

## WHAT SHOULD BE USED AS TOOLS IN WOMEN AT RISK OF AUTOIMMUNE DISEASE?

Breast implants made of materials such as ivory, rubber, or ox cartilage have been used since the 19<sup>th</sup> century. After the 1940s, direct subcutaneous silicone injections were introduced, which caused serious complications (infections and migration to distant tissues). In the 1960s, a solid silicone envelope filled with silicone gel or saline was used. Escape of silicone from the envelope of these implants could be either intracapsular or extracapsular, penetrating through the fibrous capsule formed around the implant. In 1992, the US Food and Drug Administration decided that silicone gel-filled implants could only be used in women in clinical studies, for revision after unsatisfactory saline implantation, or after mastectomy for breast cancer. In contrast, these implants have been regularly used for cosmetic purpose in Europe. Autoimmune disorders in women with silicone implants were reported in the 1970s and 1980s, including systemic lupus erythematosus, scleroderma, rheumatoid arthritis and some rheumatologic conditions (1). Several studies examined the association between implants and the development of connective tissue disease (CTD), with a relative risk of 1.24 for CTD in women silicone breast implants (1-5). In Tel Aviv, five women with CTD who had silicone implants were treated for 18 months (1). These five cases covered a wide spectrum of CTDs in women who had silicone implants for periods of up to 25 years. Two of these five cases had other possible causes of their CTD, i.e. metastatic breast cancer in patients with dermatomyositis, or drug induction (high doses of paracetamol, met-amizole, ibuprofen). The diagnoses were: morphea, dermatomyositis, systemic sclerosis, chilblain lupus/vasculitis, and eosinophilic fasciitis. In patients with fibromyalgia it has been suggested

to be related to silicone implants (1). None of the patients wanted explanation.

Because of the multifactorial nature of most autoimmune disorders, women seeking breast implants should be screened for the known triggers for developing CTD. Until we have better diagnostic tools, the women at risk of autoimmune diseases should not be considered for implantation of silicone devices for cosmetic purpose.

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## CYCLOSPORINE IN CHRONIC IDIOPATHIC URTICARIA

The treatment of chronic idiopathic urticaria (CIU) is very difficult. According Vena GA *et al.*, cyclosporine (CsA) at a dosage of 5 mg/kg *per* day progressively reduced to 3 mg/kg *per* day in addition to background therapy with cetirizine during 8 weeks may be useful in the management of CIU. This multicenter study included 99 population recruited subjects in 18 Italian outpatient clinics, all of them adult patients suffering from several relapsing CIU episodes. Exclusion criteria were other concomitant forms of urticaria, any contraindication to cetirizine and CsA (Sandimum Neoral) and relevant systemic disorders. A 1-week run-in period with cetirizine, 10 mg/day, the patients entered a 16-week double-blind period of randomized treatment in addition to the background cetirizine therapy and were randomly allocated to one of three treatments: CsA for 16 weeks; CsA for 8 weeks followed by placebo for 8 weeks (8-week CsA), or placebo for 16 weeks. Sixty (60%) patients reported adverse events with fever in the placebo group (elevated serum creatinine increased in six patients receiving CsA). The Subject's Global Assessment of relief of symptoms and Dermatology Life Quality Index (DLQI) over 24-week post-randomization period proved the efficacy and point change in total score at 16 and 24 weeks. After 8 weeks, the severity score was significantly improved by CsA with relief of symptoms and improvement in DLQI scores with CsA compared with placebo (1). This study confirmed the clinical outcome in CIU with CsA as efficient therapy at 8 weeks, as also reported by Grattan *et al.* (2), Cassano *et al.* (3), Poon *et al.* (4), Thompson *et al.* (5), and Lennox and Leahy (6).

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## ESTABLISHMENT OF THE REFERENCE CENTER FOR DERMATOLOGIC ONCOLOGY OF THE MINISTRY OF HEALTH AND SOCIAL WELFARE

On the proposal of the National Health Council, the Ministry of Health and Social Welfare of the Republic of Croatia issued a decision effective as of June 30, 2006, appointing the University Department of Dermatology and Venereology, Zagreb University Hospital Center and Zagreb University School of Medicine, a Reference Center for Dermatologic Oncology of the Ministry of Health and Social Welfare (Reference Center for Dermatologic Oncology).

In recent years, considerable progress has been made in dermatologic oncology. The incidence of malignant skin tumors, melanoma in particular, then basal cell carcinoma and squamous cell carcinoma, has been on a constant increase worldwide, including Croatia. As Croatia is a Mediterranean country, this increasing trend poses a major public health problem. Thus, the Reference Center for Melanoma has already been established at University Department of Dermatology and Venereology, Sestre milosrdnice University Hospital.

