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# Journal Watch

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## Treatment of infantile haemangioma with captopril

Tan ST, Itinteang T, Day DJ, O'Donnell C, Mathy JA, Leadbitter P.
Br J Dermatol 2012;167:619-24.

This open-labelled observational clinical trial was carried out in New Zealand to investigate the use of captopril in the treatment of problematic proliferating infantile haemangioma (IH). There were recent evidence showing the endothelium of proliferating IH had expression of constituents of rennin-angiotensin system (RAS). Therefore therapy to alter the RAS may provide another mode of targeted therapy against proliferating IH.

Infants referred to the relevant Vascular Anomalies Centre with problematic proliferating IH were recruited. Following initial baseline cardiovascular investigation for structural cardiac anomalies and renal function screening, the study subjects were admitted to hospital and a test dose of 0.1 mg/kg captopril was administered orally to study subjects with close monitoring of cardiovascular parameters. Captopril was then started at 0.15 mg/kg 8 hourly. Captopril further increased to 0.3 mg/kg 8 hourly on second day. The renal function was checked 2 days after initiation of therapy prior to discharge. The maximum dose of 0.5 mg/kg 8-hourly was given 1 week later if there was no significant involution of IH noted. Escalation of the dosage was ceased if any adverse effect or visible shrinkage of the IH was observed. Captopril was ceased if IH had completely involuted and/or when the child had reached 14 months of age. The response of IH to captopril was documented clinically and photographically.

Two boys and six girls aged 5-22 weeks with problematic proliferating IHs were included in the study. All subjects could tolerate the maximal dose of 0.5 mg/kg per dose 8-hourly. A 'dramatic response' was observed in three, 'moderate response' in two and 'slow response' in three subjects. The five subjects presented with ulcerative IH had healing of the ulcerated lesions within 2-3 weeks after therapy. The involution of IH continued during the follow-up period of 8-19 months in all subjects. In seven patients, treatment was ceased at 14 months of age and no recurrent growth observed. The authors concluded that the observed accelerated involution of problematic proliferating IH induced by captopril confirmed a significant role for the renin-angiotensin system in IH proliferation and involution and suggested further investigations with angiotensin converting enzyme inhibitor and angiotensin-II receptor antagonist may result in new treatments for challenging IH.

## Efficacy and safety of biologics in erythrodermic psoriasis: a multicentre, retrospective study

Viguier M, Pages C, Aubin F, Delaporte E, Descamps V, Lok C, et al and for the Groupe Francais de Recherche sur le Psoriasis
Br J Dermatol 2012;167:417-23.

This multicentre retrospective study was conducted between 2004 and 2009 in nine French dermatology hospitals to address the efficacy and safety of biologic therapies (BTs) in patients with erythrodermic psoriasis (EP). Patients who had EP with severity assessed by Psoriasis Area and Severity Index (PASI) or body surface area (BSA) before and after 3 and/or 6 months of treatment with biologics were included. Twenty-eight patients in nine different centres were included in the study period. Forty-two EP episodes treated with BTs were finally analyzed because nine had received several

courses of BTs: 37 with TNF-α blockers (infliximab: 24, adalimumab: 7, etanercept: 6), three with ustekinumab and two with efalizumab. The efficacy of BTs was assessed by a 75% improvement in PASI and or in BSA severity score after treatment. A third of the patients treated with infliximab showed a 75% improvement after 4 weeks and 48% of patients reached a clinical improvement of PASI 75 at 14 weeks. PASI 75 was observed in patients receiving adalimumab (50%) as well as in those receiving etanercept (40%) after 12-14 weeks. Overall, 42% of patients with erythrodermic psoriasis reached a 75% improvement 10-14 weeks after starting BTs. In the fourteen adverse events observed, twelve were considered serious adverse events (SAEs) in which consisting of bacterial infection in seven of them. One case of fatal septic shock was observed. Other SAEs include lymphoma (n=1), myocardial infarction (n=1), severe depression (n=1) and anaphylactic shock (n=1). BTs was withdrawn in 69% of cases due to adverse effects. The authors thus concluded that biologics were useful for the treatment of erythrodermic psoriasis and safety concern for infectious complications, remain the most important area when considering continuation or termination of therapy. This study is limited by the small sample size and retrospective nature.

