Yugoslavia 1969-1972. He retired on January 1, 1977. However, he remained active and linked to dermatovenerology at both national and international level. Even recently, at the opening cer-

Figure 1.

Figure 2.

Figure 3.

emony of the Second International Congress of the Croatian Dermatovenerologists “New Highlights in Dermatovenerology”, Opatija, May 16-19, 2002, it was a pleasure and honor to address Professor Dušan Jakac, a doyen of dermatovenerology, for having honored us by his presence and his occasional address to the Congress audience (Fig 1).

His classical education, his skills in dermatovenerology as well as his foreign language proficiency made him a typical European intellectual shaped in the first half of the 20th century (Fig. 2). His spirit and openness let him appear amiable, friendly and contemporary as anyone of us would wish. His long career and professional legacy place him among the few role-model dermatologists of the 20th-century Croatia (Fig. 3).

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Acta Dermatovenerol Croat 2003;11(1):10-16 ORIGINAL SCIENTIFIC ARTICLE

Identification of *Malassezia* Species Isolated from Scalp Skin of Patients with Psoriasis and Healthy Subjects

Asja Prohić

Department of Dermatovenerology, Sarajevo University Hospital Center, Sarajevo, Bosnia and Herzegovina

Corresponding author:

Asja Prohić, MD, MS

Department of Dermatovenerology

Sarajevo University Clinical Center

Bolnička 25

71 000 Sarajevo, Bosnia and Herzegovina

asjaprohic@hotmail.com

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SUMMARY The role of *Malassezia* species in psoriasis is still undetermined, but several reports have associated these lipophilic yeasts with the development of skin lesions in psoriasis. The aim of our study was to analyze the prevalence of *Malassezia* species in the scalp lesions of patients with psoriasis and assess the distribution of the species according to patient sex, age, and duration of the disease. Forty psoriatic patients with scalp involvement and the same number of clinically healthy individuals were included in the study. The samples were obtained by scraping the skin surface of the scalp of all subjects and then incubated on modified Dixon agar. The yeasts isolated were identified by their morphological and physiological properties according to Guillot *et al* method. *M.globosa* in its yeast phase was a predominant species (55%), followed by *M.slooffiae* (18%) and *M.restricta* (10%), the latter being the most common species isolated from healthy scalp skin. We found significant difference in the distribution of *Malassezia* species between psoriatic and healthy scalp skin and in the distribution of *Malassezia* species according to the severity of the scalp involvement.

KEY WORDS *Malassezia*; mycology; psoriasis; scalp

Lipophilic yeasts of the genus *Malassezia* are commensals of the microbiota found on normal skin of many warm-blooded vertebrates, but they are also associated with several skin diseases and even systemic infections (1). By means of molecular methods the genus was taxonomically revised and enlarged to seven species – in addition to *M.furfur, M.pachydermatis, and M.sympodialis,* four new taxa have been described, namely *M.slooffiae, M.globosa, M.obtusa,* and *M.restricta* (2-4). *M.pachydermatis* is the only non lipid-dependent species. It is considered zoophilic, because it is mainly isolated from animals (5), whereas the remaining six species are obligatory lipophilic and found primarily in humans.

The etiological role of *Malassezia* yeasts in pityriasis versicolor is unquestioned; the organism found in the lesions is predominantly in its mycelial phase (6-8). It seems that *M.globosa* (6-9) and *M.sympodialis* (10,11) are the species most frequently associated with pityriasis versicolor lesions. In other skin diseases, such as seborrheic dermati-

tis, *Malassezia* folliculitis, confluent and reticulate papillomatosis, atopic dermatitis, and psoriasis, neither the number of yeasts nor their morphology seems related to the skin lesions, their appearance or exacerbation.

There is evidence that psoriasis is principally a T-cell mediated skin disease (12). However, little is known about the initial stimulus that leads to the abnormal T-cell activation. Streptococcal infection can trigger guttate psoriasis or exacerbate chronic plaque psoriasis, possibly through the release of bacterial superantigenic toxins (13,14). The lymphocytes specific for group A streptococcal superantigens were identified from guttate psoriatic lesions (15) and they reacted both with streptococcal M protein and a skin determinant, possibly a variant of keratin (16). It was also demonstrated that T cells with differential reactivity to various morphological variants of *Malassezia* yeasts were present in psoriatic skin lesions, but they were not specific for the disease (17).

The beneficial effect of both oral and topical ketoconazole, followed by reduction of yeasts, indicates that *Malassezia* yeasts may represent another antigenic stimulus in psoriasis (18,19). Although this antimycotic drug may act through a direct mode of action, it has also been shown that it can suppress *Malassezia*-induced proliferation of lymphocytes in psoriatic patients and thus reduce the response to the antigenic stimulation in skin lesions (20).

The purpose of our study was to analyze the prevalence of *Malassezia* species in the scalp skin of psoriatic patients and to examine if the range of species varies with patient sex, age, and duration of the disease.

PATIENTS AND METHODS

Patients

This prospective study was conducted at the Department of Dermatovenerology, Sarajevo University Hospital Center, Sarajevo, Bosnia and Herzegovina, between April and December 2001. Forty patients with psoriasis (18 women and 22 men; age range, 7-72 years) and the same number of clinically healthy individuals (20 women and 20 men; age range, 13-76 years) were included in the study. All patients with psoriasis had chronic stationary plaque lesions with scalp involvement. We included only those individuals who had not used any topical or oral treatment in previous two months. All participants gave their informed consent in accordance with the requirements of the Institutional Ethics Committee.

Samples

All samples consisted of scales and scrapings from the scalps of both psoriatic patients and healthy subjects. Collected samples were divided into two portions – one for microscopic examination and the other for culture.

Microscopic examination of the samples was performed after the treatment with 30% solution of potassium hydroxide (KOH) and Parker blue ink.

The samples for culture were inoculated on modified Dixon agar consisting of 3.6% malt extract, 0.6% mycological peptone, 2.0% desiccated ox bile (Sigma Chemical Co. Ltd, Dorset, UK), 1% Tween 40, 0.2% glycerol, 0.2% oleic acid, 0.05% chloramphenicol, 0.05% cycloheximide, and 1.2% agar pH 6.0. The medium was always used within one week of preparation and the cultures were incubated at 32°C for seven days.

Identification of Malassezia yeasts

Malassezia species were identified according to the scheme established by Guillot et al (21), and their macroscopic and microscopic features and physiological properties were recorded. The macroscopic features of the predominant colonies included their shape, size, color consistency, and the characteristics of the medium around them. Microscopic features of the yeast cells in cultures were described after lactophenol staining and included the predominant morphology, size, and budding base of the yeasts. To assess the physiological properties of the yeasts, catalase reaction was used. A drop of hydrogen peroxide (30% solution) was added to a culture smear on a glass slide. The production of gas bubbles, indicative of release of oxygen, was considered a positive reaction.

Utilization of Tween compounds was done according to the test originally described by Guillot *et al* (21) and later modified by Gupta *et al* (10,11). Suspension of the identified yeasts (2 mL) was inoculated on Sabouraud glucose agar. The suspen-

sion was prepared by transferring a loopful of actively growing yeasts into 5 mL of sterile distilled water. The inoculum was spread evenly over the surface of a plate. Each plate was divided into four sections and 5 L of Tween 20, 40, 60, and 80 were added into a hole made in the center of each section. Utilization of Tweens was assessed by the degree of growth and/or reaction of the lipophilic yeasts around individual holes.

Statistics

Chi-squared test with Yates' correction for a small sample size was carried out to determine the statistical significance of differences in proportions. We used a statistical software package Minitab 13.0. Significance level was set at $p<0.05$.

RESULTS

Direct Microscopy

Direct microscopic examination of psoriatic scalp scales showed the presence of yeast cells in 34 (85%) patients, but short filaments were observed only in 8 (20%). Spherical and large yeast cells with a narrow budding base were found in 19 (56%) patients, together with filaments in 5 cases. Smaller yeast cells, oval or cylindrical in shape, were seen in 15 (44%) cases. In 6 (15%) slides neither yeast cells nor hyphae were observed (Table 1).

Table 1. Direct microscopy of scales from psoriatic and healthy scalp skin*

	Psoriatic scalp skin			Healthy scalp skin		
Microscopic finding	F	M		F	M	
Yeast cells and filaments	4	4	8	1	0	1
Yeast cells only	13	13	26	11	9	20
Negative	1	5	6	8	11	19
Total	18	22	40	20	20	40

*F- female; M – male.

In the scales from healthy scalp skin, yeast cells were observed in 21 (53%) patients, whereas the remaining 19 (47%) cases were negative. Short filaments were seen in only one patient. Oval and cylindrical yeast cells dominated; they were found in 14 (35%) cases. Spherical yeasts were recorded in 7 (18%) slides.

No significant statistical differences were found in the direct microscopic findings from psoriatic and healthy scalp skin (Table 1).

Cultures

Malassezia yeasts were found in 37 (93%) samples taken from scalp skin of psoriatic patients (Table 2). The most frequently isolated species was *M.globosa* found in 22 (55%) patients, followed by *M.slooffiae* (18%), *M.restricta* (10%), *M.furfur* (8%), and *M.sympodialis* (3%). Two species, *M.pachydermatis and M.obtusa,* were not isolated. The percentage of negative cultures was 8%.

Table 2. *Malassezia* species obtained from scalp skin of patients with psoriasis and normal subject

	Psoriatic scalp skin			Healthy scalp skin		
Malassezia species	F	M		F	M	
M. globosa	10	12	22	3	4	7
*M.*slooffiae	3	4	7	0	2	2
M. restricta	3	1	4	8	4	12
M. furfur	1	2	3	1	0	1
M. symodialis	1	0	1	1	3	4
M. obtusa	0	0	0	0	0	0
M. pachyderm.	0	0	0	0	0	0
Negative	0	3	3	7	7	14
Total	18	22	40	20	20	40

The results of culture obtained from healthy scalp skin were positive for *Malassezia* yeasts in 26 (65%) cases. The predominant species was *M.restricta,* found in 12 (30%) patients and the prevalence of other species was 18% for *M.globosa,* 10% for *M.sympodialis,* 5% for *M.slooffiae,* and 2% for *M.furfur.* The remaining 14 (35%) cultures showed no growth of the colonies.

Statistically significant differences were found in the distribution of the species isolated from psoriatic and healthy scalp skin – cultures from healthy skin were negative more frequently (healthy/psoriatic skin ratio, 4.7). Also, *M.sympodialis* was more frequent in the healthy scalp skin cultures (respective ratio 4.0). Other species were more commonly positive in psoriatic scalp skin cultures – *M.slooffiae* ratio 3.5, *M.globosa* ratio 3.1, and *M.restricta* and *M.furfur* ratio 3.0 (Table 2).

Distribution of Isolated Species According to Relevant Parameters

Eighteen subjects were women (45%), twenty-two men (55%), with a women/men ratio 0.8. No statistically significant differences were found between sexes in the species isolated (Fig. 1).

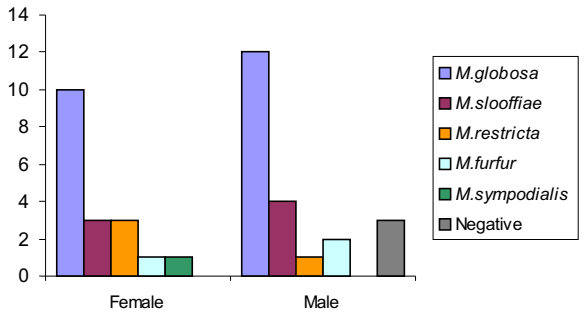

Figure 1. *Malassezia* species distribution **from psoriatic scalp skin** according to patient sex.

According to age, patients were divided into five groups, as follows: <15 (n 3; 8%), 16-30 (n 7; 18%), 31-45 (n 13; 33%), 46-60 (n 8; 20%), and >61 years of age (n 9; 22%). No statistically significant differences were found in the species isolated in these five groups (Fig. 2).

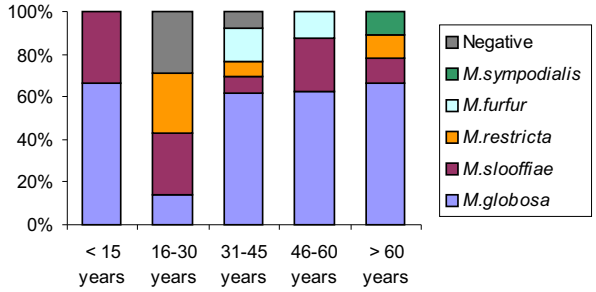

Figure 2. *Malassezia* species distribution from **psoriatic scalp skin** according to patient age.

Four groups were formed according to the duration of the psoriasis: less than one year (n 2; 5%), between 1 and 5 years (n 13; 33%), between 5 and 10 years (n 7; 17%), and more than 10 years (n 18; 45%). There was no statistically significant difference among these four groups in the distribution of the species isolated (Fig. 3).

Patients were divided into three severity groups according to the extent of scalp involvement, as follows: a) mild – seborrheic-like clinical pattern characterized by a fine diffuse scaling and erythema

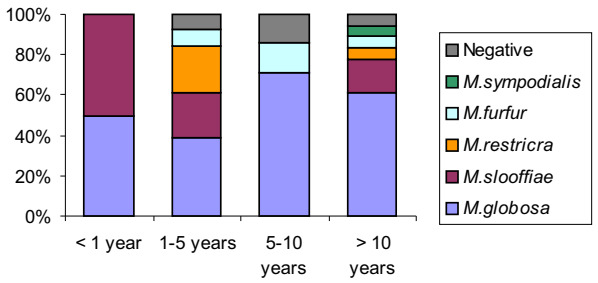

Figure 3. *Malassezia* species distribution **from psoriatic scalp skin** according to the duration of the disease.

covering the scalp (n 3; 7,5%); b) moderate – discrete plaques, or typical plaques of psoriasis that occur throughout the scalp, often with a predilection for hair margins (n 34; 85%); and c) severe – generalized plaque, or confluent involvement of the scalp with thick, scaly psoriasis (n 3; 7,5%). We found statistically significant difference in the distribution of *Malassezia* species isolated in three severity groups – *M.restricta, M.furfur, M.sympodialis* and negative cultures were found only in patients with moderate scalp involvement, whereas *M.globosa* and *M.slooffiae* were found more frequently in patients with moderate than in patients with mild or severe extent of scalp involvement (Fig. 4).

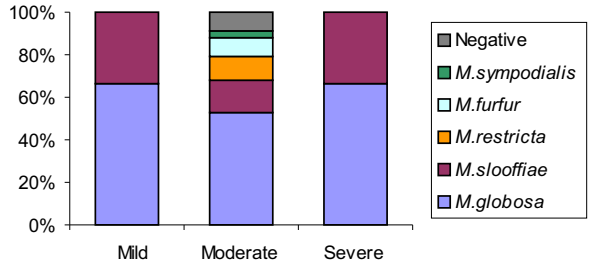

Figure 4. *Malassezia* species distribution **from psoriatic scalp skin** according to the severity/extent of the scalp involvement.

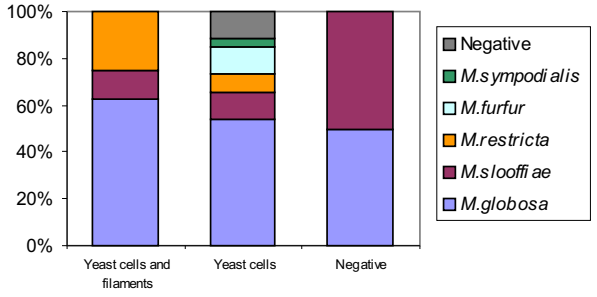

Figure 5. *Malassezia* species distribution **from psoriatic scalp skin** according to the direct microscopy findings.

We found no statistically significant difference in the distribution of isolated *Malassezia* yeasts according to direct microscopy findings: yeast cells and filaments (n 8; 20%), yeast cells only (n 26; 65%) and negative (n 6; 15%) (Fig. 5).

DISCUSSION

Rivolta (22) made the first association of the lipophilic yeasts and psoriasis in 1873. He reported on round double-contoured budding cells in the epidermis of a patient with psoriasis and named them *Cryptococcus psoriasis.* The role of *Malassezia* yeasts in psoriasis is still undetermined, but there are several reports indicating that these microorganisms are able to elicit psoriasiform lesions in both human and animals. Rosenberg *et al* (23) reported that, after heavy dense suspensions of *Malassezia* were applied to the shaved rabbits skin, lesions both grossly and microscopically similar to psoriasis developed. The same group claimed to be able to induce psoriasis-like lesions experimentally in 10 patients with psoriasis and 10 controls using patch testing with *Malassezia*. Although a Koebner phenomenon could not be excluded, their hypothesis was that psoriasis was produced by *Malassezia* yeasts through activation of the alternative pathway of complement, and also activated by other microorganisms and endotoxins (24).

Elewski (25) reported of a patient developing guttate psoriasis in sites of *Malassezia* folliculitis. In this case, pustules transformed into guttate lesions prior and during erythromycin therapy but resolved when ketoconazole was applied. Although this transformation could also be Koebner phenomenon, this case report supported the proposal that psoriasis may be included in *Malassezia*-associated diseases.

The identification of *Malassezia* yeasts to a species level is of no diagnostic value in skin diseases, as the same species form an integral part of normal cutaneous microflora in humans. However, it is of great importance to determine which species are associated with certain skin disease and whether the spectrum varies with clinical data, body site, origin of the population, etc. The results of the *in vitro* susceptibility studies have shown variations in susceptibility of the seven *Malassezia* species to ketoconazole, variconazole, itraconazole, and terbinafine. Strains of *M.furfur, M.globosa, and M.obtusa* were more tolerant to terbinafine than other species, whereas *M.sympodialis* was found to be highly susceptible (26). Therefore, correct identification of *Malassezia* species is required for the selection of appropriate antifungal therapy.

We found that the predominant species in psoriasis vulgaris lesions from the scalps of our patients was *M.globosa*, isolated in 22% of cases. This species has been recovered regularly from normal as well as diseased skin (9,10). *M.globosa* in its mycelial phase has been confirmed to be the causative agent of pityriasis versicolor (7,8). Data from United Kingdom on recovery of yeasts from scalp showed that *M.globosa* was the most frequent species in both adults and children (27). In our study, yeast cells predominated (64%), whereas filaments were observed in 23% of the scrapings from which *M.globosa* was isolated. This finding suggests that *M.globosa* in its yeast phase is the commonest species in psoriatic skin, at least from scalp. *M.slooffiae*, first isolated from animals, can be found occasionally on human skin (7,10). In our study, it was the second most frequent species (18%). The remaining three species, *M.restricta, M.furfur,* and *M.sympodialis,* were recovered in lower frequencies, as a part of normal human cutaneous flora (1).

In contrast to psoriatic scalp skin, *M.globosa* was recovered less frequently from healthy scalp skin, whereas *M.restricta* was the commonest *Malassezia* species. This species is isolated regularly from the scalp and face of patients with seborrheic dermatitis and normal individuals, but seems to be uncommon on the trunk (7,9,10). Although *M.sympodialis* is reported as one of the most frequent residents of healthy and diseases skin from trunk and scalp (6-11), in our study it was rarely isolated either from psoriatic patients or from healthy subjects.

M.obtusa and *M.pachydermatis* were not recovered from any of our samples either from psoriatic or from healthy scalp skin. However, *M.obtusa* is considered to be very rare and only infrequently isolated from the cases of pityriasis versicolor, atopic dermatitis (10), and seborrheic dermatitis (9). *M.pachydermatis* is confirmed to be clearly adapted to animals, although it has been involved in some systemic human infection (28). The presence of this species on human skin is rare and transient, occur-

ring possibly by transmission from animal pets and environmental sources (29,30).

