Report from the 60th Annual Meeting of the American Academy of Dermatology, New Orleans, February 22-27, 2002

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New Orleans, "the Great Big Easy", with a fascinating mixture of French, Spanish and southern US culture, was this year's host for the Congress. There were fewer participants than usual due to the tragic events of September 11, and this was also obvious from the last minute additions to the program: a symposium on Bioterrorism and Biodefence, which discussed anthrax, variola, plague and haemorrhagic fevers.

First a few general impressions: a) Computer projection is now more prevalent than old-fashioned slides, b) If a session was disturbed by a mobile phone, the owner could be fined 10 US$ and the money went to a summer camp for dermatologically handicapped children arranged by the AAD, c) Big pharma was very active on the television, with direct-to-consumer advertising about Lipitor, Nexium, Zoloft, Lamisil etc., even offering the first 6 pills for free when Viagra was prescribed!, d) Similarly serious-looking lawyers appeared on TV-adverts and asked patients to contact them if they had been treated with a few named medications ('…you may be entitled to money…'), and e) The sale of protective gloves has skyrocketed in the United States the last decade due to fear of hepatitis, AIDS, food poisoning and anthrax. Last year 27 billions gloves were sold for 3 billion US$ (50 gloves per American hand!). You can get dispensable gloves in all colours, with sun protection (!) and vitamin E (!) but unfortunately also containing latex – and latex allergy is becoming an ever growing problem in the USA

Fred Castrow MD was elected President for 2002. His motto is "The patient, first", which implies that a well-informed patient understands that a dermatologist provides better skin care than a gate-keeping GP paid by HMOs and with an economical incentive to treat diseases themselves rather than refer to organ specialists.

A sad reminder –on a global scale, 500 persons are infected with HIV every hour!

Topical macrolide immunomodulators: Both Protopic and Elidel are approved in the USA for use in atopic dermatitis in patients >2 years of age, Protopic for moderate–severe and Elidel for slight–moderate dermatitis. A topical steroid is still the first choice in atopic dermatitis. Protopic and Elidel will presently, according to the FDA, be second-hand modalities, and are only for short or intermittent use when conventional therapy is ineffective, causes side-effects or is considered unsuitable for some other reason. Both cause stinging/itch at the application site during the first days. None of them affects keratinocytes or fibroblasts, i.e. they don't provoke atrophy. In severe eczema, Eichenfeld recommends a start with a potent steroid and, when the disease is controlled, to try Protopic or Elidel in case of a relapse. Both are very expensive! There is still no published comparison between Protopic and Elidel. Since they cause immunosuppression in the skin in a cyclosporine-like fashion, and there has been photo-carcinogenesis following the use of cyclosporine in people with severely UV-damaged skin, this is a matter of great concern in the long-term follow-up. Protopic has been available longer than Elidel and has now been tried with impressive results in patients with severe oral lichen planus; this is however a chronic disease and most patients relapse following discontinuation.

Biologics: Patients with severe psoriasis have a profoundly reduced quality of life and are unsatisfied with their treatment. The new biologic remedies are only for those with a severe and probably lifelong psoriasis who are unresponsive to conventional therapy, including systemic agents. They are all very expensive. The '-mab' ending below means monoclonal antibody.

Inhibition of TNF-alfa: Almost all cells have receptors for TNF-alfa on their surface, and psoriatic lesions have an increased amount of TNF-alfa. Three main medications are presently available. A) Infliximab is a monoclonal IgG1-antibody against circulating and membrane-bound TNF-alfa and is ad-

ministered i.v. for 2 weeks, repeated after 2 and 6 weeks. It is approved for rheumatoid arthritis and Crohn's disease. In psoriasis: after 10 weeks, 80% were >75% improved and 48% were still so at week 26. It is not hepato- or nefrotoxic. Since latent pulmonary tuberculosis may be reactivated, skin tuberculin test and chest X-ray were recommended before therapy. Price: 12,000 US$ annually. A few patients with hidradenitis chronica suppurativa have also responded. B) Etanercept is a fusion protein between the extracellular part of the TNF-alfa receptor and recombinant Fc-portion of IgG1. It is administered subcutaneously twice a week (the patients can inject themselves). Approved by the FDA for psoriatic arthropathy, the improvement is fast and dramatic. Contrary to methotrexate, etanercept seems to prevent progressive cartilage destruction. Psoriatic skin lesions respond more slowly: a reduction of PASI scores >75% in 30% of patients after 12 weeks and in 56% after 24 weeks. According to Lebwohl, a minimum of laboratory monitoring is required during therapy. Etanercept has also yielded good results in a patient with severe cicatricial pemphigoid. C) Alefacept: a fusion protein between LFA-3 (which binds to CD2 on the T cell surface) and the Fc portion of IgG1. It inhibits activation and proliferation of T cells and stimulates the apoptosis of CD45RO+ cells, which constitute the major part of lesional T cells and mediate disease activity. Administered i.v. or i.m. Not yet approved by the FDA for monotherapy of psoriasis. It is suggested to be a remittive therapy: with 15 mg weekly during 12 weeks, 24% became clear or almost clear and the remission could last 5–17 months. The patients cannot inject themselves. Monitoring required: lymphocyte counts and CD4+ cells.

Which patients with psoriasis should be the first to be considered for 'biologics'? Lebwohl suggests it should be patients who are on cyclosporine now and those with psoriatic arthropathy who are being treated with methotrexate (which does not prevent the progressive destruction of articular cartilage).