## Oral immunotherapy for treatment of egg allergy in children

Burks WA, Jones SM, Wood RA, Fleischer DM, Sicherer SH, Lindblad RW, et al.
N Engl J Med 2012;367:233-43.

Food allergy to egg in the United States carries a cumulative prevalence of 2.6%, with allergic symptoms ranging from mild urticaria to systemic anaphylaxis. Dietary avoidance is the only approved treatment. Traditional subcutaneous immunotherapy is considered effective against certain aeroallergens but unsafe for treatment of food allergy. Oral immunotherapy has previously been evaluated to desensitize patients allergic to milk, peanut and egg. However, a sustained immune tolerance after discontinuation of oral immunotherapy was not evaluated. The following study aimed to evaluate sustained unresponsiveness in children after oral immunotherapy with egg-white powder.

A double-blind, randomised, placebo-controlled study involving 55 children of age 5-11 years with egg allergy was carried out from five centers in the United States. Forty children received oral immunotherapy of egg-white powder and 13 received placebo, following a protocol of initial dose-escalation, build-up and maintenance phase of up to 2 g of egg-white powder per day for 10 months. An oral food challenge test with 5g egg white-powder was done at 10 months, in which none of the placebo-treated group and 55% of the oral immunotherapy group passed. Those that passed clinically (no untoward reaction) and serologically (decreased wheal size on skin-prick test, decreased basophil activation and lowered egg-specific IgG4 antibody levels) were considered to be successfully desensitized. All participants were given placebo powder till 22 months, when a second food challenge test was performed, which resulted in desensitization of 75% of the oral-immunotherapy group. At 24 months, 28% of the children in oral-immunotherapy group passed another food challenge test and were considered to have sustained unresponsiveness. They continued to consume egg ad libitum (powder or cooked egg) till 36 months without clinically significant symptoms.

About 13% of children withdrew before first food challenge test at 10 months due to mild allergic reactions and anxiety reaction. No severe adverse events occurred but 25% of oral immunotherapy group experienced mild oral or pharyngeal symptoms while only 4% of placebo group suffered from adverse events. The rates of adverse events were noted to be highest during the first 10 months of oral immunotherapy.

The above study showed that a carefully-monitored oral immunotherapy can desensitize a high proportion of children with egg allergy (55%), which was therapeutically beneficial as it offered protection against allergic reaction to accidental exposure. It also showed that it could induce sustained unresponsiveness up to 36 months in a

clinical subset (28%), which was more desirable as successful incorporation of egg in diet. The authors concluded that oral immunotherapy might be a promising therapeutic intervention for food allergy. This study is limited by the small sample size.

## Re-evaluation of serological criteria for early syphilis treatment efficacy: progression to neurosyphilis despite therapy

Zhou P, Gu X, Lu H, Guan Z, Qian Y.
Sex Transm Infect 2012;88:342-5.

Nowadays, there is no effective way to assess the microbiological cure of secondary syphilis after treatment. Most authorities use clearing of clinical lesions and the 4-fold decrease in non-treponemal antibody titres to assess the effectiveness of treatment. US CDC recommends to undergo cerebrospinal fluid(CSF) examination after completed the treatment of early syphilis if patients (1) persist or recur of neuropsychiatric symptoms or signs; (2) a sustained 4-fold increase of non-treponemal antibody titres or (3) non-treponemal antibody titres do not fall by 4-fold 6 months after treatment. However, in some patients, 4-fold decrease in non-treponemal antibody titres may not predict the success of treatment since the titres may decrease even without treatment. Thus, the aim of this study is to study the cases of secondary syphilis (SS) progressed to neurosyphilis (NS) despite appropriate treatment and whose rapid plasma reagin (RPR) titres decreased 4-fold within 6 months but did not revert to negative within 24 months.

Secondary syphilis was diagnosed by (1) reactive serum RPR with reactive Treponema pallidum particle agglutination assay (TPPA) and (2) classical SS skin or mucocutaneous lesions. The patients should also fulfil the following criteria during May 2000 to April 2010: (1) serum RPR titres decreased 4-fold within 3 months but failed to revert to negative at least 24 months after treatment; (2) no history of high risk behaviours following initial syphilis treatment; (3) negative HIV test and (4) fulfilling the diagnostic criteria of NS.