The patients with psoriasis showed a low negative culture rate compared with the healthy subjects.

Our results are in agreement with report of Gupta *et al* (10), who found that *M.globosa* was the species most frequently isolated from psoriatic scalp skin, but striking difference was found in the recovery percentages: a significantly lower positive cultures from scalp were observed in Canada (28,6%) than in our study (92.5%), and consequently the species in their study were isolated in a lower frequencies.

CONCLUSION

Our results suggest that *M.globosa,* and *M.slooffiae, M.restricta* and *M.sympodialis* less frequently, represent the cutaneous yeasts flora from psoriatic scalp skin. There is still no convincing evidence of the role of *Malassezia* yeasts in psoriasis. The isolation of *Malassezia* yeasts from psoriatic lesions does not necessarily mean that they are pathogenic, but their role in the severity and extent of lesions cannot be excluded. Further studies on larger number of patients are needed to clarify the relationship between *Malassezia* species and psoriasis.

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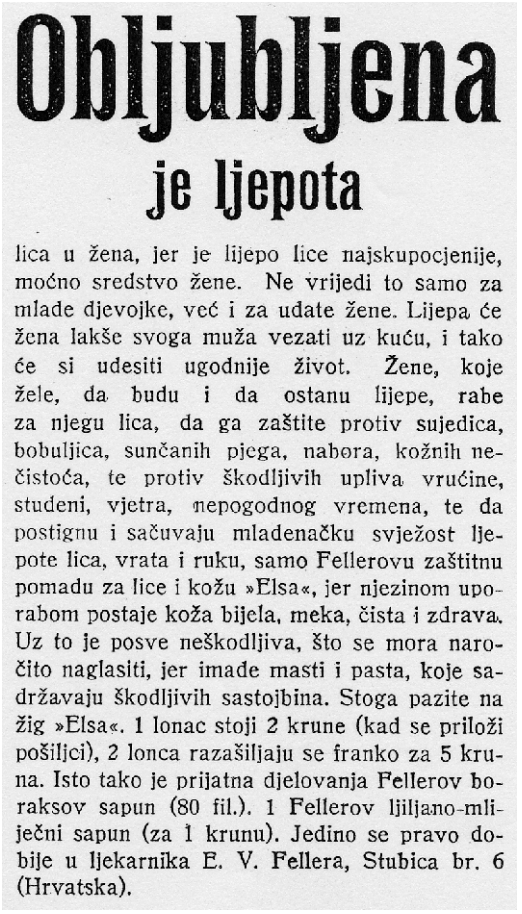

Obljubljena

je ljepota

lica u žena, jer je lijepo lice najskupocjenije, moćno sredstvo žene. Ne vrijedi to samo za mlade djevojke, već i za udate žene. Lijepa će žena lakše svoga muža vezati uz kuću, i tako će si udesiti ugodnije život. Žene, koje žele, da budu i da ostanu lijepe, rabe za njegu lica, da ga zaštite protiv sujedica, bobuljica, sunčanih pjega, nabora, kožnih nečistoća, te protiv škodljivih upliva vrućine, studeni, vjetra, nepogodnog vremena, te da postignu i sačuvaju mladenačku svježost ljepote lica, vrata i ruku, samo Fellerovu zaštitnu pomadu za lice i kožu »Elsa«, jer njezinom uporabom postaje koža bijela, meka, čista i zdrava. Uz to je posve neškodljiva, što se mora naročito naglasiti, jer imade masti i pasta, koje sadržavaju škodljivih sastojbina. Stoga pazite na žig »Elsa«. 1 lonac stoji 2 krune (kad se priloži pošiljci), 2 lonca razašiljaju se franko za 5 kruna. Isto tako je prijatna djelovanja Fellerov boraksov sapun (80 fil.). 1 Fellerov ljiljano-mliječni sapun (za 1 krunu). Jedino se pravo dobije u ljekarnika E. V. Fellera, Stubica br. 6 (Hrvatska).

Reklama E. V. Fellera, početak XX stoljeća. (Iz kolekcije S. Fatović-Ferenčić)

Acta Dermatovenerol Croat 2003;11(1):17-21 CASE REPORT

Terbinafine Exacerbates Psoriasis: Case Report with a Literature Review

Jacek C. Szepietowski

Department of Dermatology and Venereology, University of Medicine, Wroclaw, Poland

Corresponding author:

Jacek Szepietowski, MD, PhD

Associate Professor

Department of Dermatology and Venereology

University of Medicine

Ul. Chalubinskiego 1

50-368 Wroclaw, Poland

jszepiet@derm.am.wroc.pl

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SUMMARY Oral terbinafine is a widely used antifungal agent. Adverse effects occur in about 11% of patients taking terbinafine. A rare case of the exacerbation of pre-existing psoriasis after oral terbinafine treatment is reported. A 63-year-old male patient with stable psoriasis vulgaris developed extensive tinea cruris. For this reason, he was treated with oral terbinafine 250 mg/day and topical 1% terbinafine cream. After 6 days of this therapy, a widespread flare-up of psoriasis developed. Oral terbinafine was discontinued, and the psoriasis was treated with topical corticosteroids and tacalcitol. Tinea cruris was cured with topical terbinafine. This case points out that terbinafine can influence the course of psoriasis. Moreover, the literature data indicate that terbinafine may not only exacerbate pre-existing psoriasis, but may also be responsible for *de novo* development of psoriasis. Therefore, oral terbinafine should not be considered the first line drug for superficial fungal infections in psoriatic individuals.

KEY WORDS: antifungal; terbinafine; safety profile; psoriasis

INTRODUCTION

Terbinafine is an antimycotic agent of the allylamine class, with a high fungicidal activity against all dermatophytes (1,2). The drug was first introduced in 1991 and is now marketed worldwide (1,3). It is available both in oral and topical formulations (1,3). Several studies have confirmed terbinafine to be highly effective in the treatment of fungal infections of the skin, nails, and hairs (4-6). In 1996, more than 5 million patients received oral terbinafine, mostly for the treatment of onychomycosis (7,8). Five years later, in 2001, it was estimated that 18 million patients worldwide took oral terbinafine (9). Although the new generation oral antifungal agents are quite safe, adverse effects may sometimes appear (10). A survey of more than 25,000 patients receiving oral terbinafine for different reasons revealed that the incidence of its adverse effects is as high as 11% (7).

There are few reports describing exacerbation of pre-existing psoriasis after taking oral terbinafine. The case of stable psoriasis that flared after starting terbinafine therapy, presented in this report along with a short review of literature on terbinafine-induced psoriasis, could add to the general knowledge on the problem.

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CASE REPORT

A 63-year-old male patient was admitted to our Department because of erythematous lesions on upper inner thighs and groins, with minimal scaling located in the groins. The lesions appeared a week before the admission and were very itchy. Moreover, the patient had suffered from stable psoriasis vulgaris for the previous 3 years. The family history of psoriasis was negative and the patient had not required any antipsoriatic treatment for at least one and a half years before the erythematous lesions appeared.

On examination, he presented with extensive, sharply demarcated erythematous plaques limited bilaterally to the groins and upper inner thighs. The lesions showed an active edge with peripheral scaling. Small psoriatic papules with silvery-white scales were located symmetrically on the elbows, knees, and sporadically on the extensor surface of the lower legs. The psoriasis area and severity index (PASI score) was calculated as 2.2 points.

The clinical diagnosis of tinea cruris was confirmed by direct mycological examination (20% KOH with addition of DMSO), which showed typical dermatophytic hyphae. The patient was put on oral terbinafine 250 mg/day and topical 1% terbinafine cream was applied to the affected areas in the groins twice daily. In the first 5 days of terbinafine therapy, he reported marked relief of itching. However, on day 6, a widespread flare-up of the psoriasis developed. A diffuse erythematous papular eruption was present on the trunk, upper and lower extremities. No pustules were observed. The PASI score increased up to 12.4 points. As the cutaneous lesions were clinically typical for psoriasis, histopathological examination was not performed. The patient's general condition was good, basic blood laboratory tests showed no abnormalities. Two days after the first signs of the exacerbation of psoriasis, the patient discontinued oral terbianfine; topical terbinafine therapy was continued twice daily. The psoriatic eruption improved with topical application of 0.05% betamethasone dipropionate twice a day over three weeks. Afterwards, topical 4 g/g tacalcitol once a day was prescribed to control psoriatic lesions. Tinea cruris cleared with topical terbinafine and after two and a half weeks, only residual erythema was visible. On a follow-up visit, about 3 months after introduction of antifungal therapy, there were no lesions in the groins, but psoriatic papules were still present on the trunk, elbows, knees, and lower legs. The psoriasis was definitely more severe than before oral terbinafine therapy (PASI score, 3.6 points). The patient continued topical tacalcitol treatment.

DISCUSSION

Terbinafine shows highly selective activity against fungal squalene epoxidase, which is the reason for its relatively benign side-effects (9,11). In several studies, the tolerability of terbinafine was rated by most patients (88-98%) as "very good" or "good" (11). In a postmarketing surveillance study, adverse effects occurred in about 11% of patients taking oral terbinafine, whereas side-effects possibly, or probably, related to terbinafine were found in 6% of patients (7). The most commonly reported side effects were gastrointestinal symptoms, followed by cutaneous reactions. The frequency of terbinafine-related cutaneous side effects was estimated at 1.4% (7). The most common terbinafine-related complaints being different clinical manifestations of rash, pruritus, urticaria, and eczema (7,12). More severe, even serious, cutaneous reactions after treatment with oral terbinafine were reported only sporadically. They included fixed drug eruptions, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, and angio-edema (8,9,11). I agree with the opinion of Gupta *et al* (8) that the increasing use of terbinafine may result in a wider spectrum of adverse effects, including cutaneous reactions as well.

According to the PubMed database search results, by August 2002 only 6 articles had been published describing 10 patients with flare-ups of previous psoriasis or psoriasis *de novo* after taking terbinafine (Table 1). In 1995, Wach *et al* (13) first reported a female patient who developed a severe erythema anulare centrifugum-like psoriatic eruption with single pustular lesions 5 days after starting oral terbinafine 250 mg/day for onychomycosis. The lesions, localized on the trunk and extremities, completely resolved 2 weeks after discontinuation of terbinafine and treatment with oral prednisone. Shortly after this report two psoriatic patients who experienced exacerbation of psoriasis 26 and 6

Table 1. Reported patients with terbinafine-induced psoriasis (PubMed, August 2002)

No. of patient	Sex	Age (years)	Exacerbation of preexisting psoriasis	De novo development of psoriasis	Latency period (days)	Cause of terbinafine administration	Pustular lesions	Author, year (reference)
1	female	56		+	5	onychomycosis	single	Wach et al, 1995 (13)
2	male	70	+		26	onychomycosis	no	Gupta at al, 1997 (8)
3	male	52	+		6	onychomycosis	no	Gupta et al, 1997 (8)
4	female	70	+		17	suspected onychomycosis	no	Gupta et al, 1998 (14)
5	male	50		+	27	onychomycosis	generalized pustules	Gupta et al, 1998 (14)
6	female	54	+		21	suspected onychomycosis	generalized small groups of pustules	Gupta et al, 1998 (14)
7	male	34	+		12	onychomycosis	no	Gupta et al, 1998 (14)
8	male	65		+	14	suspected onychomycosis	widespread pustules	Wilson & Evans, 1998 (15)
9	female	74		+	14	suspected onychomycosis	no	Pauluzzi & Boccuzzi, 1999 (16)
10	male	70		+	10	onychomycosis	plantar pustular psoriasis	Le Guyadec et al 2000 (17)
11	male	63	+		6	tinea cruris	no	Szepietowski (present case)

days, respectively after being on terbinafine treatment were reported (8). A year later, Gupta *et al* (14) described two psoriatic patients with terbinafine-exacerbated psoriasis. Their psoriasis flared 12 and 17 days after beginning of antifungal therapy. In the next patient with stable plaque-type psoriasis pustular psoriatic lesions appeared 21 days after taking terbinafine. Moreover, additional patient developed psoriasis *de novo* on day 27 of terbinafine therapy (14). Pauluzzi and Boccucci (16) described inverse psoriasis induced by terbinafine, while others reported development of pustular psoriasis for the first time in additional two patients after 14 and 10 days of the oral terbinafine therapy (15,17). It is likely that terbinafine induced psoriasis in even more patients than it has been reported. Gupta *et al* (8) and Le Guyadec *et al* (17) were aware of 24 possible similar cases (data obtained from the World Health Organization).

The latency periods between administration of suspected agents and the flare-up or *de novo* development of psoriasis were classified into three groups: short (<4 weeks), intermediate (4-12 weeks), and long (>12 weeks) (14). The analyzed cases suggest that terbinafine should be put into the first group with the shortest latency period of 5 days, like nonsteroidal anti-inflammatory agents (14). Similarly to previously reported patients with terbinafine-induced psoriasis, no provocation test with oral terbinafine was performed in our patient. So far, the mechanism of psoriasis exacerbation due to terbinafine intake has remained unknown.

The majority of patients who developed terbinafine-induced psoriasis took this oral antifungal agent because of onychomycosis. However, in some patients, terbinafine was prescribed only for clinically suspected onychomycosis without mycological confirmation (4,6,9,15). A widely accepted rule is that mycological examination must give a positive result before therapy with oral antifungal drugs, including terbinafine, can be started (10). The patient described in this case report received

oral terbinafine to control tinea cruris diagnosed by direct mycology. This is the first patient with terbinafine-induced psoriasis who developed psoriatic lesions during the course of tinea cruris therapy.

Several cases of terbinafine-induced psoriasis showed to be very difficult to control, with some of them requiring hospitalization and/or systemic corticosteroid therapy (13-15). One of these patients developed widespread pustular eruption, fever, and laboratory abnormalities (increased white cell count and disordered liver function tests) (15). In the patient described in this case was in good general condition without any blood abnormalities and his psoriasis significantly improved with potent topical corticosteroid and tacalcitol. However, the PASI score was 3 months after starting terbinafine therapy higher than before the disease exacerbation. Resistance to the therapy of psoriasis induced by drugs, such as antimalarial agents, corticosteroids or lithium, has been reported (14,18). The above mentioned patients with terbinafine-induced psoriasis indicate that psoriasis exacerbated by terbinafine could also be difficult to treat.

Several patients developed pustular psoriasis (14,15,17). Pustular eruption is a known adverse effect of oral drugs (18). As many as 5 patients have been reported who developed acute generalized exanthematous pustulosis – an entity often indistinguishable from acute generalized pustular psoriasis - associated with oral terbinafine (19-22).

To the best of my knowledge, no reports have been published of psoriasis exacerbation after treatment with other oral antifungal agents, such as itraconazole, fluconazole or ketoconazole. Interestingly, itraconazole has even been suggested to be beneficial in sebopsoriasis (23) and palmoplantar pustular psoriasis (24). Moreover, ketoconazole could potentially affect psoriasis in seborrheic areas of skin directly by an antifungal action or indirectly by suppressing fungal antigen-induced lymphocyte-mediated immune responses affecting the skin (25).

In conclusion, terbinafine, in contrast to other oral antifungals, may be responsible for the exacerbation or *de novo* development of psoriasis, frequently pustular psoriasis. Although it is widely used in psoriatic patients (mainly for onychomycosis) without any adverse effects (26), the cases of terbinafine-induced psoriasis indicate that oral terbinafine should not be considered a first line drug for superficial fungal infections in psoriatic individuals.

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Acta Dermatovenerol Croat 2003;11(1):22-28 CASE REPORT

Psoriasis Vulgaris and Arthritis Psoriatica Gravis Mutilans

[1]Pero Vržogić, [2]Aida Pašić, [1]Tea Podobnik-Takač

[1]Naftalan Special Hospital for Medical Rehabilitation, Ivanić Grad, Croatia
[2]Department of Dermatology and Venerology, Zagreb University Hospital Center, Zagreb, Croatia

Correspondence to:

Pero Vržogić, MD

"Naftalan" Special Hospital for Medical Rehabilitation

Omladinska 23a

10310 Ivanić Grad, Croatia

Received: 18. 12. 2002
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SUMMARY A 33-year-old man with generalized vulgar psoriasis type I and psoriatic arthritis was admitted to the Naftalan Special Hospital on February 21, 2000. He was immobile and complained of severe pain in all his joints. Since the patient had suffered from the disease for 10 years without showing any improvement after different therapies, his cutaneous and joint lesions gradually worsened and eventually resulted in generalized psoriasis and mutilating arthritis. Nevertheless, the patient was discharged from our hospital in better condition. To avoid such severe consequences of psoriatic arthritis, we believe that patients with either type I or type II psoriasis should undergo locomotor system screening. It would significantly decrease the number of unrecognized and undiagnosed cases of psoriatic arthritis and allow their early treatment, and prevention of more severe forms. Administration of new therapeutic agents, e.g. Alefacept (IgG1 fusion protein), Etanercept (inhibitor of TNF activity), and Efalizumab (monoclonal antibody that blocks the leukocyte integrin CDIIa/CD18(LFA-1), could provide successful management of the disease in future.

KEY WORDS psoriatic arthritis; psoriasis; cell migration inhibition; infection

INTRODUCTION

Psoriasis is an inflammatory dermatosis, which develops due to genetic susceptibility and affects 1-3% of the population (1-4). Although psoriasis may occur at any age, it is most common at the age of 20, and occurs 3-4 years earlier in women than in men. In 75% of patients, the onset of psoriasis occurs before the age of 40 (4,5). Familial clustering of the disease has been documented in about 30% of patients (2). Vulgar psoriasis of a chronic stationary type (chronic plaque psoriasis) shows an equal sex distribution (2,4).

Based on the age at onset, familial affection, and association of psoriasis with some HLA antigens, especially HLA Cw6, psoriasis can be divided into two types: type I and type II. Type I is characterized by early occurrence, positive family history, and association with HLA antigens, whereas type II is characterized by late occurrence, no family his-

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tory, ungual lesions, and associated arthritis. Moreover, according to the latest genetic studies of gene expression (psors1, psors2, psors3) and significant occurrence of particular chromosomes at the specified gene loci (6p, 17q, 4q), there could also be type III psoriasis (4-6,8).

Although psoriasis may affect any skin region, the predilection sites are the scalp, elbows, knees, and sacral region. Nails can also be involved. Arthropathic psoriasis, or psoriatic involvement of joints, occurs in 10% of patients (2,9-13). The basic lesion is a papule or plaque with silver-whitish scales. There are various clinical forms of psoriasis, such as psoriasis in placibus, psoriasis guttata, psoriasis nummularis, psoriasis geographica; psoriasis inversa, psoriasis erythrodermica, psoriasis pustulosa, psoriasis cum pustulatione, psoriasis palmoplantaris; and arthritis psoriatica associated with HLA-B27 (1,6,7).

Psoriatic arthritis is a specific type of arthritis that can either start slowly, with mild symptoms, or develop quickly. Generally, patients complain about one or more of the following symptoms: discomfort, stiffness, pain, throbbing, swelling, and tenderness in one or more joints, reducing the joint motion. When psoriatic arthritis starts early in life, the prognosis is poor. Affection of distal joints (closest to the finger nail or toe nail), lower back, wrists, knees, or ankles with swelling of the fingers and toes produces a sausage appearance of the affected fingers. Morning stiffness and tiredness are frequent. Nail changes may also occur, e.g., pits in the nail bed. Inflammation of the eye, such as conjunctivitis, is rare (9,10).