There are more 'biologics' already in clinical use or in the drug companies' pipelines awaiting clinical trials or FDA approval. Among the indications are mycosis fungoides, CD20+ B-cell non-Hodgkin lymphoma, head and neck cancer, allergic asthma and allergic rhinoconjunctivitis.

Isotretinoin: Lookingbill recommends an onset of 0.5 mg/kg/day for 4 weeks and then an increase according to each patient's tolerance up to a maximum of 1 mg/kg/day, with the cumulative dose >120 mg/kg (to prevent the severe acne flare-ups occasionally seen when a nodulocystic acne is started on 1 mg/kg/day). Many of us probably already do this, in accordance with the guidelines from one of the world's leading 'acneologists,' Bill Cunliffe. 250,000 fertile women with acne were treated with isotretinoin in the USA in the year 2000, and 150 became pregnant during therapy. Surprisingly 90% of the latter were treated by dermatologists! The FDA started serious discussions with the manufacturer, Roche, which resulted in more stringent rules, called SMART (system to manage Accutane related teratogenicity). They include: 2 pregnancy tests before therapy, with the last during the first 5 days of the next menstruation; a new test each month; 2 different anticonception modalities to be used one month before, during and one month after therapy; a special consent form to be signed; the dermatologist can take the responsibility for these measures or the patient can be referred to a gynaecologist (paid for by Roche); when all this has been done, the doctor puts a special yellow SMART sticker on the prescription, which allows the pharmacist to deliver isotretinoin pills for 30 days. The patient must return to the doctor after one month for a new pregnancy test, another prescription with the yellow sticker etc. In addition, all female patients are requested to report to a special epidemiological registry for fertile women (they get 10 US$ when they do).

Depression, suicide: It was headline news when a 17-year-old boy,the son of a USA congressman, shot himself. He had been on isotretinoin for several months. The congressman has since worked hard to forbid isotretinoin (but not shotguns in homes?). Suicide is the No. 3 leading cause of death in American teenagers, 11.4/100,000, and the corresponding figure for isotretinoin-treated is 1.8/100,000. Depression is also common among teenagers, some of the causes are said to be alcohol, drug abuse, relation problems, etc. There was no increase of depression

in published comparisons between groups of isotretinoin–treated youths and untreated control subjects. There are however about 25 cases of depression reported to the FDA describing onset during therapy, improvement upon discontinuation and relapse when isotretinoin was reintroduced. This is no proof, considering that >4 million people have been treated in the USA during the last 20 years, but the latter cases are still disturbing. Cunliffe and Schwayder speculate that there may be a few, rare persons who metabolize isotretinoin differently. Until more is known, it was recommended that candidates for isotretinoin be carefully informed not only about the risk for mood shifts and depression, but that they must sign a special consent leaflet. The doctor should watch for signs of depressions at each visit.

Community-derived skin infections due to MRSA are now seen more frequently. The most common presentations are as abscesses, cellulitis, impetigo and infected atopic eczema. These were previously seen mostly in children with kidney transplants, but the last 10 years in children without such risk factors as well. The cause is presumed to be the ever-increasing use of antibiotics. The hospital-acquired MRSAs are multiresistant and a few strains even vancomycin-resistant. However the community-acquired skin infections are sensitive to clindamycin and sulphonamides. In a Florida study of children with impetigo, 153 of 170 of the kids were culture-positive for Staph. aureus and 12% of the Staph. cultures consisted of MRSAs!

Subacute cutaneous LE: Callen presented an elegant review: There is a lack of randomized controlled trials, but he suggested the following as standard treatment: a) triggering drugs? Most commonly hydrochlorotiazide, terbinafin, calcium channel blockers, b) the clinical efficacy of chloroquine is reduced in smokers, c) camouflage: wig, make-up, d) sunscreen: a combination of common sense, protective clothing and broad-spectrum sunscreens, e) chloroquine or hydroxichloroquine (Callen prefers the latter, refers to lower toxicity), f) if a–e are not sufficient, he suggests thalidomide, g) if thalidomide also ineffective, he suggests gold (auranofin) or dapsone (particularly in bullous LE).

Quo vadis, dermatology? Klaus Wolff was a guest lecturer. He spoke of how health care reforms in plain language mean that money must be saved, and dermatology and its patients risks being on the losing end when life-threatening diseases come first and there is less interest (verbally yes, financially no) in quality-of-life aspects. He painted a future scenario where oral immunomodulators control psoriasis and atopic eczema so these diseases can be treated by GPs, effective screening and early diagnosis of skin cancers reduce cutaneous oncology to simple excisions, autoimmune diseases are more and more taken over by internists and immunologists, and genetic diseases go to molecular genetics. What is left for the dermatologist to take care of: seborrhoeic dermatitis, pityriasis rosea and hand eczema? Life-style corrections, e.g. eliminating wrinkles and furrows, inject a little here and there, remove excess skin etc., requires less training than to become a clinical dermatologist but generates more money. Wolff suspects these aspects will increase at the expense of clinical dermatology and academic research. He urges us to fight back: we should strive for excellence in dermatology and widen our interest and knowledge in clinical fields bordering on dermatology (he coined the word 'skinternists'). To sum up, dermatology, in Wolff's opinion, should be at the forefront of quality-of-life medicine based on science, not primarily a life-style medicine.

It is always a vitalizing experience to join our American colleagues, to learn and to share experiences. Let's hope that next year's meeting in San Francisco, on March 21–26, will not be affected by more politically tragic events. Looking forward to seeing you there!