Lumber puncture was performed if patient had neuropsychiatric symptoms and signs or those with serofast state of RPR more than 24 months after treatment. The diagnostic criteria of NS included: (1) reactive CSF VDRL and TPPA in absence of substantial contamination of CSF with blood; (2) with or without elevated CSF white blood cells; (3) with or without elevated CSF protein.

Total 17 patients were included with 14 males and 3 females. They were all responded to treatment serologically but developed NS later. During the SS stage, seven patients were treated by Benzathine penicillin 2.4 MU IMI weekly for 2 or 3 doses; four treated by IMI procaine penicillin 0.8 MU/day for 15 days; two treated by IMI ceftriaxone 250 mg daily for 10 days; three were given azithromycin 2 gm for 7 days or 1 gm daily for 14 days and one was given minocycline 200 mg/day for 15 days. All serum RPR titres decreased 4-fold within three months but remained serofast for more than 24 months. CSF examination revealed all had reactive CSF VDRL and TPPA. Nine of them also had elevated CSF protein and white blood cells, three had increased CSF protein and one had elevated CSF white blood cells only. The remaining four showed normal CSF protein and white blood cells. Four patients had neuropsychiatric symptoms and signs and other 13 were asymptomatic.

All these 17 patients received treatment of NS. Thirteen were by IV penicillin G, 4 MU every 4 hours for 14 days and 4 were given IV ceftriaxone 2 gm daily for 10 days because of penicillin allergy. All of them had significant dropped in serum RPR and CSF VDRL titres 3 months after completion of NS treatment. Thus, the authors suggested that NS may be detected in immunocompetent patients despite given appropriate treatment and clinicians should be aware and consider CSF examination in any treated patients with evidence of progression irrespective of prior treatment regime or serological response.

## Multilevel and spatial analysis of syphilis in Shenzhen, China, to inform spatially targeted control measures

Wu X, Tucker JD, Hong F, Messina J, Lan L, Hu Y, et al.
Sex Transm Infect 2012;88:325-9.

Syphilis is still a major sexually transmitted infection in China especially in Guangdong Province, Shenzhen city. The reported incidence in Shenzhen was 48.9 cases per 100,000 people in 2008 which was 2.3 times higher than China (21.1 cases/100,000 people). The purpose of this study is to identify spatial and socio-demographic subpopulations that have a higher burden of syphilis.

There were 6496 syphilis cases among Shenzhen residents with 16.9% primary syphilis, 18.9% secondary syphilis, 0.3% tertiary syphilis, 63.7% latent syphilis and 0.5% congenital syphilis. Among all cases, 48.8% were men and 51.2% were women. The mean age was 34.3±12.3 years old. Men were significantly more than women to have primary and secondary syphilis. Younger people and migrant labourers were also more likely to have primary and secondary syphilis. By analysis of the surrounding neighbouring cities around Shenzhen, there was a significant spatial clustering of primary, secondary and latent syphilis cases. Moreover, those living in the districts with higher gross domestic product (GDP) were a significant predictor of primary and secondary syphilis. This might be that areas with higher GDP tended to have more commercial sex and extra-marital affairs. However, the clustering of primary and secondary syphilis was disproportionately low in Hong Kong when compared with other Shenzhen's neighbouring cities. The number of entertainment venues, high risk sex venues and MSM venues in the cities were not associated with the syphilis infection. The authors postulated that these venues might be more targeted by officials to have more condom promotion programme, health outreach and related sex health programme. The sex workers in these venues might also shift to the underground venues that were not easily identified by the officials.

The authors concluded that there is substantial clustering of primary and secondary syphilis cases at the neighbourhood of Shenzhen. Greater sexually transmitted disease health services and programme may be needed in these neighbourhoods.

## Moderate to severe plaque psoriasis with scalp involvement: A randomised, double-blind, placebo-controlled study of etanercept

Bagel J, Lynde C, Tyring S, Kricorian G, Shi Y, Klekotka P.
J Am Acad Dermatol 2012;67:86-92.