The diagnosis of psoriatic arthritis is made on the basis of medical history, physical examination, laboratory findings (e.g., antibody testing), and x-rays of the symptomatic joints. Differential diagnosis includes rheumatoid arthritis, gout, and Reiter's syndrome, which are similar to psoriatic arthritis and may occur with psoriasis. However, the antibody generally present in rheumatoid arthritis is usually not found in the blood of patients with psoriatic arthritis, whereas analysis of the fluid obtained from the affected joints can help discern between gout and psoriatic arthritis (11).

Psoriatic arthritis may develop at any age, but usually begins between the age of 30 and 50. A number of factors seem to be associated with the development of arthritis, especially heredity. Recent studies have shown that some genetic markers are more common in people who develop psoriatic arthritis, and immune system is also believed to play a role. Some bacteria, as well as trauma, were identified as the possible triggering factors (11-13).

There are five types of psoriatic arthritis: symmetric arthritis and polyarthritis, asymmetric arthritis, distal interphalangeal predominant (DIP) arthritis, spondylitis, and arthritis mutilans (13,14). Narrowing of the joint cavities, marginal erosions, and periarticular osteoporosis develop, depending on the type of psoriatic arthritis. The diagnosis is made by a radiologist, and rheumatologist is in charge of the treatment.

CASE REPORT

A 33-year old man from Narta, near Čazma, was admitted to our hospital due to psoriasis vulgaris and psoriatic arthritis in February 21, 2000. He was immobile, subfebrile, and complained of severe pain in all the joints. Patient's medical history revealed that the patient's mother suffered from psoriasis and carcinoma of the uterus, which was surgically treated. The patient's father was an alcoholic, whereas his younger brother was healthy. The patient had no other severe disease in his history. Of childhood diseases, he had had measles and varicella. The patient did not smoke and did not consume alcohol over the previous 10 years (before, he had occasionally drunk beer or wine).

The disease started 10 years ago, with the appearance of typical psoriatic lesions on the scalp. As early as 2-3 months afterward, he had arthritic attack accompanied by fever of up to 38 C: the interphalangeal joints of his fingers and toes swelled, as well as ankle joint and knee joint. The cutaneous and joint lesions worsened over years and resulted in generalized psoriasis and mutilating arthritis. Between 1991 and 1993, the patient was treated irregularly for 3-4 months with medium doses of prednisone in combination with sulfasalazine and nonsteroidal anti-inflammatory agents (NSAR), but without any success. In 1993, the patient received methotrexate and NSAR for 2 months, but this therapy had to be discontinued because of hepatic lesion. Auropan (gold salt) and

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NSAR he received the same year also proved inefficient. In 1994, oral prednisone was reintroduced, but it had to be discontinued due to the development of Cushing's syndrome. The patient had also been receiving antimalarial drug, chloroquine tablets, but could not recall for how long. Then, he turned to alternative medicine. In 1996, he became bed-ridden and remained on home care, taking high doses of analgesic drug Fortral (pentazocin) and NSAR without any medical control.

On February 21, 2000, the patient was referred to the "Naftalan" Special Hospital for the treatment of his disease, with very poor clinical condition of his skin and joints, and remained hospitalized until March 27, 2000.

On admission, he was immobile, conscious, subfebrile (37.2 – 37.6 C), eupneic, and cardially compensated. He complained of severe pain in all his joints, for which he was taking Fortral (3x1 tablet) daily, along with NSAR-indomethacin. Visible mucosa was well-perfused, and general neurologic status normal, with no neurologic events. Physical examination showed normal eyes and ears, heart and lungs. His blood pressure was 130/80, abdomen meteoristic at the thorax level, without any pathologic changes palpable. The liver and spleen were normal on palpation.

Dermatologic Status

The entire skin was atrophic and erythematous. Diffuse scaling with infiltrates was found on the scalp, with visible erythema on the face. Erythema with squames of a coin size was found marginally on the forehead, and erythema only intertriginously on the neck (Fig. 1). Axillary skin was also reddish, partly macerated, whereas large squamous lesions along with erythema spread over the extensory sides of the extremities (Figs. 2 and 3).

Squames with rhagades and crusts were present on the palmar surfaces of both hands. The skin was laterally inflamed, with pustular necrotic plaques along both thighs and thick, infiltrated squames and crusts. On both lower legs, the skin was inflamed and atrophic, with adherent squames and crusts. The skin of both feet showed necroses with pustular necrotic plaques. Under the dried discharge, swelling of abundant necrotic pustular content could be seen on both dorsal and plantar sides of both feet. The nails showed deformities and were covered with dried purulent discharge. Interdigitally, the skin was sticky and of bad odor. The intertriginous folds, inguinal and gluteal regions showed inflammatory changes and macerations, with gluteal region covered with abundant squamous infiltrates and crusts.

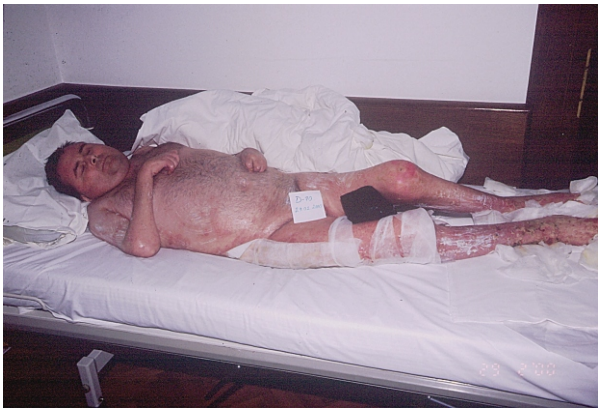

Figure 1. Diffuse scaling and erythematous skin of the body.

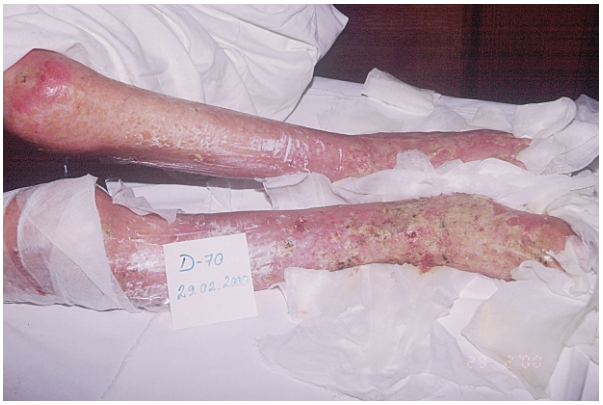

Figure 2. Erythematous and large squamous lesions on the lower extremities.

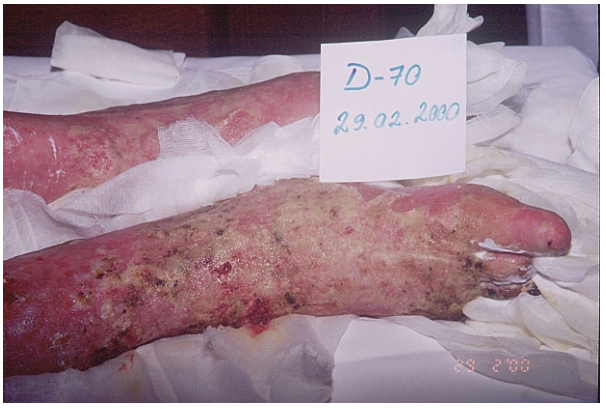

Figure 3. Detail of erythematous and large squamous lesions along distal extensory sides.

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Locomotor Status

The patient was immobile, lying on his back. He could not sit independently, even with support, and could not turn aside. Both temporomandibular joints were painful, and yawning limited. The cervical and lumbar spine motion was minimal and painful. There were contractures of both shoulders and both elbows. Both radiocarpal joints were swollen and painful, with minimal motion. Pain and deformities of small joints of the hand were also found, with fingers in flexion contracture (Fig. 4).

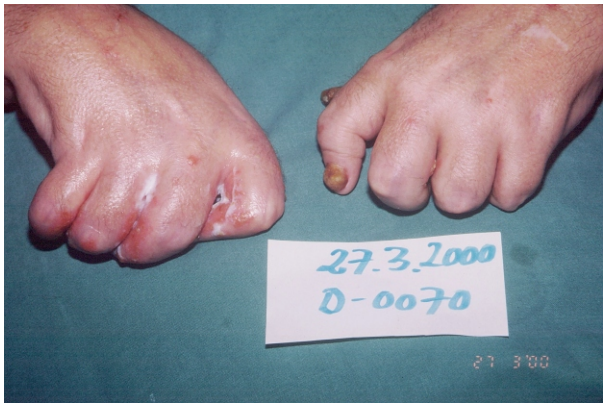

Figure 4. Deformities of small joints of the hand, with fingers in flexion contracture.

The hips were in flexion contracture, with motion block, and the knees swollen, malformed, extremely painful on palpation and motility, and also in flexion contracture. Both ankles and dorsa of the feet were swollen, and toes in flexion contracture showed sausage-like thickening.

Laboratory Findings

His laboratory findings on February 28, 2000, were as follows: ESR 108; leukocytes 6.4; erythrocytes 3.24; hemoglobin 105; hematocrit 322; platelets 399; PCT 277; granulocytes 75%; lymphocytes 18.8%; monocytes 3.1%; nonsegmented 3% (rough granules in most granulocytes); BG 4.9; urea 1.5; uric acid 258; AST 17; ALT 12; sodium 152.1; potassium 4.99; and urine findings normal.

Mupirocin sensitive *Proteus mirabilis* was isolated from the bacteriologic swab of a foot lesion.

X-ray

Oblique posterior-anterior projection of cervical spine showed complete ankylosis of small joints. Posterior-anterior projection of thoracic spine did not reveal any major pathologic alterations, whereas posterior-anterior projection of lumbosacral spine in supine position showed right-sided convex scoliosis. Intervertebral spaces seemed to be preserved, whereas small joints were affected with ankylosis. X-ray of the hips and pelvis showed ankylosis of the coxofemoral articulations with protruding acetabula bilaterally (Fig. 5). The right shoulder x-ray obtained with the patient lying down without grid showed demineralization of the head of the humerus and scapula. X-ray of the clenched right hand showed deformities of proximal phalanges of all fingers, with subluxation. The left hand also showed deformities of proximal phalanges and subluxation of the metacarpophalangeal articulations (Fig. 6). There was a pathologic fracture of the distal ulnar bone and along carpal bones. On a single x-ray of the right knee in oblique projection articulation fis-

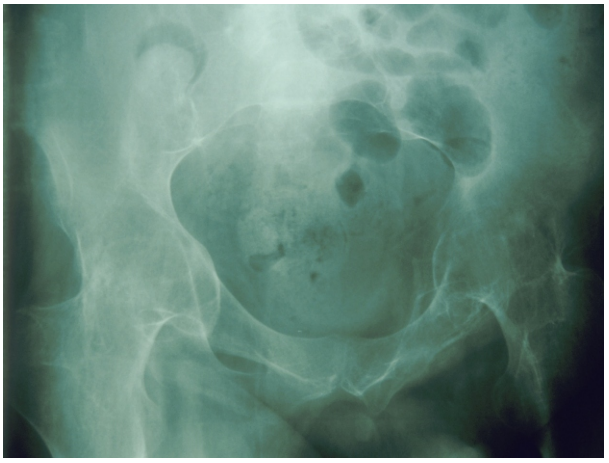

Figure 5. X-ray of the hips and pelvis showed ankylosis of the coxofemoral articulations with protruding acetabula bilaterally.

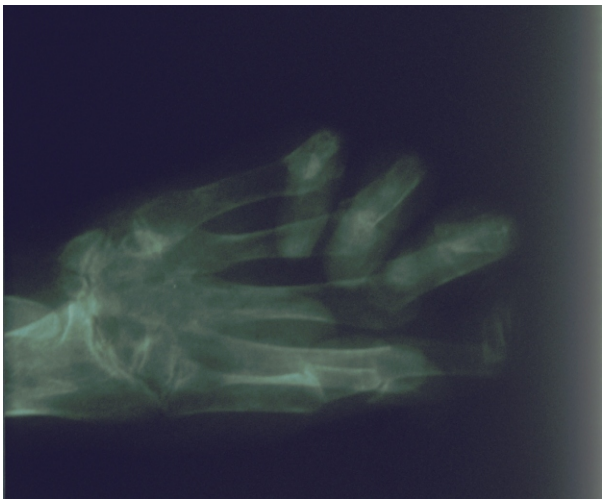

Figure 6. Deformities of proximal phalanges and subluxation of the metacarpophalangeal articulation.

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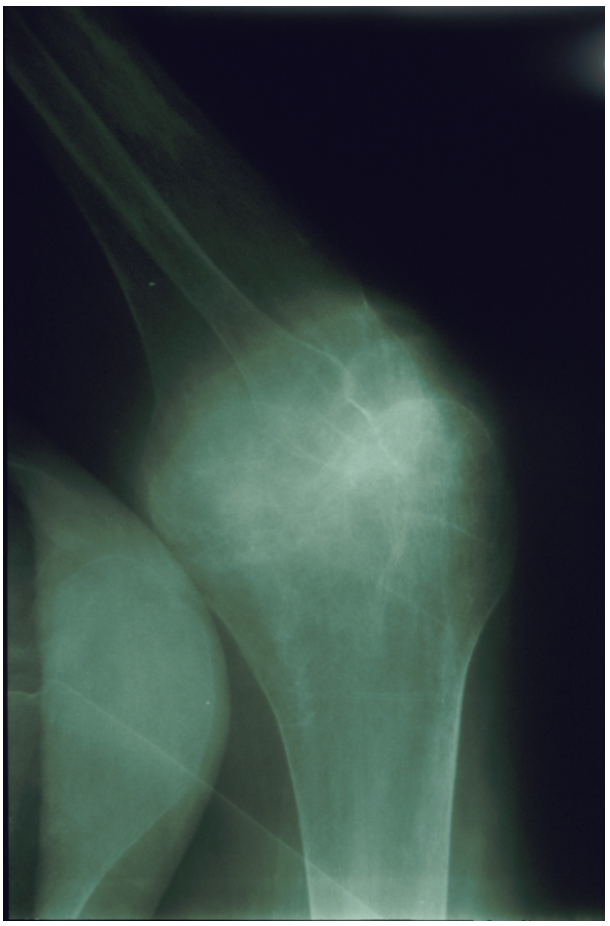

Figure 7. Right knee without articulation fissures.

sures could not be differentiated (Fig. 7). X-ray of the right foot in oblique projection showed severe skeletal demineralization with inflammatory changes of the articulatory areas of the tibia, deformities of the talus and tarsal bones, and ankylosis of the metatarsophalangeal articulations bilaterally (Fig. 8).

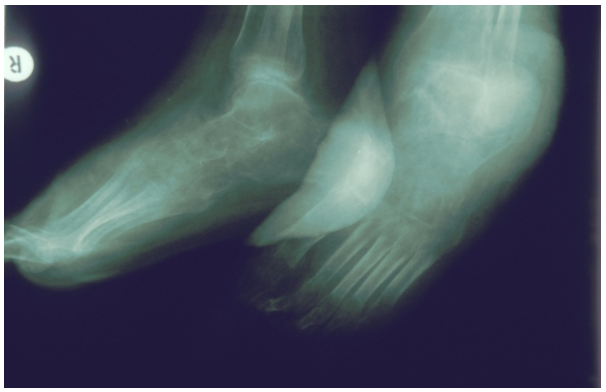

Figure 8. Deformities of the talus and tarsal bones and ankylosis of the metatarsophalangeal articulations bilaterally.

Therapy

Daily baths in KMnO4, antibiotic ointments (Betrion, mupirocin) and neutral creams (Belobase) were abundantly applied locally, in combination with the Beloderm corticosteroid cream (betamethasone dipropionate), 5% salicylic ointment in emollient, zinc oxide paste, oil compresses, and 5% salicylic oil on the scalp.

Oral antibiotic therapy administered for 11 days consisted of 625 mg (3x1 tablet) Klavocin (amoxicillin with clavuronic acid) daily, but it had to be discontinued due to diarrhea. Throughout his hospital stay, the patient received NSAR (Lubor – piroxicam tablets) and Fortral (pentazocin) 3x1, which he had been using before admission, as well as Praxiten (oxazepam) and Apaurin (diazepam). NSAR (Lubor) was also administered intramuscularly for 15 days.

This combined therapy slowly but steadily resulted in considerable regression of cutaneous lesions, with gradual epithelization (Fig. 9). Fortral was successfully withdrawn and substituted by oral Tramal (tramadol) 2-3x1 tablets a day. In addition, physical therapy with passive movements was introduced, allowing for active movement and enabling the patient to continue exercising at home.

On discharge from the hospital, the patient was recommended to continue with the following therapy: application of Betrion ointment with bandage on the remaining non-epithelialized areas of the skin, daily washing of both feet in $KMnO_4$, very careful hygiene of other skin areas with the use of Belobase, and application of 30% Beloderm in Belobase on the possible minor psoriatic lesions on the back and in the gluteal region. The zinc oxide paste was applied only on particular areas of the trunk to prevent the possible decubitus (ulcers) formation. Belosalic (betamethasone dipropionate with salicylic acid) lotion twice a week was recommended for the scalp, in addition to washing it with Oronazol (ketoconazole) shampoo.

The patient was administered Methotrexate (methotrexate), 7.5 mg/week, with transaminase, ESR and CBC control testing every 2 weeks. He used Lubor (piroxicam), 20 mg 1x1, Praxiten 15 mg 2x1 tbl daily, and Tramal as needed.

Although control examinations by the patient's doctor, visiting nurse care, and physiotherapist's

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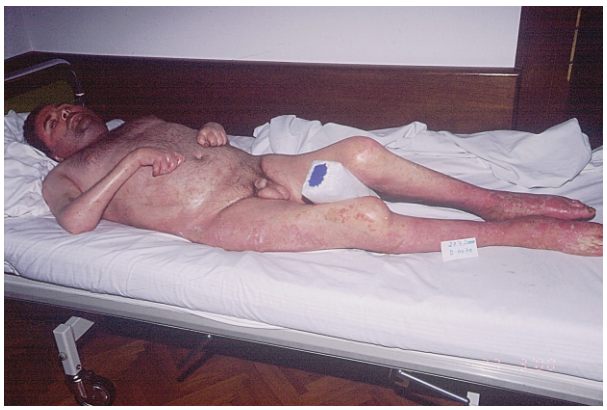

Figure 9. Considerable regression of cutaneous lesions with epithelization.

home visits were recommended, the patient failed to do physical therapy and visit an orthopedic surgeon for additional treatment.

DISCUSSION

The aim of this report was to highlight the importance of screening for joint disease in patients with psoriasis type I or II. Although our patient developed psoriasis type I, the history of the disease, its extent, and early development of radiologically evident joint involvement demonstrate the characteristics of psoriatic arthropathy. We believe that appropriate screening for joint disease in patients with psoriasis has important implications for clinical practice and genetic studies. Literature data show a high prevalence of undiagnosed psoriatic arthropathy in patients with psoriasis (15). The prevalence of symptomatic sacroileitis is of particular interest. The patients with joint involvement are older than those with psoriasis alone. In our patient, the onset of both psoriasis and psoriatic arthritis occurred ten years before admission, with bilateral sacroileitis, inflammatory backache, peripheral joint inflammation, and positive family history of both psoriasis and arthritis. Previous unsuccessful therapy imposed the need of a new therapeutic approach, e.g. administration of TNF blockade and reduction of many proinflammatory cytokines, adhesion molecules, and destruction factors.