The program of activities of the Reference Center for Dermatologic Oncology includes numerous actions in the field of dermatologic oncology related to non-melanoma malignant tumors and primary skin lymphomas. Exact data on the incidence of malignant epidermal tumors in Croatia are lacking; therefore, the Board on Dermatology and Venereology at Ministry of Health and Social Welfare has already established collaboration with the National Cancer Register. This collaboration has now been additionally encouraged and included in the regular activities of the Reference Center for Dermatologic Oncology. Processing of data on malignant epidermal tumors in Croatia is under way. Data have been collected from reports submitted by dermatologists, ENT specialists, surgeons and other specialists treating patients with malignant epidermal tumors, with special reference to promotion of team approach in the diagnosis and treatment of malignant epidermal tumors and primary skin lymphomas.

Attention will be especially focused on the early diagnosis of malignant epidermal tumors as a

major factor influencing therapeutic outcome and patient's quality of life. This can be successfully implemented at University Department of Dermatology and Venereology, Zagreb University Hospital Center, with properly equipped Laboratory of Skin Dermatologic Histopathology and Electron Microscopy Unit. Outpatient Clinic for Dermatologic Radiotherapy is part of the Reference Center of Dermatologic Oncology. It is an appropriate therapeutic modality for elderly patients with malignant epidermal tumors, recurrent or inoperable malignant epidermal tumors, and some primary skin lymphomas, mycosis fungoides in particular.

Photodynamic therapy as a treatment modality for precancerous lesions and some forms of basal cell carcinoma is also performed at the Center.

Current diagnosis and treatment of primary skin lymphomas is an important segment of dermatologic oncology. Clinical and histopathologic diagnosis has been developed at the Department for years, using a variety of modern methods of treatment for primary skin lymphomas. Efforts will be made to upgrade team approach in the field, to the benefit of our patients.

Nowadays, prevention of malignant skin tumors is an important task of every dermatologist/venereologist. The program of the Reference Center includes prevention actions, which are focused on the respective education of the population at large, with special reference to young population groups, on the methods of protection from sunlight exposure as a major factor in the etiology of malignant epidermal tumors. Special attention will be paid to secondary prevention, including early diagnosis and early therapy, which is closely associated with better prognosis.

Another aspect of the Center activities is education of dermatologists/venereologists in part serving their residency at the Reference Center for Dermatologic Oncology. In addition, mention should be made of the rich professional, scientific and publishing activities of the Center for Dermatologic Oncology.

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## ESTABLISHMENT OF THE REFERENCE CENTER FOR PHOTODERMATOLOGY OF THE MINISTRY OF HEALTH AND SOCIAL WELFARE

Upon the Ministry of Health and Social Welfare of the Republic of Croatia decision effective as of June 30, 2006, University Department of Dermatology and Venereology, Zagreb University Hospital Center and Zagreb University School of Medicine, has been appointed Reference Center for Photodermatology of the Ministry of Health and Social Welfare, thus recognizing our Department as the leading institution in the field of photodermatology in Croatia.

Many new diagnostic and therapeutic modalities in the field of photodermatology, e.g., phototherapy, photochemotherapy, phototesting, photodynamic therapy, and laser therapy, with the use of ultraviolet light (300-320 nm, 311±1 nm, 365 nm), visible light (400-700 nm) and laser light of various wavelengths, have been employed at the Department.

Outpatient Clinic for Phototherapy was established at University Department of Dermatology and Venereology in 1978, when the first unit for UVB and UVA therapy was purchased. Since then, the development of photodermatology and photomedicine at the international level has been closely followed. These activities have been intensified in the past decade. Currently, all modern phototherapy and photochemotherapy modalities, i.e. UVB, UVB 311 nm, UVA+UVB, PUVA, PUVA-bath, phototherapy of palmoplantar dermatoses, and phototherapy in children, have been successfully applied at the Department.

In 2003, the Unit for Laser in Corrective Dermatology was established to provide treatment for almost all indications for the use of laser in dermatology/venereology. The most important

advantages of laser therapy over other methods of treatment include selective removal of skin lesions, excellent tolerability, short-term treatment and favorable cosmetic effects.

In January 2004, local photodynamic therapy (PDT) was introduced at Department. PDT is a novel phototherapeutic modality that includes photochemical reactions with interaction of visible light, photosensitizing substances and oxygen. The aim of PDT is selective destruction of the target, abnormal cells while preserving normal ones.

Teaching activities for undergraduate students of the School of Medicine and postgraduate education for physicians of various specialties have for years been performed at Outpatient Clinic for Phototherapy. Work at Outpatient Clinic for Phototherapy is part of residency in dermatology/venereology. In addition, physicians and nurses working at phototherapy clinics established in Croatia to date have received respective training and education at our Department.

Besides work with patients, attention has also been paid to professional and scientific activities in the field of photodermatology.

The newly established Reference Center for Photodermatology of the Ministry of Health and Social Welfare will invest all efforts to upgrade therapeutic and diagnostic methods in the field of photodermatology, to continue providing education for professionals in the field of photodermatology, to engage in professional and scientific activities, and to publish the results achieved.

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