Biologics are effective in treating moderate to severe plaque psoriasis but evidence of its efficacy in managing scalp disease is limited. In this multicenter, randomised, double-blinded, placebo-controlled trial, the authors aimed at evaluating efficacy and safety of Etanercept in treating scalp symptoms in patients with moderate to severe psoriasis using Psoriasis Scalp Severity Index (PSSI) as the assessment tool.

A total of 124 patients were recruited and they were randomly assigned to receive subcutaneous Etanercept 50 mg twice weekly for 12 weeks followed by once weekly for another 12 weeks (group A) or placebo in first 12 weeks and Etanercept 50 mg twice weekly in subsequent 12 weeks (group B).

Etanercept-treated patients (group A) achieved significantly higher improvement in mean PSSI score at 12 week (80.8% vs 20.4%, $p<0.0001$). And the effect still persisted in the subsequent 12 weeks when a lower dosage of Etanercept was given. On the other hand, patients in group B also experienced significant improvement in PSSI score from baseline after they switched to Etanercept from week 13 onwards. Patients with higher body mass index (BMI) did not appear to have a compromised result in this study, although the sample was small.

Etanercept was generally well tolerated and the side effect profile was similar in both groups at 12 weeks. Five patients from group A withdrew due to adverse events, of which 2 experienced serious events namely cholecystitis and metastatic malignant melanoma. The authors concluded that Etanercept is an effective and well-tolerated

treatment for psoriatic patients with scalp involvement. However, the study was limited by the insufficient power to detect rare adverse reaction associated with Etanercept and the effect of high BMI on its efficacy.

## Wet dressing therapy in conjunction with topical corticosteroids is effective for rapid control of severe paediatric atopic dermatitis: Experience with 218 patients over 30 years at Mayo Clinic

Dabade TS, Davis DM, Wetter DA, Hand JL, McEvoy MT, Pittelkow MR, et al.
J Am Acad Dermatol 2012;67:100-6.

Intensive topical treatment had been used for decades in treating flare of atopic dermatitis. The authors in this study reviewed their experience in using hospitalised intensive wet dressing and topical steroids in the management of paediatric atopic patients over the past 30 years.

A total of 218 paediatric patients were reviewed. Most of them had tried topical therapies, dietary manipulation, phototherapy and systemic steroids prior to admissions. 'Closed' wet dressing method was utilised, where moist gauze was applied over topical steroids or emollient and dry cotton flannel clothing was used to cover the gauze to maintain moisture. It was done 5-8 times per day initially and slowly weaned according to patients' response. Most patients (over 90%) had remarkable improvement (more than 50%) over short period of time with a mean hospital stay of 3.6 days. They were usually well tolerated and only some patients complained of mild discomfort initially.

Despite its promising efficacy, wet dressing was still under-utilised. The authors explained the possible reasons include the limited literature on wet dressing. Labour intensiveness and insurance coverage also discourage its use. This study was limited by its retrospective nature, incompleteness of data and lack of standardisation of assessment.

## Childhood- and later-onset vitiligo have diverse epidemiologic and clinical characteristics

Nicolaidou E, Antoniou C, Miniati A, Lagogianni E, Matekovits A, Stratigos A, et al.
J Am Acad Dermatol 2012;66:954-8.

Vitiligo occurred early in life is not uncommon. However, there were only few reports studied the difference between childhood- and later-onset vitiligo. In this cross-sectional study, patients with a vitiligo onset before 12 years old were included as childhood-onset group while those had a disease onset after the age of 12 were selected as later-onset group.

A total of 394 patients were examined during a period of 5 years in which 126 of them had disease onset at childhood and 107 patients with later-onset disease were randomly selected. It was found that childhood-onset vitiligo more commonly affected the eyelids and lower extremities and they were usually segmental, while later-onset vitiligo affected upper extremities more. However, the reason for this difference in clinical pattern remained unclear. Moreover, childhood-onset vitiligo showed a slower rate of progression, lower connection with stressful events at initial presentation and associated more with allergic diseases but less with thyroid problem when compared to later-onset group. It was found that within the childhood vitiligo group, the presence of thyroid disease was associated with positive family history of thyroid disease and duration of vitiligo. Hence, the authors suggested that children with vitiligo should be followed up later in life for the emergence of thyroid disease, especially those with positive family history.