In our patient, the onset of vulgar psoriasis type I, associated with HLA DR7 and DR6, occurred at age 23. The disease took a very severe course, with parallel involvement of skin and joints. During the 10-year period, the values of ESR ranged from 80 to 110. He had been hospitalized on several occasions at different departments, i.e. at Department of Dermatology and Venerology, Zagreb University Hospital Center; Department of Physical Medicine and Rehabilitation; Dubrava University Hospital; Naftalan Special Hospital in Ivanić Grad; and Department of Orthopedics in Lovran.

The patient was administered various drug treatments, which could be properly traced from his medical records. The patient failed to comply with therapeutic recommendations. Methotrexate, taken overall for 2-3 months, had to be discontinued because of increased transaminases. Oral corticosteroids also had to be discontinued because the patient developed severe Cushing's syndrome.

Since the patient developed a negative attitude towards official medicine, as evidenced by his refusal to seek medical help for the past 4-5 years, the disease progressed to its terminal stage: immobility, inflammatory activity and strong pain in the affected joints. The poor outcome resulted from the patient's psychological profile. The consequence of all these factors was total and permanent disability in the most productive age.

Hopefully, the new therapeutic approach with Alefacept (human LFA-3/IgG_1 fusion protein), administered intravenously at a dose of 7.5 mg per week for 12 consecutive weeks, will soon become the treatment of choice for psoriatic arthritis and psoriasis (15). Alefacept has been shown to improve the clinical joint score, skin psoriasis, and T-cell subsets in synovial fluid (16, 17). Etanercept (Enbrel1), an inhibitor of TNF activity, given as monotherapy at a dose of 25 mg s.c. twice a week, may prove useful in the management of psoriasis (18). Infliximab, a chimeric anti-TNF- antibody and Etanercept neutralized rhTNF- effectively (18). Efalizumab, a monoclonal antibody, blocks the leukocyte integrin CD11a/CD18 (LFA-1) in patients with psoriasis vulgaris (19).

In conclusion, the case we presented points to the significant role of an early diagnosis and timely treatment of psoriatic arthritis, with individualized approach to and proper education of each patient to prevent permanent debilitating lesions. In our patient, his unfavorable psychologic profile contributed to the poor outcome of the disease.

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Acta Dermatovenerol Croat 2003;11(1):29-31 CASE REPORT

The Baboon Syndrome Due to Nickel

Tomasz Kolodziej, Jacek C. Szepietowski, Julita Sikora, Rafal Bialynicki-Birula

Department of Dermatology. University of Medicine, Wroclaw, Poland

Corresponding author:

Tomasz Kolodziej, MD

Department of Dermatology,
University School of Medicine

Chalubinski 1 str

50-368 Wroclaw, Poland

tj-kolodziej@wp.pl

SUMMARY The "baboon syndrome" is a rare variant of systemic contact dermatitis and is characterized by general exanthema with particular involvement of buttocks and flexures. Here we present a 25-year-old female with contact allergy to nickel, who developed baboon syndrome after systemic administration of this allergen.

KEY WORDS nickel hypersensitivity; systemic contact dermatitis; baboon syndrome.

INTRODUCTION

Hematogenous contact eczema, the 4th type of allergy reaction, may be caused by a systematical exposure to an allergen of a person previously sensitized to it. The term "baboon syndrome" is a variant of such eczema characterized by general exanthema, with particular involvement of buttocks, which may resemble the red gluteal region of a baboon (1). Diffuse erythema also involves anogenital area, upper inner side of the thighs, and armpits (1).

CASE REPORT

A 25-year-old woman with previously proven contact allergy to nickel was referred to our Department because of itchy and painful generalized rash that had developed 2 days before admission. Several days before developing skin lesions, she had been exposed to components that might have contained nickel: she had eaten significant amount of canned beans, drunk tap water, and inhaled vapors of water-based paints.

Physical examination revealed erythematous, maculopapular, symmetrically distributed patches involving sacral region and lateral aspects of trunk, buttocks, anogenital area, groins, and the major flexural areas (Figs. 1-3).

There were also numerous vesicles on her left wrist where she had worn a watch before hypersensitivity to nickel developed (Fig. 4).

She was treated with intravenous injection of hydrocortisone (5 days, from 200 mg to 50 mg), systemic antihistaminics, and mild topical corticosteroids. This treatment resulted in pronounced clinical improvement within 3 days. The lesions disappeared completely after 7 days of therapy. Three weeks later patch testing revealed a highly positive reaction to 1-%-nickel sulfate.

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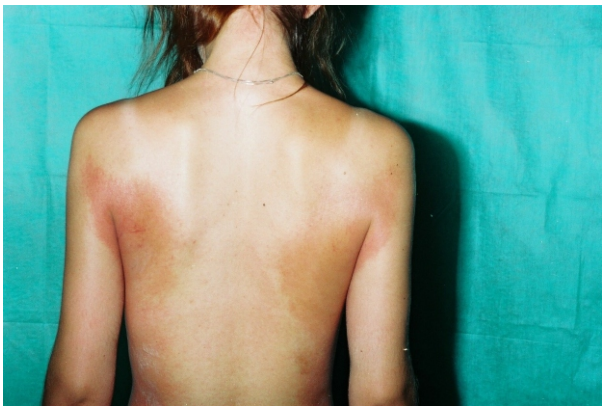

Figure 1. The baboon syndrome due to nickel. Flexural exanthema.

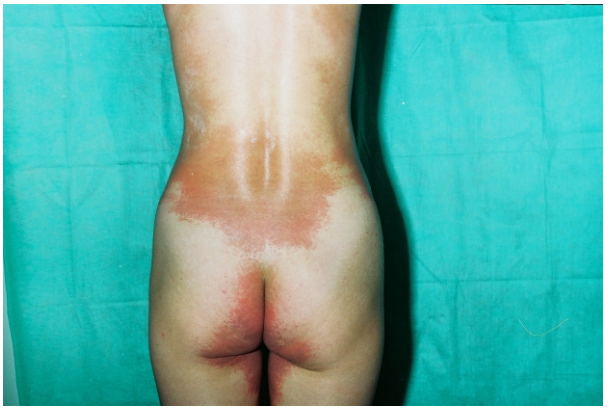

Figure 3. The baboon syndrome due to nickel. Erythema of underpants area.

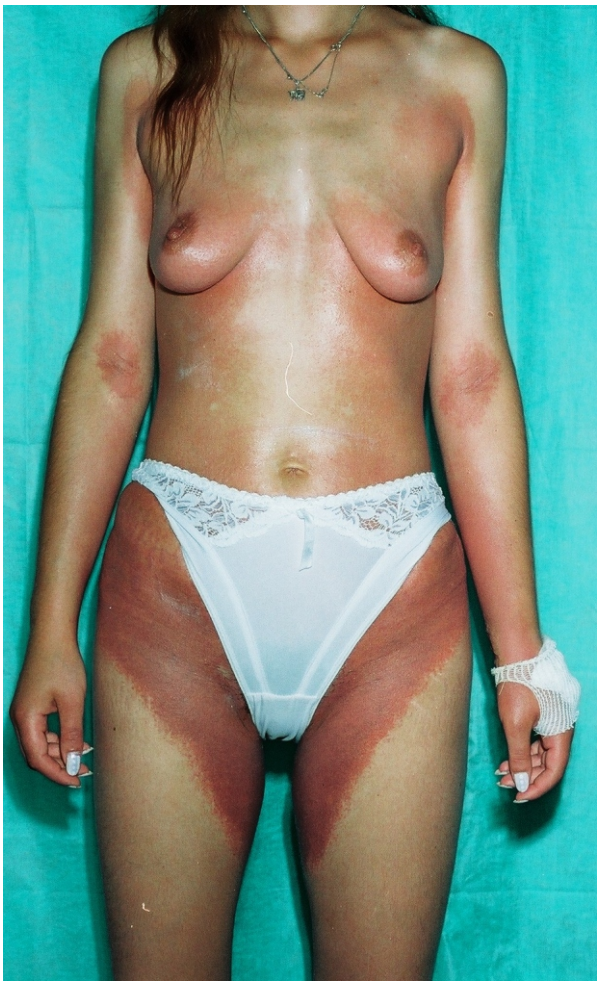

Figure 2. The baboon syndrome due to nickel. Skin lesions resemble the baboon red buttocks.

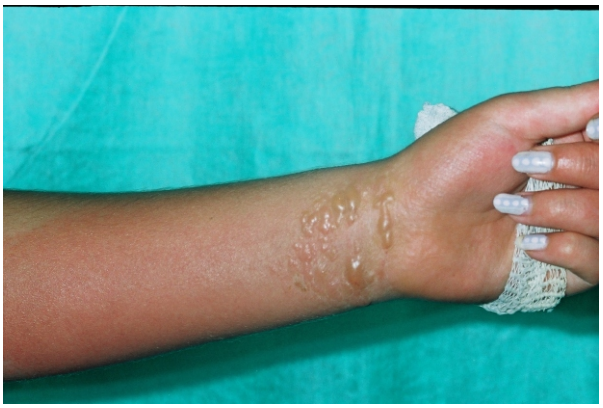

Figure 4. The baboon syndrome due to nickel. Numerous vesicles on the patient's wrist, where she had worn a hand-watch before she developed hypersensitivity to nickel.

DISCUSSION

Systemic exposure to contact allergen, such as water-based paints, may cause various hypersensitive skin reactions, such as generalized eruptions, palmo-plantar dyshydrotic lesions (pompholyx), and contact-type dermatitis with different distribution, mostly involving hands and rarely involving anogenital region, flexures, and buttocks (baboon syndrome) (1,2). The onset of the baboon syndrome is acute, ranging from several hours to 2-4 days after systemic exposure to the allergen (3).

The microscopic findings are not specific and show sparse superficial and perivascular lymphocytic and histiocytic infiltration. There is no involvement of the epidermis and no signs of leukocytoclastic vasculitis (4).

The reason of such an unusual distribution of eczema in the baboon syndrome is unclear. Occlusion by underwear and sweating are more prominent in those regions, but their influence is only speculative.

The baboon syndrome has been described in over 20 reports, although in some it was described as eczema with flexural pattern (5). Systemic exposition to mercury (1,6) and antibiotics, particularly amoxicillin (4,7), present the most common causes of the syndrome. The baboon syndrome develops particularly often after exposure to mercury and mercury derivates, such as antiseptics used in newborns (1,6). Cases of the syndrome due to exposition to terbinafine (8), intravenous human immunoglobulins (9), and hydroxyurea (10) were also described, but very rarely.

To the best of our knowledge, there has been only one report of baboon syndrome provoked by a systemic exposure to nickel (1) before ours. It seems that this pattern of eczema is not characteristic for this allergen.

The frequency of baboon syndrome is unknown. This condition is probably often overlooked, although it should be considered in the differential diagnosis of erythematous eruptions in flexural areas and on the buttocks.

CONCLUSION

Baboon syndrome is a rare form of systemic contact dermatitis. The frequency of baboon syndrome is unknown because it is rarely included into differential diagnosis of erythematous eruptions. Our case of baboon syndrome provoked by nickel is the first one ever recorded in our country.

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Acta Dermatovenerol Croat 2003;11(1):32-40 REVIEW

Skin Photodamage and Lifetime Photoprotection

Ivana Nola, Lena Kotrulja

Department of Dermatovenerology, Sisters of Mercy University Hospital, Zagreb, Croatia

Correspodending author:

Ivana Nola, M.D., M.S.

Department of Dermatovenerology

Sisters of Mercy University Hospital

Vinogradska cesta 29

10 000 Zagreb, Croatia

ivana_nola@hotmail.com

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SUMMARY Ultraviolet (UV) radiation is a very small part of the electromagnetic radiation spectrum, released and transported from the source in the form of photons. Disposal of these photons within the skin causes cutaneous photodamage, which leads to clinical, histologic, and biochemical changes. Aging is a complex process characterized by cellular attrition, decreased cellular reserve capacity, and compromised ability to perform normal cellular function. Intrinsic aging, which steadily develops with time, is linked to chronologic age; it is the result of a genetic program. Photoaging, on the other hand, develops as a consequence of UV radiation-induced degenerative changes in the skin. Intrinsic aging is a universal, inevitable process, whereas photoaging is neither universal nor inevitable and can be prevented. UV radiation can also suppress the immune system in both local and systemic way and lead to simultaneous and sequential biochemical events that ultimately cause photocarcinogenesis. Therefore, everyday use of products that protect against UV radiation is necessary to prevent acute and long-term photodamage (clinical and cellular changes) leading to photoaging, photoimmunosuppression, and photocarcinogenesis.

KEY WORDS skin; skin aging; sunlight; sunscreening agents; ultraviolet rays

INTRODUCTION

Photoaging denotes macroscopic and microscopic skin changes, which develop as a consequence of chronic solar radiation. Photoaging has unique and distinctive features, quite different from normal aging. With the exception of senile angiomas, which normally accompany aging and develop on the trunk areas, practically all major skin tumors originate from photoaged skin (1).

In the 20th century, natural light and UV radiation from artificial sources were thought to be good for both our psyche and our skin, and that, by generating a healthy looking tan, they enhance the photoprotective properties of melanin in our skin. Yet, excessive exposure to this life-supporting radiation can be very damaging to the skin of those individuals whose natural photoprotective defenses are poor (2,3).

Despite the fact that the incidence of skin cancer is increasing in the West, the protection from sunlight, the primary cause of skin cancer, is still largely ignored by the public. The reasons for such an attitude are dictates of fashion, the ease of access to the sun, and the increasing longevity of the population. Even if solar protection soon becomes the

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norm, there is nothing that can be done to reverse the damage already done (3).

THE NATURE OF ULTRAVIOLET RADIATION

Solar ultraviolet (UV) radiation and visible radiation, which together comprise a very small part of the electromagnetic radiation spectrum, are energy released and transported from the source, usually the sun, as photons. Cutaneous photodamage occurs as the consequence of the disposal of these photons within the skin. UV radiation exposure varies according to altitude, geographic latitude, season, time of day, and proximity to snow or water (1,2).

The UV radiation from sun, which spans wavelengths from 100 to 400 nm, is divided into three wavebands: UVB (280-315 nm), UVA (315-400 nm), and UVC (100-280 nm) (2).

UVC radiation is heavily absorbed by molecular oxygen, ozone, and water vapor in the upper atmosphere and does not reach the terrestrial surface in measurable amounts. It is the most potent UV radiation in terms of damage it inflicts on living material (3).

UVA is adjacent to visible light and makes 95% of solar ultraviolet radiation. It is subdivided into two regions: short-wave UVA, or UVA II (320-340 nm), and long-wave UVA, or UVA I (340-400 nm) (1-3). UVA penetrates much deeper into the skin, contributes substantially to chronic sun damage, and can have immunologic effects. Longer wavelengths of UVA penetrate cloud cover, light clothing, and untinted glass relatively easily and thus may induce moderate continuing skin damage over longer periods, even when UV radiation exposure is not obvious (4). UVA is partially responsible for a sun-induced erythema (Morison). It is also called “long-wave UV radiation”, or “black-light”, because it cannot be seen (5,6).

UVB is the most important component of sunlight for human skin. Although it does not penetrate as deeply as UVA, nor does it interact as vigorously with the epidermis as UVC, UVB combines the depth of penetration and reactivity with macromolecules in a way that makes it biologically the most potent portion of the UV spectrum in terms of short- and long-term consequences (3). UVB is significantly attenuated by dense clouds, close-weave clothing, and window panes. Absorption and scattering in the atmosphere occur when the sun is low, at high latitude during the winter months, and in early summer mornings and evenings (4).

UVB is greatest in the summer, whereas UVA is more constant over the year (1). Eighty percent of UVB and 70% of UVA radiation occur between 10:00 a.m. and 2:00 p.m. (5).

Visible light (400-760 nm) probably plays an insignificant role in photodamage, as well as infrared radiation (760-1,700 nm) (4).

Solar radiation incident upon the Earth’s atmospheric envelope is either reflected or transmitted and attenuated (2) by gas molecules and water droplet scattering, ozone absorption, and oxygen absorption (1).

Thus, the major source of the damaging effects of sunlight is the UV portion of the spectrum between 290 and 400 nm (UVB and UVA). The different UV wavelengths penetrate the skin to different depths and have different biologic consequences (4).

PHOTOREACTIONS IN TISSUE

Solar radiation seems to cause two types of reaction – one is beneficial and the other is harmful. Photoreactions involving photosynthesis, vision, vitamin D synthesis, killing of pathogens, phototherapy, and photochemotherapy, are considered good and beneficial, but sunburn, skin cancer, drug- or chemically-induced phototoxic and photoallergic reactions and mutations are recognized as harmful (1,2).

Understanding light as photons that must be absorbed by molecules of tissue determines photobiologic responses. With the absorption of energy, a molecule reaches the excited state. The molecule that absorbs the energy from the photon is called chromophore, and the biologic process itself is determined by the energy of the photon and the characteristic wavelength of the UV radiation (1).

Our understanding of light-chromophore interaction in the skin is still incomplete. DNA is thought to be the principal skin chromophore; it can absorb

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and be mutated directly by UVB. Other endogenous chromophores that may absorb UV radiation include NADH/NADPH, triptophan, riboflavin, and melanin. Absorption of UVA radiation by these chromophores may lead to the release of reactive oxygen species, such as singlet oxygen, hydrogen peroxide, and superoxide anion. These reactive oxygen species may cause oxidation of lipids and proteins that, in turn, may affect DNA repair, induce matrix metalloproteinases, produce dyspigmentation, and result in skin photoaging and carcinogenesis (7). According to many authors, oxygenated free radicals play a significant role in skin aging and development of cancer as well as in inflammatory skin disorders, such as eczema and psoriasis (8). Antioxidant cellular systems resort to micronutrients, such as vitamins and oligoelements working through metalloenzymes, zinc and cuprum superoxide dismutase (Zn-Cu SOD), and selenium-glutathione peroxidase (Se-GSH Px) (9). However, in some diseases or following environmental stresses, these systems can be overloaded. In such situations, oxygenated species are liable to initiate chemical or structural modifications of protein, nucleic acids or membrane lipids leading to changes in the morphology and function of the cells (1,10).

Urocanic acid has been reported to be a chromophore for UVA I absorption (11). It is a derivative of histidine and produced by keratinocytes. The action spectrum for single oxygen generation after excitation of trans-urocanic acid is similar to the UVA action spectrum for photodamage in animal models. This suggests that UVA excitation of trans-urocanic acid may initiate changes that lead to photoaging of the skin (12,13).

Many immunologic assays have been used to measure UV-induced immune suppression, including tumor rejection, contact and delayed hypersensitivity responses, antibody production, and changes in the number and function of epidermal Langerhans' cells (6). However, UV directly affects the function of epidermal cells, including melanocytes and keratinocytes. Many of its effects are mediated via induction of soluble mediators. In addition to cytokines, neuropeptides are produced by many different cells, including epithelial and inflammatory cells, and are part of the network of mediators regulating immune and inflammatory reactions (1,10).

Keratinocytes have recently been shown to produce propiomelanocortin in addition to several other neuropeptides, such as substance P, vasointestinal peptide, calcitonin gene-related peptide. Propiomelanocortin is the precursor for adrenocorticotropin (ACTH), beta-endorphin (-E), beta-lipotropic hormone (-LPH), and melanocyte-stimulating hormones (-, -, and -MSH). The precursor of propiomelanocortin undergoes cleavage via proteolytic activities of the family of prohormone-converting enzymes, which have also been found to be expressed in keratinocytes (14). The immune system plays an important role in UV carcinogenesis by contributing to host resistance against tumor growth. Individuals sensitive to UVB-induced immunosuppression are at an increased risk of the development of skin cancer. Thus, both UV-induced DNA alteration and immune regulation are important for cutaneous carcinogenesis. UV radiation alters antigen-presenting cell function either directly by affecting epidermal Langerhans' cells or indirectly by inducing keratinocytes to release immunomodulatory cytokines (15).

THE REASONS FOR SKIN AGING – INTRINSIC AGING AND PHOTOAGING

There are two reasons for skin aging. One is natural aging, or intrinsic aging, which is a universal and inevitable process linked to our chronologic age (10). The other and most common reason for skin aging are external factors. Exposure to UV radiation is the greatest source of skin damage, while environmental pollutants, cigarette smoke, alcohol, and heavy metals all play significant roles (4,10).

Intrinsic aging

The chronological degenerative changes in the skin are genetically predetermined and steadily develop with time. Aging is the result of a genetic program. During cell mitosis, the enzyme DNA polymerase cannot replicate the final base pairs of each chromosome and the result is the shortening of the terminal portion of the chromosome after each cell division. Thus, critically short telomeres compromise the transcription and signal cellular senescence or apoptosis. Telomere shortening may thus be viewed as an internal "clock" that predetermines the functional lifespan of the cell (16).

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Clinically, chronologically aged skin appears dry, pale, and finely wrinkled, with a certain degree of laxity and a variety of benign neoplasms.

At tissue level, the changes resulting from chronologic aging occur in the dermis and epidermis. The most consistent and striking change of intrinsic cutaneous aging is flattening of the dermoepidermal junction, reflecting in part the reduction of the proliferative pool of keratinocytes that are located in rete ridges. Regarding the stratum corneum, neither average thickness nor its degree of compaction appear to change with age. The rate of formation of neutral lipids, those that contribute to the barrier function of the stratum corneum, is slower. Also, there is a progressive decrease in melanocyte density (2).

However, the main modifications due to chronologic aging occur in the dermis, the supportive element of the skin, a tissue responsible for the mechanical properties of the skin (12,13). The modifications take place in the extracellular matrix. These modifications alter the dermis architecture and thus the mechanical properties of the skin: rigidity, elasticity, and resilience. Such alterations to the extracellular matrix result in the formation of wrinkles (10).

So, the characteristic of intrinsic aging is epidermal thinning, and the opposite holds for photoaging, where the epidermis thickens in response to chronic stimulation (1,10).

Photoaging

Skin photodamage refers to the adverse cutaneous changes induced by exposure to UV radiation. Photoreactions lead to clinical, histologic, and biochemical changes (1). UVB radiation produces the most harmful effects. Acute adverse effects of UVB radiation include inflammation, sunburn, pigmentation changes, and hyperplasia. Chronic adverse effects of UVB include photoaging, immunosuppression, and photocarcinogenesis, including squamous cell, basal cell and melanoma skin cancers. UVB radiation is responsible for 98% of delayed erythema development (17). UVA radiation is also linked to acute and chronic skin injury. Acute damage produced by UVA includes erythema (to a much lesser extent than by UVB), photoallergic responses, and phototoxic reactions. Chronic UVA injuries include photoaging and photocarcinogenesis (1).

Apart from acute sunburn inflammation associated with secondary skin tanning, thickening, immunologic dysfunction, and vitamin D production, these changes have two distinct cumulative clinical manifestations: skin photoaging and skin cancer (10).

The propensity for solar damage depends upon the patient's skin type, the cumulative exposure to ultraviolet light, the intensity of exposure, and the years of exposure (1,10).

People with skin types 1 and 2 are most susceptible. A red-headed, blue-eyed, fair-skinned individual who burns and freckles easily is most probably at risk, but appearances are deceptive. Although dark-haired, brown-eyed, and olive-skinned people are usually exempt, it is their response to sunlight that matters. If they burn, their skin type may be 1 or 2, therefore, they belong to a high risk group. UV induced skin cancer does not occur in the Negro type of skin (type 5) (1).

The amount of exposure is important. The link between sunlight and skin cancer was first established in sailors. Thus, solar keratoses and squamous cell carcinoma occur as the result of chronic exposure and are commonest in those who spend a lot of time outdoors and whose skin is chronically weather-beaten (10). The intensity of exposure is also relevant. Thus, certain forms of malignant melanoma are most common in workers ensconced in their offices or factories most of the year, who intensely expose their white, non-tanned skin to the sun during vacation and often burn (5).

The timing of exposure may be important, since much of the damage may be done in childhood (3).

From the histologic point of view, UVB rays stimulate the division of cells, resulting in the epidermis becoming thicker and more leathery, lacking luster. Acanthosis is accompanied by cellular atypia, loss of polarity, and marked irregularities in cell size and staining properties. Various neoplastic alterations are observable, such as solar lentigines and early actinic keratoses. Melanin is accumulated on the surface of all new cells and acts as a parasol against sunlight. This response is what we call tanning (3,18).

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In normal aging, cells in the dermis become depleted. Hypocellularity is the rule. Fibroblasts are scanty and shrunken, and mast cells are more scattered. The metabolism of fibroblasts slows down with aging and their ability to synthesize extracellular matrix decreases, resulting in atrophy of the dermis. Simultaneously, the balance between elastase and collagenase enzymes and their inhibitors is disrupted, leading to modifications of the skin mechanical properties. One of the major histologic consequences is alteration of the elastic network, predominant papillary dermis. It not only thins down the dermoepidermal junction, but also contributes to the skin loss in elasticity and resilience (10).

This contrasts photoaging, in which fibroblasts are numerous and hyperplastic, mast cells abundant and partially degranulated, and histiocytes and other mononuclear cells also increased. One might say that the photoaged skin is chronically inflamed, a process called heliodermatitis (2).

While elastin increases in photoaged skin, collagen decreases. It is evidently solubilized by the enzymes produced by inflammatory cells, so that it practically disappears from most damaged areas. The formerly collagen-containing areas of actinically damaged dermis are now occupied mainly by elastic fibers and glycosaminoglycans (GAGs). In normal aging, collagen, far from disappearing, becomes more stable and resistant to enzymatic digestion, and its bundles become larger, forming rope-like structures (1,2,10).

Finally, actinic radiation is exceedingly damaging to the microcirculation. Many vessels become completely obliterated, and few that survive are variably dilated and scraggy; the normal horizontal plexuses are extinguished (2).

SKIN CANCER FORMATION

Skin cancers are among the most common of human cancers. It is now well established that the UV radiation components of sunlight provide a major contribution to skin tumor induction and development (10,19,20)

Actinic rays, especially in the sunburning range (280-320 nm) are carcinogenic. Human epidemiological and animal irradiation studies strongly suggest that chronic cutaneous UVB and, to a lesser extent, UVA exposure either to sunlight or to artificial sources, are responsible for the induction of most non-melanoma skin cancers, and probably of melanomas as well, although it has recently been suggested that UVA may play a relatively more important part in the latter (2). UVA efficiently penetrates the basal layer of the epidermis where the actively dividing cells reside. UV radiation acts by altering the DNA and also the cell functions involved in cell differentiation (6,21).

Photocarcinogenesis represents the sum of complex, simultaneous and sequential biochemical events that ultimately lead to the occurrence of skin cancer. The photons of sunlight begin a series of genetic events in the skin leading to cancer (19). These events, initiated by UV radiation of appropriate wavelength, include the formation of DNA photoproducts, DNA repair disturbances, mutation of proto-oncogenes and tumor suppressor genes, UV-production of radical species with subsequent effects on mutation and extra-nuclear function, and other epigenetic events that influence the course of carcinogenesis. The epigenetic influences may include immune responses, antioxidant defenses, and dietary factors (22).

Biologically, DNA appears to be the most important target of radiation-induced damage in the skin. When DNA molecule absorbs the photons of UV light, it reaches an excited state followed by rearrangement of electrons to form a photoproduct (23,24). The best described photoproducts are two dipyrimidine structures: cyclobutane dimers and 6-4 pyrimidine-pyrimidone adducts that result in single base-pair changes (or point mutations) in the genetic sequence following DNA repair. These two photoproducts comprise 95% of UV-induced lesions and are believed to be responsible for most of the carcinogenic effects of UV radiation (23,24). The cyclobutane (or pyrimidine) dimer is the predominant UV photoproduct, accounting for 85% of primary lesions in UV treated DNA (23-25). It is formed when UV photons are absorbed by the carbon-carbon double bond at the 5-6 position of two adjacent pyrimidines, and redistribution of electrons results in single bond ring closures between the two 5-positions and two 6-positions, giving rise to a pair of cyclobutane rings that are covalently linked (22). A clear relationship between the formation of pyrimidine dimers and carcinogenesis has been well es-

tablished in various animal studies (26) and cell culture systems (19) in which enzymatic repair of these lesions reduced the incidence of tumor formation. The 6-4-pyrimidine-pyrimidone adduct is the second most common UV photoproduct, accounting for 10% of UV-induced lesions (27). It is formed when absorption of UV photons causes reaction of the carbon-carbon double bond at pyrimidine 5-position with the carbon-nitrogen double bond of the adjacent 3'pyrimidine, and redistribution of electrons results in covalent linkage between the 6- and 4- positions of the respective pyrimidine. Both photoproducts lead to a mutation that is virtually pathognomonic for UV radiation, as well as to incomplete repair of cellular DNA damage, impaired function through mutation of the cutaneous cell cycle regulating intranuclear p53 protein, and possible alterations in immune surveillance (as apparently occur in exaggerated form in the skin cancer-prone disorder xeroderma pigmentosum). Other photoproducts include reactive oxygen species (7,8) and cytosine photohydrates and purine photoproducts (24,28), but these are less common and have not been well described (25).

In addition, other lesions including single-strand breaks, double-strand breaks (25), and DNA-protein crosslinks (26), can occur but these are usually irreparable and interfere with transcription and replication, resulting in cell death (21).

Mutations in the p53 tumor suppressor gene contribute to the development of human and mouse UV-induced skin cancers. Such mutations are also found in sun-damaged skin and actinic keratosis, suggesting that p53 mutations arise early during UV skin carcinogenesis. p 53 mutations can serve as a surrogate early biologic endpoint in skin cancer prevention studies (27). UVB has been shown to affect p16 expression, which impairs cell cycle regulation in vitro and in vivo. Altered expression patterns of p16/CDKN2A following UVB exposure could be of value for identifying people at an increased risk of UV-induced skin cancer (29).

Sunburn cell formation in the epidermis is a characteristic consequence of UV radiation exposure at doses around or above the minimum erythema dose. Sunburn cells have been identified morphologically and biologically as keratinocytes undergoing apoptosis. There is evidence that sunburn cell formation is a protective mechanism to eliminate cells at risk of malignant transformation (30). The level of DNA photodamage is a major determinant of sunburn cell induction by a process controlled by the tumor suppressor gene p 53. UV radiation triggers death receptors either by direct activation of these surface molecules or by inducing the release of their ligands, such as CD95 ligand or tumor necrosis factor. Induction of apoptosis in keratinocytes by UV light is a critical event in photocarcinogenesis. UV light directly stimulates CD95 and thereby activates CD95 pathway to induce apoptosis independently of the natural ligand CD95L. These findings further support the concept that UV light can affect targets at the plasma membrane, thereby even inducing apoptosis. UV radiation also interferes with skin homeostasis, which is maintained by a unique distribution pattern of apoptosis-inducing and apoptosis-preventing molecules (31).

Recently, it has been demonstrated that keratinocytes can release tumor necrosis factor-alfa (TNF-alfa), which is known to cause apoptosis in particular cells. In addition, it has been shown that UVB light induces the release of TNF-alpha by keratinocytes and that keratinocytes express the 55-kD receptor for TNF-alfa (32).

Oxidative stress also appears to be involved, probably via mitochondrial pathways, resulting in the release of cytochrome C. The sunburn cell with its pyknotic nucleus and eosinophilic cytoplasm is characteristic of mammalian epidermis after exposure to UVC and UVB radiation or UVA radiation in the presence of psoralens (30).

UV radiation modulates the immune system of the skin that is also important for tumor promotion. UVB and UVA radiation can induce DNA damage with the resulting squamous cell carcinoma and malignant melanoma by causing mutations as well as immunosuppressive effects that presumably contribute to photocarcinogenesis (20). UVB radiation-induced immunomodulation effects are limited to the epidermis, whereas UVA radiation affects both epidermal and dermal cell populations. In particular, UV radiation has been shown to affect the production of soluble mediators and expression of cell-surface receptors, and to induce apoptosis in pathogenetically relevant cells (32).

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PHOTOPROTECTION

There is overwhelming evidence that exposure of human skin to UV radiation leads to the development of cutaneous photoaging and neoplastic changes. This has led to the development of skin care products providing good protection against UVA radiation, associated with the high photoprotective level against UVB radiation (1,33). Protection from UV radiation is an important part of every program to prevent skin cancer (28). The measures that can be taken to diminish the risk of UV radiation exposure include: reduction through the limitation of sun exposure, through the use of appropriate clothing, and through the careful use of sunscreen products (4). So, during daily activities, an appropriate protection against solar exposure should prevent the clinical and cellular changes leading to photoaging, photoimmunosuppression, and eventually photocarcinogenesis (10).

Sun Exposure Habits

For people in developed countries, most consequences of UV radiation occur by short, multiple exposures of the hands, head, and neck (1). Sufficient recurring cutaneous sun exposure results in skin photoaging and in due course potentially in nonmelanoma skin cancers and perhaps melanoma in all individuals. Modification of this exposure by adjusting to the time of the day and year is likely to have a major impact in reducing these disorders. Clearly, encouraging good sun exposure habits in children at early age is particularly vital from the scientific standpoint, since adults have an established behavior pattern that is more difficult to alter (4).

Clothing As Sunscreen

Photoprotection with clothing is demonstrable in patients with severe dermatoheliosis on the exposed areas as compared with normal-appearing skin on the areas protected by clothing. Clothing remains an excellent means of sun protection. Cotton and polyester/cotton blends are equally effective. Lycra may block UV radiation 100% when lax, but if stretched, it is significantly less effective, with a calculated sun protection factor (SPF) 2. The color of fabric contributes to sun protection: dark colors provide greater sun protection than light ones. Hats and visors provide some protection for the head and neck. Glass filters UVB, but to block UVA radiation, protective coatings are needed. Glass treatment products are helpful adjuncts for patients with multiple skin cancers, transplanted patients with skin cancers, and patients with photosensitive dermatoses. To maximize sun protection using physical means, one should wear a hat with a large brim and clothing with sufficiently tight weaves, dark color, loose fit, and dryness. Shade devices, such as awnings or umbrellas, add further to sun protection, but even shade may contain 50% of ambient UV light. Care must be taken to avoid exposure to light-colored reflective surfaces, including sand, snow, and ice, to avoid reflected UV radiation (1).

Sunscreens

Sunscreens (SS) are UV radiation-absorbing chemicals that attenuate the amount and nature of UV radiation reaching viable cells in the skin. Chemical sunscreens have been shown to prevent UV induced sunburn, actinic keratosis, photoaging, and DNA damage. Sunscreen strategies are useful for protection against UVB and short-wave UVA, but complete protection against long-wave UVA has not been achieved. Their regular, appropriate, prophylactic application is an effective means to minimize the short- and long-term effects of UV radiation exposure. Absorbent products have traditionally been most popular; they act well against UVB and are cosmetically satisfactory. However, some users can develop cutaneous irritation and occasional contact or photocontact dermatitis to such products (34).

Efficacy of sunscreens is typically denoted by a sun protection factor (SPF). It is the ratio of the UV radiation exposure dose necessary to produce minimally detectable erythema in sunscreen protected skin compared with that of unprotected skin. The importance of sun protection in childhood cannot be overstated. It has been predicted that the use of an SPF 15 for the first 18 years of life can potentially reduce the risk of non-melanoma skin cancer by 78%. While photoaging would also presumably be reduced, since regular sunscreen use may reduce lifetime UV radiation exposure by 80%. Adults are more likely to use sunscreens than children, but their peak sun exposure years have already passed by adulthood and the visible signs of photoaging have already begun to appear (17).

Modern sunscreens and moisturizers containing sunscreens undergo massive premarketing toxicological and clinical assessment to determine their efficacy and safety. Major manufacturers provide products which have short- and long-term benefits in photoprotection (35).

There is increasing scientific evidence that people should use sunscreens prophylactically with adequate SPF (ICSS).

The presence of significant levels of UV radiation-induced molecular, cellular and extracellular damage (from single or repeated suberythematous UV radiation exposure) suggests that successful photoprotection from the chronic effects of solar exposure may require SPFs significantly greater than those necessary to prevent a minimal erythema dose (4).

Sunscreen use protects against most UV-induced non-melanoma skin cancer and actinic keratoses but its activity against malignant melanoma is not clear. More studies with broad-spectrum stable sunscreens and better models for the investigation of malignant melanoma are required (34).

Sunscreens can ensure variable protection but they cannot repair the UV-induced damage at the molecular level, which is the initiating event of the biological effects. The ultimate goal of photoprotection should be the suppression of photons to come in contact with the skin surface (17,34).

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Topical procedures, innovations, and mistreatments in dermatovenerology

Lokalna terapija, novosti i greške u liječenju u dermatovenerologiji

HISTORICAL SATELLITE SYMPOSIUM

VENERAL DISEASE: REALITY AND TABOO

FINAL PROGRAM AND BOOK OF ABSTRACTS

OCCASION ON 20 ANNIVERSARY DEATH OF ACADEMICIAN FRANJO KOGOJ

IN THE PALACE OF CROATIAN ACADEMY OF SCIENCES AND ARTS, ZAGREB,
MAY 28, 2003 AT 4.00 PM

HISTORICAL SATELLITE SYMPOSIUM

VENEREAL DISEASE: REALITY AND TABOO

ON THE 20th ANNIVERSARY OF DEATH OF ACADEMICIAN FRANJO KOGOJ

Palace of the Croatian Academy of Sciences and Arts, Zagreb,

May 28, 2003, at 4.00 p.m.

CROATIAN ACADEMY OF SCIENCES AND ARTS

DEPARTMENT OF MEDICAL SCIENCES

INSTITUTE OF HISTORY AND PHILOSOPHY OF SCIENCES

DIVISION OF HISTORY OF MEDICAL SCIENCES

CROATIAN SOCIETY FOR HISTORY OF MEDICINE OF THE CROATIAN MEDICAL ASSOCIATION

and

CROATIAN DERMATOVENEROLOGICAL SOCIETY OF THE CROATIAN MEDICAL ASSOCIATION

organize

Symposium with International Participation

VENEREAL DISEASE: REALITY AND TABOO

Investigations in venereal diseases surpass the limits of medicine and reveal the complexity in biology as much as in sociology and culture. The Symposium will place a special emphasis on multidisciplinary approach to the phenomenon of venereal diseases and demonstrate the intertwining of medical and cultural fabric, past as well as present. Contributions will be dedicated to the **memory of Academician Franjo Kogoj (1894-1983)**, the founder of dermatovenerology in Croatia, on the occasion of the 20th anniversary of his death.

Zagreb, Wednesday, May 28th, 2003

16.00 – 20.00

Palace of the Croatian Academy of Sciences and Arts Conference Hall

Trg Nikole Šubića Zrinjskog 11

Program

16.00 – 16.20 Welcome Reception

I. Venereal diseases: realities

16.20 -16.40 Michael Waugh (Leeds)

An historical study of why venerology and not dermatovenerology in Great Britain: an evolution

16.40 – 17.00 Marcia Ramos e Silva (Rio de Janeiro)

Facial and oral aspects of some venereal and tropical diseases

17.00 – 17.20 Mihael Skerlev (Zagreb)

The HPV genital infections – what do we really know, what can we really do?

17.20 – 17.40 Josip Begovac (Zagreb)

The success and failure in combating the HIV/AIDS epidemic

17.40 – 18.00 Discussion

18.00 – 18.20 Coffee break

II. Venereal diseases: Taboos

18.20 – 18.35 Aleksandar Štulhofer (Zagreb)

Recent research on sexual risk taking in Croatia

18.35 – 18.50 Marija Ana Dürrigl, Stella Fatović-Ferenčić (Zagreb)

The perilous love: silence on sexual matters in Croatian medieval writing

18.50–19.05 Amir Muzur, Ante Škrobonja (Rijeka)

The Skerlievo disease between myth and reality

19.00 - 19.10 Agata Maković (Zagreb)

AIDS in public journals in Croatia

19.10- 19.20 Mihael Mišir (Osijek)

AIDS in medical journals in Croatia

Discussion and concluding remarks

BOOK OF ABSTRACTS

OS1

WHY VENEREOLOGY RATHER THAN DERMATOVENEREOLOGY IN GREAT BRITAIN – AN EVOLUTION: A HISTORICAL STUDY

M. Waugh

Consultant Venereologist, Leeds General Infirmary, Leeds, UK

England, an off shore part of the British Isles, temperate in weather and not inclined to look to Continental Europe, has always had rather different traditions to the rest of Europe.

From the 16th to the 20th century, it was at war some of the time with Spain, France, Holland, and then the Central Powers. Today, it has a quaint relationship within the European Economic Community.

It built up the world's largest Empire by the end of the 19th century on piracy, envy of Spanish gold, trade, dislike of French imperialism, and Napoleonic centralisation: an envy and then, an understanding for Dutch business acumen, the loss of its American colonies, the rise of sugar production in the slave islands of the West Indies, the rise of the Industrial Revolution, the necessity of finding markets, the gaining of Empire, i.e., India, Australia, Canada, and New Zealand, and colonies all round the World backed by the financial acumen of the City of London and the British Navy.

England was therefore not really bound to follow European ways, and the British Isles, later the Empire, was not bound by European traditions.

Venereal diseases and especially knowledge on syphilis from the 16th century onwards were continental concerns and new ideas were often late into England. There is a multitude of records of the ravages of Morbus gallicus in England in the 16th century. However, the name *syphilis,* coined in 1530, had not come to England until 1686, when Nahum Tate translated Fracastor's work. The first medical writer was Daniel Turner, who wrote on syphilis in 1717.

Gonorrhoea, following the faulty teaching of Paracelsus, was thought to be part of the common venereal disease and ,as the poet Pope quotes in the 18th century, "time that at last matures a clap to a pox". John Hunter's scientific experiment that went wrong did not really help matters in that before Ricord, he considered gonorrhoea to be in common with syphilis as part of the venereal disease. Surgeons not known for intellectual curiosity looked after venereal diseases. They usually got their experience in the army or navy.

The amazing revolution and progress in 19th century Europe in microbiology and dermatology were in fact European first and taken up slowly in England.

What really startled the medical establishment were the scientific discoveries, *T.pallidum*, serology for syphilis, and the magic bullet of Ehrlich, Salvarsan. These were German discoveries, England was loosing out in the race.

Then along came the Royal Commission on the Venereal Diseases, which started to get evidence about the parlous state of the population with regard to venereal diseases from 1912 onwards. Since its report in 1917, the system of confidential and free countrywide STD Departments has first started to look after syphilis and gonorrhoea, only to become a separate specialty staffed by doctors with training in internal and genitourinary medicine looking after STDs and HIV/AIDS. Dermatovenereology in England lost out about 80 years ago, but dermatologists in many parts of the world now realise they have to do more public health medicine if they are to regain the confidence of their governments and ministries.

OS2

FACIAL AND ORAL ASPECTS OF SOME VENEREAL AND TROPICAL DISEASES

M. Ramos-e-Silva

Sector of Dermatology HUCFF-UFRJ and School of Medicine, Federal University of Rio de Janeiro, Brasil

Diseases of the tropical areas include some venereal diseases, which are still prevalent in some countries; Brazil is one of them. Some patients come from large cities like Rio de Janeiro. However, at the University Hospital of the Federal University of Rio de Janeiro, we also see patients who come from the interior of the State of Rio de Janeiro, or from other states, to seek medical care at better equipped hospitals for therapy of this type of condition.

Venereal and tropical dermatoses have many different cutaneous manifestations and may affect skin in several locations. The face is one of the affected areas, especially when the disease has a predilection for cartilage, oral and/or nasal mucosa.

Alterations observed on the facial skin and mucosa of the mouth of the following tropical diseases are presented and discussed: syphilis, donovanosis, leishmaniasis, paracoccidioidomycosis, leprosy, larva migrans, and myiasis.

OS3

THE HPV GENITAL INFECTIONS – WHAT WE REALLY KNOW, WHAT CAN WE REALLY DO?

M. Skerlev

Department of Dermatology and Venereology, Zagreb University Hospital Center and School of Medicine, Zagreb, Croatia

Sexually transmitted infections (STIs) are as old as human history. Anogenital *Human papillomavirus* (HPV) infections are most frequently diagnosed STIs of viral origin, and the HPV types associated with such lesions have been studied extensively over the last years. HPV-associated genital

pathology represents one of the major problems among STIs, mostly due to the high recurrence rate, difficult eradication, and oncogenic potential. Besides, the young, sexually active population in the generative period is mostly affected.

HPV genital infections are also among most frequent diagnoses in the Sexually Transmitted Diseases (STD) Outpatient Clinic of the Department of Dermatology and Venereology at Zagreb University School of Medicine. The frequency of HPV genital infections ranged from 125 patients in 1991 to 175 in 2002. Careful and friendly manner of taking medical history and performing clinical examination showed rather important to obtain the exact data. Clinical variations ranged from various types of genital warts to bizarre forms of giant condyloma of Buschke-Löwenstein type. In spite of the fundamental importance of the clinical examination itself, we wanted to identify the HPV DNA type in these lesions. Over the last few years, different diagnostic tools have been used in patients with HPV genital infection, including pathohistology and, in some cases, penoscopy. However, the results were not always precise enough to help us decide whether the lesion was HPV-induced or not. Thus, we wanted to evaluate the significance of viral tests (PCR, *in situ* hybridization) for anogenital warts in men. Hereby we present the results of HPV DNA detection and typing of biopsy specimens on the anogenital location in 100 men with HPV-induced, clinically visible lesions (condylomata acuminata, condylomata plana, and Buschke-Löwenstein). According to these results, HPV 16 and 18 can also be isolated from “benign" HPV-associated genital lesions more than it is usually expected. Therefore, the diagnostic approach to HPV genital infections needs to be complex, including HPV DNA typing whenever it seems appropriate.

Different methods for the treatment of genital warts are presented, such as cryotherapy, podophyllotoxin, curettage, and imiquimod (in the smaller group, as compared to other treatment modalities). So far, none of the treatments has been found clearly superior.

Over the last decades, the oncogenic properties of HPVs have been intensively studied, and a significant but pragmatically insufficient progress has been achieved, especially in the field of HPV diagnostics. Treatment should be provided in accordance with available resources, the experience of the provider, and the preference of the patient. Thus, the clinical approach to HPV genital infections, complex as it is, raises many questions regarding HPV genital infections, which remain to be answered.

OS4

THE SUCCESSES AND FAILURES IN COMBATING THE HIV/AIDS EPIDEMIC

J. Begovac

“Dr. Fran Mihaljević”University Hospital for Infectious Diseases, Zagreb, Croatia

New advances in basic and clinical research in human immunodeficiency virus (HIV) infection have had a dramatic impact on the HIV/AIDS epidemic in developed countries. HIV infection is no longer perceived as a progressive and fatal disease, it is now sought to be a treatable illness. New anti-HIV drugs given in potent combination regimens have demonstrated impressive efficacy in both clinical and laboratory terms, and have provided evidence that appropriate drugs can suppress HIV replication and disease manifestations. New techniques for measuring HIV RNA have been developed, which allowed more accurate and effective clinical management and shortened the time required to accumulate evidence for drug efficacy in a clinical trial. However, there is still no vaccine. In addition, benefits from recent advances are not available to the majority of HIV-infected people in the world. More than 95% of all HIV-infected people now live in developing countries and 95% of all deaths take place in developing countries. The world has now entered the third decade of the HIV/AIDS epidemic and the evidence of its impact is unprecedented. Wherever the epidemic has spread unchecked, it is now affecting the resources and capacities of countries upon which both human security and development depend. In some regions, HIV/AIDS, in combination with other crises, is driving ever-larger parts of nations towards poverty. Most of the time, the world stood silently by as HIV/AIDS swept through these countries. According to UNAIDS estimates, the HIV/AIDS epidemic claimed more than 3 million lives in 2002, and an estimated 5 million people acquired HIV infection in 2002 – bringing the number of people globally living with the virus to 42 million. By far the worst affected region, sub-Saharan Africa is now home to 29.4 million people with HIV/AIDS; approximately 3.5 million new infections occurred in 2002, while the epidemic claimed the lives of an estimated 2.4 million Africans. Ten million people aged 15–24 and almost 3 million children under 15 years of age are living with HIV. Only a tiny fraction of the millions of Africans in need of antiretroviral treatment actually receive it. Many millions are not receiving medicines to treat opportunistic infections, either. These figures reflect the world’s continuing failure, despite the progress made in recent years, to mount a response that matches the scale and severity of the global HIV/AIDS epidemic. In Eastern Europe and Central Asia, the number of people living with HIV in 2002 was 1.2 million. HIV/AIDS is expanding rapidly in the Baltic States, the Russian Federation, and several Central Asian republics. In Asia and the Pacific, 7.2 million people live with HIV. The growth of the epidemic in this region is largely caused by the growth of epidemic in China, where a million people live with HIV and official estimates foresee a manifold increase in that number over the next decade. There remains considerable potential for growth in India, too, where almost 4 million people live with HIV. In several countries experiencing the early stages of the epidemic, significant economic and social changes are giving rise to conditions and trends that favour the rapid spread of HIV, e.g., wide social disparities, limited access to basic services, and intensified migration. Best current projections suggest that an additional 45 million people will become infected with HIV in 126 low- and middle-income countries between 2002 and 2010—unless the world succeeds in mounting a drastically expanded, global prevention effort. It is now vital that HIV/AIDS-related activities become an integral part of world efforts to prevent and overcome the humanitar-

ian crises. Also, providing antiretrovirals to patients in developing countries should be a global humanitarian priority and failing in providing life-saving treatment to those mostly affected can not be justified.

OS5

SEXUAL RISK-TAKING RESEARCH AND ITS SOCIAL IMPACT: THE CASE OF CROATIA

A. Štulhofer

Associate Professor of Sociology, Zagreb University Philosophical Faculty, Zagreb, Croatia

A short history of sexual risk-taking research in Croatia and its social impact, particularly in terms of HIV/AIDS prevention campaigns and sex education programs, are presented. The early behavioral and attitudinal studies of adolescent sexuality carried out in the 1970s are discussed, followed by a detailed analysis of a number of studies published in the 1990s. The overview also includes the most recent RAR (rapid assessment and response) study of HIV/AIDS-related risk behaviors (2002).

The analysis of previous studies focuses primarily on their theoretical shortcomings and methodological limitations, suggesting steps necessary for improving future research in this area. Underdeveloped interdisciplinary cooperation remains a serious impediment to sexual risk-taking research.

The second part of the presentation offers a concise analysis of the (lack of) research related to social outcomes. Two cases will be elaborated: the enigmatic HIV/AIDS public campaign introduced in 1997 and a conspicuous non-existence of school-based sex education. In conclusion, a possible explanation is offered for the lack of ties and coordination between research and (sexuality related) health initiatives.

OS6

THE PERILOUS LOVE: SILENCE ON SEXUAL MATTERS IN CROATIAN MEDIEVAL WRITING

M.A. Dürrigl[1], S. Fatović-Ferenčić[2]

[1]Old Church Slavonic Institute and [2]Department for the History of Medicine of the Institute for the History and Philosophy of Sciences, Croatian Academy of Sciences and Arts, Zagreb

Medieval writers were not explicit and were often using rather "cryptic" and formulaic language in mentioning sexuality issues. Although there is always somehow a "caveat" for a person writing about sexuality, there is no absence on such issues in Croatian medieval texts. In the Middle Ages, human sexuality fell within the domains of physician, natural philosopher, moralist, and theologian. This paper sheds light on some aspects of sexuality based on evidence from Croatian Glagolitic medieval writing. Analyzing literature, i.e. works belonging to the genres of hagiography, *visions, exempla,* and the so-called *Miracles of Our Lady* from the 15th and early 16th century, we tried to pin-point their main characteristics and their relation to preserved medical compilations and setting, which articulated notions of *sex and punishment, body and spirit, disease and sin.* Although they belong to a completely different cultural sphere, they can be used as basis in understanding conceptual framework for research on stigma with a focus on health research and selected health problems for which stigma is a major concern.

OS7

THE SKERLIEVO DISEASE: BETWEEN MYTH AND REALITY

A. Muzur, A. Škrobonja

Rijeka University School of Medicine, Rijeka

At the end of the 18th century, the epidemic of an unknown disease broke up in Western Croatia. It was named "Skerlievo disease," after a village nearby the city of Rijeka. The illness was spreading quite rapidly and, at its peak, the number of diseased reached around 14.000. Dozens of papers, books, and dissertations were written about it all over Europe, trying to elucidate the nature and cause of the epidemic. By the end of the 19th century, the disease mostly disappeared, but the questions remained. In this brief overview, we intend not only to present the rise and fall of a curious illness (now generally accepted as endemic syphilis), but also of the rise and fall of fashionable diagnosing. Moreover, the story of the Skerlievo disease in numerous epidemiological, ethical, and popular aspects resembles the story of AIDS.

OS8

AIDS IN PUBLIC JOURNALS

A. Maković

"Merkur" University Hospital, Zagreb

The aim of this study was to investigate the topic of AIDS in Croatian public journals, since the day it was first noted until today. The study included 6 different journals published in Croatia. The year to begin with was 1978. Although AIDS has been known since the late 1970s, in Croatian media it was first mentioned in 1983. On June 29, 1983, *Vjesnik* brought highlights from the Belgian press. Although the disease became widespread in a very short time, there was not much information about it in our public journals until the 1984, when Robert Gallo and Luc Montagnier found a possible causative agent – a virus, which they named "a new retrovirus".

Show business, film industry, and famous movie stars were often used as a convincing and expressive medium in communicating messages in AIDS campaigns. Popular journals were another important vehicle for transferring the information. Their role was particularly important in spreading public health education messages and uncovering certain behavioral mechanisms, stigmas, and taboos in Croatia regarding AIDS. Although often sensational and inaccurate,

public journals were recognized as a good medium for public education, presentation of AIDS-related facts, and introduction of pertinent news.

*The investigation was carried out under the supervision of Assist. Prof. Stella Fatović-Ferenčić.

OS9

AIDS IN BIOMEDICAL JOURNALS IN CROATIA

M. Mišir

ER, Department of Emergency Medicine, Osijek

Appearing in the early 1980s, AIDS became one of the most threatening diseases of our time. It brought fear of stigmatization and drama, which could be easily compared to similar pandemics in past periods. Fear and traces of medical investigations on AIDS, ranging from surprise and helplessness to triumph, are noted in a large number of medical journals all over the world. This investigation dealt with traces that AIDS research has left on the pages of Croatian biomedical journals since the first appearance of AIDS until today.

The aim was to analyze the impact and transfer of international medical information on AIDS to Croatian medical journals, and to investigate the quality and structure of such information. The analysis included 25 Croatian biomedical journals, found in the libraries of Zagreb School of Medicine, *Andrija Štampar* Zagreb School of Public Health, Osijek University Hospital, and Zagreb School of Stomatology.

Most Croatian medical journals included in the analysis were a good source of quality information, which implies their important role in preparing medical community to AIDS in our country long before first patients appeared in our hospitals.

*The investigation was carried out under the supervision of Assist. Prof. Stella Fatović-Ferenčić.

Topical procedures, innovations, and mistreatments in dermatovenerology

Lokalna terapija, novosti i greške u liječenju u dermatovenerologiji

MEĐUNARODNI KONGRES
INTERNATIONAL CONGRESS

HOTEL JEZERO, PLITVICE / CROATIA
May 29-31, 2003
www.cybermed.hr/3dermkh

POD POKROVITELJSTVOM AKADEMIJE MEDICINSKIH ZNANOSTI HRVATSKE
UNDER THE AUSPICES OF THE CROATIAN ACADEMY OF MEDICAL SCIENCES

organizira organized by
HRVATSKO DERMATOVENEROLOŠKO DRUŠTVO HRVATSKOG LIJEČNIČKOG ZBORA
CROATIAN DERMATOVENEROLOGICAL SOCIETY OF THE CROATIAN MEDICAL ASSOCIATION

u suradnji s in cooperation with
INTERNACIONALNOM AKADEMIJOM ZA KOZMETIČKU DERMATOLOGIJU
THE INTERNATIONAL ACADEMY OF COSMETIC DERMATOLOGY IACD

Under the auspices of the Croatian Academy of Medical Sciences

International Congress

TOPICAL PROCEDURES, INNOVATIONS, AND MISTREATMENTS IN DERMATOVENEROLOGY

organized by

Croatian Dermatovenerological Society of the Croatian Medical Association

in cooperation with

The International Academy of Cosmetic Dermatology

IACD

Hotel Jezero, Plitvice/Croatia,

May 29-31, 2003

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Scientific Information:

The Scientific Program consists primarily of Plenary lectures and lectures, Satellite Symposia, Free Communications and Posters. The general theme of the Congress are highlights in local therapy in dermatovenerology. A number of distinguished scientists have been asked to present their lectures related to the main Congress topic. The time allotted for each presentation is 8-20 minutes.

Technical information for presentations:

Slide Reception/Preview Desk will be located near by Congress Hall

For presenters giving a lecture or oral presentation with slides, a slide reception and preview desk is available during the Congress hours. Speakers are kindly requested to hand in their slides at least one hour before the beginning of this session. Slides 5x5 cm must be fitted in the plastic frames. Specialized personnel will check the order of the slides together with the speaker, seal and label the carrousel and take it to the Meeting room. Double projection will be provided in all sessions. LCD projection will be provided in Congress hall.

If you are a Chairman

- Please be at your session room 10 minutes prior to commencement of the session. We would like to remind you that time allotted for presentation is:
- 15-20 minutes for plenary
- 8- 15 minutes for other lectures
- You are kindly requested to make sure that speakers strictly adhere to the time scheduled.

If you are Speaker

- Please be certain that the length to your lecture/oral presentation stays within the allotted time given in Scientific Program. We remind you that you should turn in your slides at least one hour before the commencement of the session. You must collect your slides from the slide reception immediately after the end of the session. Please follow the time schedule for your presentation.

Instructions for PC

- Congress Hall will be fully equipped with the necessary equipment for presentation through PC. Speakers are kindly requested to bring their diskette or CD Rom with their presentation.

Technical equipment:

- Single slide projection (carusell 24x36), double slide projection (carusell 24x36), overhead projection, LCD projection (PC Power Point).

Posters & Meeting Hall

- All posters will be on display for the entire duration of the Meeting. Each poster board is 1 meter wide x 1,50 meters high. Each board will be labeled with your poster presentation number, which is assigned to you (refer to your personal letter).
- Material for mounting posters (double-sided Scotch tape) will be available at the Congress Secretariat.

Poster mounting and removal schedule:

- Mounting: Thursday, May 29, 2003, between 8,00 - 19,00
- Removal: Saturday, May 31, 2003, between 16.00 - 18.00
- Poster Award for the best three posters, Saturday, May 31, 2003 at 17.00

SCIENTIFIC CONGRESS PROGRAM

Thursday, May 29, 2003.

14,00-20,00 Registration at the Registration Desk in front the Reception of the Hotel Jezero

Poster set up in the Exhibition area

Main hall hotel Jezero

17,30-17,45 Opening Ceremony in the Congress Hall

Welcome: J. Lipozenčić, President of the Croatian Dermatovenerology Society of the Croatian Medical Association and Congress President

Welcome: L. E. Millikan, Secretary and treasurer general of International Academy of Cosmetic Dermatology

17,45-18,00 Short video program on the National Park Plitvice on the occasion of the Opening Ceremony

18,00-19,00 PLENARY LECTURES

18,00-18,20 **I. Dobrić, S. Murat-Sušić:** Basic principles of local therapy in dermatovenerology

18,20-18,40 **H .P . M. Gollnik:** Pathogenesis and current global treatment strategies for acne - recommendations of the global alliance to improve outcomes in acne

18,40-19,00 **M. Ramos-e-Silva:** Ethnic skins and their management

19,00-20,00 Satellite symposium OKTAL PHARMA

Hair and scalp problems

V. Siboud: Androgenetic alopecia and hair follicle growth - an update

M. Skerlev: Microbiological background, pathogenesis and treatment of dandruff

Importance of cosmetic dermatology

A. Stanimirović: Cosmetic dermatology: instead of cosmetics or better of cosmetic

20,00-22,00 Welcome reception

Friday, May 30, 2003.

8,00-20,00 Registration at the Registration Desk in front the Reception of the Hotel Jezero

Main hall hotel Jezero

1. THE ROLE OF LOCAL TREATMENT IN DERMATOLOGY

09,00-10,45

Chairpersons: H. Nakayama, M. Ramos-e-Silva, R. Wolf, V. Milavec-Puretić

08,45-09,00 **V. Milavec-Puretić, I. Lakoš-Jukić:** Optimization of the topical therapy in dermatology

09,00-09,15 **S. Murat-Sušić, K. Husar:** Neonatal and infant skin care

09,15-09,30 **I. Nola, K. Kostović, L. Kotrulja, L. Lugović:** Emollients as sophisticated therapy in dermatology

09,30-09,50 **R. Wolf, H. Matz, E. Orion:** Sunscreens – the ultimate cosmetic

09,50-10,00 **J. Lipozenčić:** What's new in topical therapy?

10,00-10,15 **C. R. Celebi:** The project of consumer attitudes on cosmetic prodicts and applications in Balkanian countries

10,15-10,30 **M.Ramos-e-Silva:** Photoaging – myths and facts

10,30-10,45 **Discussion**

10,45-11,00 Coffee break

11,00-12,00 Satellite symposium SPIRIG

Extemporaneous prescriptions

M. Gloor: Update on extemporaneous prescriptions in dermatology

P. Huber: Quality management in extemporaneous prescriptions

12,00-14,00 Lunch time and poster viewing

2. THERAPY OF INFLAMMATORY SKIN DISEASES

14,00-16,00

Chairpersons:J. Ring, A. Pašić, G. Trevisan, J. Lipozenčić

14,00-14,20 **J. Ring, U. Darsow:** New approaches in treatment of atopic eczema

14.20-14.35 **I. Lawrance:** Tacrolimus ointment is safe and effective in the treatment of atopic dermatitis: Results of 2 large long term open label study in pediatric and adult patients

14,35-14,50 **F. Kokelj, G. Trevisan:** UV combined therapy in psoriasis

14,50-15,05 **V. Kuzmanovska, L. Biserkoska-Atanasovska:** A new combination in local treatment for psoriasis vulgaris

15,05-15,15 **P. Vržogić, A. Pašić, T. Podobnik-Takač, J. Lipozenčić:** Psoriasis vulgaris et arthritis psoriatica gravis mutilans – case report

15,15-15,30 **Z. Jukić, V. Barišić-Druško, I. Ručević, N. Šustić, D. Biljan, A. Ageel, R. Vukadin:** Local therapy of psoriasis vulgaris-historical review

15,30-15,45 **A. Pašić, R. Čeović, D. Hrsan:** The light in the treatment of dermatoses

15,45-16,00 **Discussion**

16,00-17,00 Satellite symposium VICHY

Improving our Knowledge of Healthy Skin: UV-Induced Skin Damage and Public Awareness of Photoprotection

I. Bartenjev: The importance of photoprotection

A. Bakija-Konsuo, Z. Bukvić-Mokos, M. Kaštelan, L. Prpić-Massari, I. Sjerobabski-Masnec, L. Stojanovič, B. Žgavec: Educating people about the harmful effects of the sun and the importance of photoprotection: Results of the “Sun Prevention Center” campaign

17,00-17,30 Coffee break

3. TREATMENT OF VIRAL, BACTERIAL AND PARASITIC DISEASES AND STD

17,30-19,00

Chairpersons: A. Horváth, A. Stary, M. Waugh, M.Šitum, V. Hegyi

17,30-17,50 **A. Horváth, K. Nagy:** Unusual cases of immunodermatologic diseases: retroviral background?

17,50-18,05 **M. Waugh:** Syphilis in Europe setting the scene

18,05-18,20 **R. Wolf, H. Matz, E. Orion: Scabies:** The diagnosis of atypical cases and their treatment

18,20-18,35 **A. Stary:** Antibiotic resistance in gonococcal infection

18,35-18,45 **M. Potočnik:** The efficiency of local treatment in genital lesions

18,45-19,00 **Discussion**

19,00-20,00 Satellite symposium BELUPO

Itrac 3 in Dermatology

M. Skerlev: The novel treatment strategies significance of Itraconazol

20,30 Gala Dinner with live music

Saturday, May 31, 2003.

Main hall hoteL Jezero

4. TREATMENTS AND MISTREATMENTS IN COSMETOLOGY

09,00-12,30

Chairpersons: H. P. M. Gollnik, A. Basta-Juzbašić, A. D. Katsambas, L. Oremović, F. Gruber

09,00-09,20 **H. Nakayama: Melasma:** Its causation and treatment

09,20-09,40 **A. D. Katsambas:** Topical corticosteroids old and new guidelines

09,40-09,55 **A. Basta-Juzbašić:** Pro et contra topical corticosteroids on the face

10,10-10,25 **L. Oremović, I. Sjerobabski Masnec, L. Lugović, G. Novak Bilić:** Cosmetics and acne vulgaris

10,25-10,40 **N. Arslanagić, R. Arslanagić:** Side effects of local glucocorticosteroids therapy on the skin of the face

10,40-11,00 **V. Hegyi, L. Hegyiva:** Laser in dermatology, past, present and future

11,00-11,10 **I. Sjerobabski Masnec, L. Oremović, L. Kotrulja, I. Nola, J. Meštrović-Štefekov:** Mistreatment in acne therapy – a case report

11,10-11,20 **N. Puizina-Ivić, T. Stipić, A. Čarija, S. Perić-Sušak, V. Gotovac:** Peelings of ageing skin: what's new?

11,20-11,35 **I. Bartenjev:** Laser in dermatology

11,35-11,50 **M. Šitum:** Approach to dermatosurgery in Croatia

11,50-12,10 **L .E. Millikan:** Surgical treatment-cosmetic

12,10-12,20 **S. Ljubojević, J. Lipozenčić, A. Basta-Juzbašić, V. Milavec-Puretić:** Contact sensitivity in facial dermatitis

12,20-12,30 **Discussion**

12,30-13,30 Satellite symposium URIAGE-Formasana

Atopic dermatitis and skin care

J. Lipozenčić: Etiopathogenesis of atopic dermatitis - the phenomenon of dry and irritable skin

S. Murat-Sušić: Treatment and skin care of patients with atopic dermatitis

S. Škrinjar: URIAGE products in skincare of dry and atopic skin

13,30-14,00 ANNUAL MEETING OF THE CROATIAN DERMATOVENEROLOGICAL SOCIETY

14,00-15,00 Lunch time and poster reviewing

15,00-16,00 Satellite symposium BEIERSDORF

New Scar Reducer Therapy

B. Marinović: Common scars and keloids

J. Lipozenčić: Hansaplast - scar reducer in prevention of keloids

5. TREATMENTS AND MISTREATMENTS IN DERMATOMYCOLOGY

16,00-17,00

Chairpersons: M.Skerlev, A.Prohić, V.Barišić-Druško, N.Arslanagić

16,00-16,20 **M. Skerlev:** The appropriate and inappropriate teatment of dermatomycoses

16,20-16,30 **A. Prohić, M. Kantor:** Tinea incognita caused by Trichophyton verrucosum

16,30-16,40 **J. Radoš, M. Skerlev, D. Celić, I. Dobrić:** What do we really know about tinea incognita ? – a case report

16,40-16,50 **D. Biljan, V. Barišić-Druško, Z. Jukić, N. Šustić, I. Ručević, R. Vukadin, A. Ageel:** Clinical experience with promogran

16,50-17,00 **Discussion**

17,00-17,15 M. Sijerčić, F. Gruber, M. Šitum: Poster award for the best three posters

17,15 J. Lipozenčić: Final Conclusion and Closing Ceremony

Closing Cocktail

Posters:

1. T. Batinac, J. Lipozenčić, G. Zamolo, F. Gruber, A. Stašić, M. Lenković: P53 and ki-67 in proliferative skin diseases
2. I. Kuljanac, E. Knežević, H. Cvitanović: Erythema annulare centrifugum (a case report)
3. I. Kuljanac, E. Knežević, H. Cvitanović: Lichen planus linearis – a case report
4. J. Lipozenčić, D. Bobek, V. Milavec-Puretić, J. Jakić-Razumović, A. Basta-Juzbašić, S. Ljubojević: Expression of CD30+ and CD45+ Ro in atopic dermatitis lesions
5. L. Lugović, J. Lipozenčić: Mixed and pure atopic dermatitis
6. I. Manola, S. Ljubojević, J. Lipozenčić, N. Pustišek: Naevus commedonicus – a case report and review of therapeutical approach
7. S. Simeonova, V. Lazarevic, L. Biserkoska-Anasovska, M. Nikolovska: Complications in tattooing with different aproaching in healing
8. M. Šitum, Ž. Bučan, S. Levanat: Gorlin's syndrome and therapeuthical possibilities
9. M. Šitum, Ž. Bučan, K. Kostović, D. Štulhofer Buzina: Congenital giant nevus- therapeutic approach
10. I.Vukšić, N. Puizina-Ivić, D. Marasović, D. Anđelinović, T. Stipić, D. Pezelj, G. Pavičić, V. Gotovac, A. Čarija, S. Perić-Sušak: The efficacy of table sugar in treatment of venous ulcers
11. K. Kostović, Ž. Bučan, I. Nola, N. Troskot: Vitiligo - new approaches in phototherapy
12. I. Ručević, V .Barišić-Druško, D. Biljan, Z. Jukić, N. Šustić, R. Vukadin, A. Ageel: Convatec in local therapy-case report
13. J. Meštrović-Štefekov, M.Šitum, B.Marinović, G.Novak-Bilić, L.Kotrulja, I.Nola: Therapeutic difficulties in diagnosis of pemphigus foliaceus
14. G.Novak-Bilić., M.Šitum, A.Soldo-Belic, J.Meštrović-Štefekov, L.Kotrulja, L.Lugović: Vasculitis with mutilation; part of leprosy clinical findings?
15. L. Kotrulja, L. Oremović, I. Sjerobabski Masnec, M. Šitum, M. Vurnek, Ž. Bučan, M. Tadinac Babić, N. Jokić Begić, R. Gregurek: Correlation between quality of life and psychological impact of patients in acne vulgaris
16. H. Cvitanović, E. Knežević, I. Kuljanac: Dermatomycoses in Karlovac county 1995-2002
17. J. Lipozenčić, S. Ljubojević, N. Pustišek, T. Batinac: Erythromelalgia provoked by influenca vaccine
18. A. Smeh-Skrbin, I. Dobrić, G. Krnjević-Pezić, P. Vržogić: Naphthalan in the treatment of patients with atopic dermatitis (neurodermitis)

AWARDS

On 111 General Assembly of the Croatian Medical Association (CMA) in Zagreb, February 22, 2003, the following active Members of CMA and Croatian Dermatovenerological Society were awarded:

Prof. Franjo Gruber for "Ladislav Rakovac";

Prof. Jasna Lipozenčić and **Prim. Aida Pašić, MD**, for "Diploma"; and

Bogumil Cezarović, MD for "Zahvalnica".

The Croatian Dermatovenerological Society of the Croatian Medical Association, Zagreb

and

"Naftalan" Special Hospital for Rehabilitation, Ivanić Grad, Croatia

organize

International Symposium

Current State on Psoriasis and Naphthalanotherapy

Ivanić Grad, Croatia

Main topics:

- New aspects in etiopathogenesis of psoriasis
- Immunohistopathologic diagnosis in prognosis of psoriasis
- Antiproliferative effect of naphthalan combined ultraviolet B (UVB) light and naphthalan therapy
- Other therapeutic options in treatment of psoriasis.

Contact:

Prof. Jasna Lipozenčić
Department of Dermatology and Venerology
Šalata 4
10000 Zagreb, Croatia
Tel/fax.: +385-1-4920-014
E-mail: *jasna.lipozencic@zg.tel.hr*

September 19, 2003.

Bus transportation from Zagreb to Ivanić Grad will be organized for all participants of the Symposium.

Continuing Medical Education Course on

Sexually Transmitted Diseases and Infections

Zagreb, Croatia

November 21-22, 2003

The Continuing Medical Education Course is organized by the Chair of Dermatovenerology, University School of Medicine Zagreb and the Croatian Dermatovenerological Society of the Croatian Medical Association **under the auspices of Academy of Medical Sciences of Croatia**.

There has been a resurgence of sexually transmitted infections (STIs) in all age groups, which makes diagnostic procedures in venerology ever more important. Great efforts are needed in service provision, health promotion, and research to identify the interventions most likely to succeed. The prevalence of the most frequent STIs will be discusses on the Course.

World known expert in the field of STIs, Prof. James Bingham will also participate in Course.

Contact:

Prof. Jasna Lipozenčić
Department of Dermatology and Venerology
Šalata 4
10000 Zagreb, Croatia
Tel/fax: +385-1-4920-014
E-mail: *jasna.lipozencic@zg.tel.hr*

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10th ANNIVERSARY OF THE CROATIAN DERMATOLOGICAL SOCIETY OF THE CROATIAN MEDICAL ASSOCIATION

AND

10th ANNIVERSARY OF THE FIRST PROFESSIONAL JOURNAL IN THE HISTORY OF THE CROATIAN DERMATOVENEROLOGISTS - *ACTA DERMATOVENEROLOGICA CROATICA*

July 10, 1992- July 10, 2002

It has been ten years since the foundation of the Croatian Dermatologic Society (CDS) of the Croatian Medical Association (CMA) and *Acta Dermatovenerologica Croatica (ADC)*, the first professional journal in the history of the Croatian dermatovenerologists.

To mark this occasion, on July 10, 2002, the Professional Board organized a celebratory meeting at the Department for Dermatology and Venerology of the Zagreb University Hospital Center and Zagreb University School of Medicine. The agenda ran as follows:

1. Reading the excerpts from the report published in *ADC* No 1, pages 3-4 and 37, on the foundation of the CDS-CMA and the foundation of the professional journal *ADC*. Dr. Mirna Bradamante, the youngest resident at our Department, read the texts;
2. Report by Dobrić I, Labar B, Pašić A, Skerlev M: "Graft-versus-Host Disease – Dermatological Aspects";
3. Prof. Dobrić personally congratulated Prof. Jasna Lipozenčić, the current Head of Croatian Dermatovenerological Society, and expressed his hopes for the continuation of the Society's successful work, as well as the success of the *ADC* journal.

At the end of the meeting, Prof. Dobrić read a fax by Prof. Mario Gligora from Rijeka who contributed greatly to the foundation of the CDS, but could not attend the meeting.

As it was agreed at the meeting, Prof. Dobrić would write a short article for *ADC* regarding this anniversary.

Our intention was not only to celebrate the anniversary, but also to remember these events of cultural significance. Ten years of *Acta Dermatovenerologica Croatica* have been very successful. The Journal, published in English and indexed in Index Medicus/MEDLINE and Excerpta Medica/EMBASE, with an international Board of Editors, is our contribution in terms of culture as well as in terms of developing cultural relations between our county and other countries in the world.

After the first ten years, we are facing the future determined not to give up.

Ines Lakoš-Jukić, MD

Professor Ivan Dobrić, MD, PhD

Emergency States in Allergology and Clinical Immunology in Dermatology and Venerology

A continuous medical education course "Emergency States in Allergology and Clinical Immunology in Dermatology and Venerology" for dermatovenerologists, residents in dermatology and venerology, and general practice specialists was held at the Zagreb University School of Medicine on October 25-26, 2002, under the auspices of the Academy of Medical Sciences of Croatia. The Course was organized by the Chair of Dermatology and Venerology, Zagreb University School of Medicine, and Croatian Dermatovenerological Society of the Croatian Medical Association.

The Course was attended by 115 physicians from Croatia, Bosnia and Herzegovina, and Slovenia. Professors Werner Aberer from Graz and Karl Holubar from Vienna were invited lecturers from abroad. The scientific program included lectures, seminars, moderated discussions, printed material, and conclusive questionnaire. The participants were introduced into the latest concepts in the etiology, pathogenesis, modified environmental factors, and particularly appropriate treatment of emergency states as well as prevention of allergic diseases. Considering the increasing incidence of allergic diseases, modern diagnostic methods and especially emergency therapeutic procedures were presented.

The following topics were covered: emergency states in dermatology and venerology; SSS *vs* toxic epidermal necrolysis; acute vasculitides; current approach to urticaria/angioedema and therapeutic procedure; bullous dermatoses; allergic reactions to insect stings and emergency intervention; acute manifestations of steroid dermatitis; current *in vitro* diagnosis of allergic diseases; the role of CAST-ELISA test in diagnosis and management of allergic diseases; new concepts in the diagnosis and treatment of atopic dermatitis; primary photodermatoses; testing for UV hypersensitivity; hereditary angioedema; infectious dermatoses – acute states and management; acute manifestations and treatment of medicamentous exanthemas; and specific immunotherapy.

The experts from particular fields presented novel concepts from the literature as well as their own results and recommendations for approach to and treatment of the aforementioned dermatologic conditions. The objective of the Course was to develop the algorithm for emergency states in dermatology and venerology. According to the questionnaire distributed to the participants at the end of the Course, the meeting was appraised as highly successful and useful. The next course, dedicated to sexually transmitted diseases, will be held on November 21-22, 2003.

The Croatian Dermatovenerological Society of the Croatian Medical Association takes active part in the continuous education of dermatologists and venerologists as one of the Course organizers.

The Chair of Dermatology and Venerology at Zagreb University School of Medicine devoted this year's Course to the 10th anniversary of both the Croatian Dermatovenerological Society and *Acta Dermatovenerologica Croatica*, the official journal of the Society.

Prof. Jasna Lipozenčić, MD, PhD

Course Director

President of the Croatian Society of Dermatovenerology

Head of the Chair of Dermatology and Venerology

Zagreb University School of Medicine

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2003;11(1):56-57

Melanoma Malignum – New Findings and the Coordination of Treatment Protocols

The Symposium on Coordination of Melanoma Malignum Treatment Protocols took place at "Dubrava" University Hospital in Zagreb, Croatia, on December 13, 2002, under the sponsorship of Croatian Society of Plastic, Reconstructive and Esthetics Surgery, Croatian Dermatovenerological Society of the Croatian Medical Association, and Croatian Medical Chamber. The symposium was organized by the Department for Plastic, Reconstructive and Esthetic Surgery, Dubrava University Hospital, and Department for Dermatovenerology, Sisters of Mercy University Hospital. The chairs were Sandra Stanec and Mirna Šitum.

The event was attended by a large number of physicians, specialists in dermatology, surgery, pathology, oncology, cytology, maxillofacial surgery, and ENT.

In their welcome speech, Prof. J. Lipozenčić, President of Croatian Dermatovenerological Society, and Prof. Z. Stanec, President of Croatian Society of Plastic, Reconstructive and Esthetic Surgery, emphasized the importance of multidisciplinary approach in the treatment of melanoma. Chairs of the Symposium, Mirna Šitum and Sandra Stanec, pointed out the increased incidence of this malignant tumor and the need for having a unique therapy protocol in all Clinical Centers.

The program was divided into morning and afternoon sessions, as follows:

- Epidemiology and etiology of melanoma malignum (Pašić A)
- Molecular biology of melanoma malignum (Levanat S)
- Pathohistological forms of melanoma malignum (Lambaša S)
- Problems in differential diagnosis of melanoma malignum (Krušlin B)
- Clinical findings, risk factors, and prevention of melanoma malignum (Šitum M)
- TNM classification and prognosis of melanoma malignum (Stanec Z)
- Surgical therapy of different stages of melanoma malignum (Unušić J)
- Sentinel lymph node biopsy (Stanec M)
- Melanoma malignum of the head and neck (Virag M)
- Therapy protocol in Slovenia (Arnež Z)
- Radiotherapy and chemotherapy of melanoma malignum (Šantek F)
- Immunotherapy and genetherapy of melanoma malignum (Đaković N)
- Local recidives – control of the patients with melanoma malignum (Nola I)

Each presentation was followed by an educative discussion, with specialists from various fields sharing their experience and presenting their cases. Colleagues from Slovenia also took an active part in the symposium, showing their results and experience in diagnostic methods and therapy of melanoma malignum.

A round table at the end of the meeting was attended by Stanec Z, Virag M, Arnež Z, Unušić J, Pašić A, Lambaša S, Krušlin B, Levanat S, Đaković N, and Šantek F. The purpose of the round table was to work up the protocol for melanoma malignum treatment according to the world standards. The discussion that developed was very fruitful and despite certain disagreements, the group eventually came up with the acceptable protocol. It still needs to be improved, though, as some questions remained unanswered. However, we believe that the participants will have the answers needed by the next meeting in 2003, when the protocol will be completed and, hopefully, introduced into practice soon afterwards.

Assistant Professor Mirna Šitum, MD, PhD

Co-organizer of the Symposium

Marko Polo´s Diary

Stella Fatović-Ferenčić, ESHDV representative of Croatia

On close neighbourhoods, on *Zlata Praha*, and green eyes

The complexity of skin, the largest body organ, kept me again in touch with the world this year. The terrorist attack on America occurred just before last year's Munich EADV Congress, and this year we were faced with general flood inundating vast areas of Central and Eastern Europe. Prague, the venue of our 2002 EADV meeting was badly overflown during the summer, but it did not stop the organisers of 11th Congress of the EADV to continue with preparations. Eastern countries were politically separated from the rest of Europe and the liberation after the collapse of Berlin wall started the chain of political changes in different parts of Eastern Europe. In Croatia, we experienced a war and paid for our liberty in blood and suffering. After the Velvet Revolution, Czechs started developing a rapid *return to Europe*, although they, like Croats, never really left it as far as their culture, history, and spirit were concerned.

11th EADV Congress, Prague, October 2-6, 2002

The EADV was a Western orientated dermatological society. The event in Prague was the first one that took place in one of the former Soviet block countries, the Czech Republic. Another remarkable fact, for the first time in the history of EADV, there was a lady president of the meeting – Jana Hercogova. During the 14th century, the Emperor and King Charles IV turned Prague much into a magnificent metropolis, the *Zlata Praha* of legendary fame, of people like Jan Hus and Jan Žižka, Antonín Dvořák, Leoš Janáček, and Franz Kafka. Prague got its university in 1348, 16 years before Krakow, or 17 years before Vienna. This *Alma mater Carolina Pragensis* hosted the participants of the 11th Congress EADV under the patronage of the Rector Magnificus. The Charles University medals were given at this occasion to prominent international dermatologists, as well as honorary memberships of the Czech Society of dermatology. A unique experience indeed, for all participants of this magnificent ceremony.

The History Day, as usual, began with meeting friends and colleagues and sightseeing. The excursion went onto the observatory tower of the Klementinum, the old Jesuit monastery and university. It was a beautiful sunny day. The sight of the golden hundred-towered city spreading before our eyes was worth every step of endless old stairway that took us all the way up to the top. After that, we crossed Charles Bridge and touched Saint Ioannes Nepomucenus Memorial, uttering wishes. Our meeting proceeded with the 3rd Alibert Oration delivered by Prof. Mauricio Goihman Yahr from Caracas, Venezuela and, of course, ended with a delicious lunch. When the joy of seeing new places and making acquaintances embraces me at different corners of the world, I completely forget that the history was too often a bloody matter, actually. I rather see it as a sequence of events, and in medicine, as a network of overt or hidden relations. These relations motivate competitions, ambitions, they inspire the intellect and work, and without them nothing would ever be the same. Dermatovenerology in Croatia, for example, was closely linked to dermatovenerology in Czechia. Suffice it to mention that Croatian pioneers in dermatology, Pavel Šavnik

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and Franjo Kogoj, were educated in Prague's clinics and students of Professor Šamberger.

During that stay in Prague, I was invited at the meeting of the Editorial Board JEADV. Jean-Paul Ortonne, Nice, took over editorial office of the journal from Torello Lotti, Florence. It was decided that henceforth there would be a new section in the JEADV – History of Medicine. Karl Holubar, Vienna, and me would be section editors.

Prague's EADV Congress, the first one held in Eastern Europe, was rather overwhelming, but emotions are usually those that move our spirit.

Upon my return to Zagreb, I was immediately swallowed by daily routine. The conference on *Tuberculosis, its past and present,* which I organised in the Croatian Academy of Sciences and Arts on October 10th fulfilled my expectations**:** more than a hundred people gathered to hear the lecturers.

In November I went to Vienna. The traditional *Jahrestagung* this year hosted Croatian dermatovenerologists, another step in getting closer to our closest neighbours. We are all looking forward to our country having no borders that separated us for more than half a century from our natural neighbours and to open ourselves to Europe.

The end of 2002 is approaching, perspectives regarding world peace are not optimistic. Wars are waged, bioterrorism is a common issue. In 2003, it would be 730 years since *Marko Polo was passing through what is now Afghanistan. He noted and described beautiful marble houses in Balkh one of the world's oldest cities, alas destroyed later.* Since then, particularly in last two decades, destruction has been very much a synonym for Afghanistan, and the Afghan refugee Sharbat Gula's eyes, like those of a threatened wild animal, are certainly the most moving and symbolic reflection of it. The green shine of these eyes and the reflection of fear in them are ingrained in my memory. Hardly any other message I ever saw urging the world to keep piece was so painful and striking.

ANNOUNCEMENTS

5th Symposium on Sexually Transmitted Diseases with international participation, Opatija, Croatia, April 14-16, 2003. Contact: Jasminka Blaha, "Dr. Fran Mihaljević" University Hospital for Infectious Diseases, Mirogojska 8, Zagreb; e-mail: *jblaha@bfm.hr*

Prague Dermatological Days, Prague, Czech Republic, April 25-26, 2003. Contact: Dr. Jana Hercogova, e-mail: *jana.hercogova@infmotol.cuni.cz*

IX International Congress Allergy, Asthma, Immunology and Global Network, Antalya, Turkey, April 27-30, 2003. Contact: *acicis@ibch.ru; http://www.isir.ru*

7th CSCC (Croatian Society of Cosmetic Chemists) Meeting 2003, Hvar, Croatia, May 7-10, 2003. Contact: Vera Sekulić, M. Gupca 2, Osijek, Croatia; e-mail: *vera.sekulic@saponia.hr*

3rd World Congress of the International Academy of Cosmetic Dermatology, Beijing, China, May 15-17, 2003. Contact: IACD2003 Secretariat, Chinese Medical Meetings International, 42 Dongsi Xidajie, Beijing 100710, China; e-mail: *lillian.lee@263.nrz; www.chinamed.com.cn/IACD*

14th Ljudevit Jurak International Symposium on Comparative Pathology, Zagreb, Croatia, June 6-7, 2003. Contact: Prof. Mladen Belicza, M.D., Ph.D., Department of Pathology, Sisters of Mercy University Hospital, Vinogradska cesta 29, 10000 Zagreb, Croatia; *www.kbms.hr/Jurak/symposium.htm*; e-mail: *juraks@kbsm.hr*

XXII Congress of the European Academy of Allergology and Clinical Immunology, Paris, France, June 7-11, 2003. Contact: Congrex Sweden AB, Attn: EAACI 2003, P.O. Box 5619, SE-11486 Stockholm, Sweden; e-mail: *eaaci2003@congrex.se, www.congrex.com/eaaci2003*

9th International Psoriasis Symposium, New York, USA, June 17-22, 2003. Contact: Skin Disease Education Foundation, 233 East Erie Street, Suite 700, Chicago, Illinois 60611; e-mail: *sdef@sdefmail.com; www.sdefderm.com*

Second Dermatology Update, National Skin Centre Singapore, Singapore, June 28-29, 2003. Contact: www.ilds.org

First World Congress on Work-Related and Environmental Allergy (1st WOREAL) & Fourth International Symposium on Irritant Contact Dermatitis, Helsinki, Finland, July 9-12, 2003. Contact: secretariat@woreal.org; www.woreal.org

International short course in dermoscopy, Graz, Austria, July 15-19, 2003. Contact: Lorenzo Cerroni, Department of Dermatology, University of Graz, Auenbruggerplatz 8, A-8036 Graz.

Summer Academy of Dermatopathology, Graz, Austria, July 21-25, 2003. Contact: Lorenzo Cerroni, Department of Dermatology, University of Graz, Auenbruggerplatz 8, A-8036 Graz.

15th Biennial Congress of the International Society for Sexually Transmitted Diseases Research (ISSTDR), Ottawa, Canada, July 27-30, 2003. Contact: 2003 ISSTDR Congress Secretariat, 251 Bank Street, Suite 401, Ottawa, Canada; e-mail: information@isstdr.org; www.confersense.ca

International Symposium on Atopic Dermatitis, Rome, Italy, August 29-31, 2003. Contact: Alberto Giannetti, giannett@unimore.it; Giampiero Girolomini, giro@idi.it

XVIII World Allergy Organization Congress ICACI, Vancuver, Canada, September 7-12, 2003. Contact: Sally Kolf, 611 East Wells Street, Milwaukee, WI 53202, USA; e-mail: congress@worldallergy.org; www.worldallergy.org

Current State on Psoriasis and Naphtalanotherapy, International Symposium organized by Croatian Dermatovenerological Society of the Croatian Medical Association and Special Hospital for Rehabilitation "Naftalan", Ivanić Grad, Croatia, September 19, 2003. Contact: Prof. Jasna Lipozenčić, Šalata 4, 10000 Zagreb, Croatia. Tel./Fax: +385-1-4920-014; e-mail: jasna.lipozenčić@zg.tel.hr

12th Congress of European Academy of Dermatology and Venerology, Barcelona, Spain, October 15-18, 2003. Contact: Unicongress, Calvet, 55, Baixos, 08021 Barcelona, Spain. *www.eadv.org*. E-mail: *eadv2003@unicongress.com*

6th Tergestinum Symposium on Psoriasis and 2nd Alpe Adria Meeting on Psoriasis, Bibione, Italy, November 7-8, 2003. Contact: Organizing Secretariat, Via San Nicolo 14, 34121 Trieste, Italy. Tel +39 40 368343, Fax: +39 40 368808

Sexually Transmitted Diseases and Infections, Continuing Medical Education Course organized by the Cahir of Dermatovenerology, Zagreb University School of Medicine and Croatian Dermatovenerological Society of the Croatian Medical Association, Šubićeva 9, 10000 Zagreb, Croatia, November 21-22, 2003. Contact: Prof. Jasna Lipozenčić, Šalata 4, 10000 Zagreb, Croatia. Tel./Fax: +385-1-4920-014; e-mail: *jasna.lipozenčić@zg.tel.hr*

9th Alple-Adria-Danube Congress of Sexually Transmitted Diseases and Infections of the Skin, Prague, November 27-30, 2003. Contact: *jana.hercogova@lfmotol.cuni.cz*

4th World Congress of IACD, Cairo, Egypt, April 12-18, 2004.

9th International Congress of Dermatology, Beijing, China, May 2004. Contact: ICD2004 Secretariat, Dept. of Foreign Relations, Chinese Medical Association, 42 Dongsi Xidajie, Beijing 100710, China. *www.chinamed.com.cn/dermatology.* E-mail: *ICD2004@chinamed.com.cn*

23rd Congress of the European Academy of Allergology and Clinical Immunology, Amsterdam, Netherlands, June 12-16, 2004. Contact: Dept. Allergology, University Hospital Rotterdam, dr. Molewaterplein 40, NL-3015 GD Rotterdam, The Netherlands. *www.congrex.com/eaaci2004.* E-mail: *degroot@algo.azr.nl*

X World Congress of Pediatric Dermatology, Rome, Italy, July 7-10, 2004. Contact: Triumph Congressi, Via Lucilio, 60, 00136 Rome, Italy; e-mail: *dermo@gruppotriumph.it, www.gruppotriumph.it*

American Academy of Dermatology, Academy '04, New York, USA, July 28-August 1, 2004.

13th Congress of the European Academy of Dermatology and Venerology, Florence, Italy, November 17-21, 2004. E-mail for contact: *president@eadv2004.org; info@eadv2004.org*

10th World Congress on Cancers of the Skin, Vienna, Austria, March 19-23, 2005. Contact: Elfriede Pomp, Department of Dermatology, University of Vienna, Vienna General Hospital, Waehringer Guertel 18-20, A-1090 Vienna. *www.wccs.at.* E-mail: *info@wccs.at*

6th World Congress on Melanoma, Vancouver, B.C., Canada, September 2-9, 2005. Contact: Venue West Conference Services Ltd., Vancouver, B.C., Canada; e-mail: *congress@venuewest.com*

INSTRUCTIONS TO AUTHORS

ACTA DERMATOVENEROLOGICA CROATICA (ADC) is a quarterly peer-reviewed journal, indexed in Index Medicus/MEDLINE and Excerpta Medica/EMBASE. It publishes original scientific articles, short scientific communications, clinical articles, case reports, reviews, reports, news and comments, and announcements in the fields of dermatology and venerology.

General Guidelines

Type the complete manuscript double-spaced, on one side of A4 bond paper, with a left side margin of at least 4 cm.

The manuscripts should not exceed 12-15 typed pages in case of original scientific papers, and 6-8 pages in case of short communications, clinical articles, case reports, and reviews.

The manuscripts should be written in English. The authors are responsible for ensuring that the English used is suitable for publication. All material is assumed to be submitted exclusively to this journal.

All manuscripts are subject to peer review.

Preparation of Manuscripts for Submission

Title Page

The title page should carry (a) the title of the paper, which should be concise but informative; (b) full name of each author, with institutional affiliation; (c) name(s) of department(s) and institution(s) to which the work should be attributed; (d) name and address (with telephone and fax numbers as well as the e-mail adress) of the author to whom requests for reprints should be addressed; (f) source(s) of support in the form of grants, equipment, drugs, or all of these; and (g) a short running head of not more than 40 characters (count letters and spaces) at the foot of the title page.

Second Page

The second page should carry a summary of not more than 250 words, followed by three to six key words from the Medical Subject Headings (MeSH) list of Index Medicus.

Manuscript

The text of observational and experimental is usually, but not necessarily, divided into sections with the headings Introduction, Material (Patients) and Methods, Results, and Discussion. Long articles may need subheadings within some sections to clarify their contents, especially Results and Discussion sections. Other types of articles, such as case reports, reviews, and editorials, are likely to need other format.

Abbreviated terms should be written in full the first time they are used in the text, with abbreviation in parentheses.

Underline the words that must be printed in italic.

References should be identified in the text by arabic numerals in parentheses, and be numbered and listed consecutively at the end of the manuscript in the order in which they are first cited in the text.

Indicate in the text where the illustrations (figures and tables) should be inserted.

Tables and figures should be provided each on a separate sheet of paper after the references. Descriptive legends to figures should be typed double-spaced on a separate sheet of paper, whereas figures should be submitted in an envelope, with the number, the name of the (first) author, and title of the manuscript on the back: each table should be typed on a separate sheet of paper, numbered in the order in which they are first cited in the text, with a title and descriptive legend. Terms used in tables should not be abbreviated.

Ethics

When reporting experiments on human subjects, indicate whether the procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) or with the Helsinki Declaration from 1975 as revised in 1983. Do not use patients, names, initials or hospital numbers, especially any illustrative material.

Statistics

Describe statistical methods and provide enough data to enable a knowledgeable reader to assess the reported results him or herself. Please state the statistical package (version, manufacturer) used for statistical analysis.

Acknowledgements

Please specify: (a) contributions that need acknowledging but do not justify authorship, such as general support by a departmental chairman; (b) acknowledgements of technical help; (c) acknowledgements of financial and material support, specifying the nature of support; (d) financial relationship that may be a source of conflict of in-

terest. Technical help should be acknowledged in a separate paragraph as well as other contributions.

References

References should be typed double-spaced on a separate sheet of paper. The Vancouver style, proposed by the International Committee of Medical Journal Editors, is used (Engl J Med 1991,324:421-8, BMJ 1991,302:338-41, or *www.icmje.org*) . Examples of correct forms of references are given below:

Journal article

Standard journal article (list all authors, but if their number exceeds six, give six followed by et al.)

You CH, Lee KY, Chey RY, Menguy R. Electrogastrographic study of patients with unexplained nausea, bloating and vomiting. Gastroenterology 1989;79:311-4.

Chapter in a book

Weinstein L, Swartz MN. Pathologic properties of invading microorganisms. In: Sodeman WA Jr, Sodeman WA, editors. Pathologic physiology: mechanisms of disease. Philadelphia: Saunders; 1974. p. 457-72.

Article not in English

Massone L, Borghi S, Pestarino A, Piccini R, Gambini C. Localisations palmaires purpuriques de la dermatite herpetiforme. Ann Dermatol Venerol 1987;114:1545-7.

Conference paper

Harley NH. Comparing radon daughter dosimetric and risk models. In: Gammage RB, Kaye SV, editors. Indoor air and human health. Proceedings of the Seventh Life Sciences Symposium; 1984 Oct 29-31; Knoxville (TN). Chelsea (MI):Lewis, 1985:69-78.

Disertation

Youssef NM. School adjustment of children with congenital heart diseases (dissertation). Pittsburgh (PA): University of Pittsburgh; 1988.

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