This study was limited by selection bias because the subjects were selected from the tertiary centre where some of the milder cases could be missed out.

## Ocular adverse effects of systemic treatment with isotretinoin

Neudorfer M, Goldshtein I, Shamai-Lubovitz O, Chodick G, Dadon Y, Shalev V.
Arch Dermatol 2012;148:803-8.

This study aimed at determining whether isotretinoin treatment might result in significant ocular adverse effects. Isotretinoin was reported to be associated with ocular adverse effects such as dry eyes (due to meibomian gland abnormality), blepharoconjunctivitis, keratoconjunctivitis sicca, photosensitivity, intolerance to contact lens, refractive changes, papilloedema and more severely benign intracranial hypertension. These adverse effects were readily reversible upon cessation of therapy.

This is a retrospective case-control study. The patients were recruited from the databases of a large health maintenance organisation in Israel serving a population of 2 million. The data were drawn from January 2000 through December 2007. A total of 14682 new patients using isotretinoin for acne were identified and analyzed. Another 14682 isotretinoin-free patients having acne and 14682 acne-free patients, all matched with sex and age, were also chosen for comparison.

The isotretinoin group had a significantly higher risk of ocular adverse effects (both inflammatory and structural adverse effects) than the isotretinoin-free group and acne-free group. The overall hazard ratio was 1.70 ($p<0.001$) for any ocular adverse effects in one year follow-up period. The hazard ratio was 2.33 (95%CI: 2.06-2.64) for inflammatory adverse effects and 2.10 (95%CI: 1.52-2.91) for structural adverse effects. There was increase in ophthalmologic medication used within one year period in isotretinoin group when compared with the other two control groups. The increase risk of ocular adverse effects in isotretinoin group was noted to begin from the first month and continue throughout the one year period. The most frequent ocular adverse effects were conjunctivitis, hordeolum, chalazion, blepharitis, eye pain and dry eyes. The adverse effects were likely due to the meibomian gland dysfunction induced by isotretinoin.

The authors suggested that ocular lubricants should be prescribed along with systemic isotretinoin use. Ophthalmologist should be referred for any ocular problems after starting isotretinoin and the treatment reviewed if symptoms persist or progress. The study may be limited by the fact that patients with severe acne have a higher risk for ocular diseases and this is the group that was indicated for treatment with isotretinoin.

## Dabrafenib in BRAF-mutated metastatic melanoma: a multicenter, open-label, phase 3 randomised controlled trial

Hauschild A, Grab JJ, Demidov L, Jouary T, Gutzmer R, Millward M, et al.
Lancet 2012;380:358-65.

Metastatic melanoma carries a high and rapid mortality rate. About 50% of melanomas have an activating mutation in serine-threonine protein kinase BRAF gene, in which, 80-90% of such have a V600E mutation and 10-20% have V600K mutation. Vemurafenib, the first BRAF-inhibitor, showed improvement in overall survival and progression-free survival in 48% of patients. It was recently approved by the US Food and Drug Administration and European Medicines Agency for treatment of metastatic melanoma.

Dabrafenib is a reversible, ATP-competitive inhibitor of mutated BRAF V600E, which was shown in phase 2 studies to have a confirmed response rate of 59% and manageable safety profile. An open-label, phase 3, randomised controlled trial was carried out from December 2010 to September 2011 to assess whether dabrafenib was better than standard chemotherapy in the treatment of metastatic melanoma. Patients of age 18 or above, with previously untreated, stage IV or unresectable stage III BRAF V600E mutation-positive melanoma were recruited. A total of 250 white Caucasians from 12 European and Northern American countries, with a median age of 50-53 years were randomly assigned (3:1) to receive dabrafenib (150 mg twice daily, orally) or dacarbazine (1000 mg/$m^2$ intravenously every 3 weeks).

Patients with central nervous system (CNS) metastasis, poor performance status, organ dysfunction and use of other anti-tumour therapy (except interleukin) were excluded. Treatment was continued until disease progression, death, or treatment withdrawal, with cross over to dabrafenib allowed if disease progression was confirmed.

The primary endpoint was progression-free survival. It was 5.1 months for dabrafenib and 2.7 months for dacarbazine, with a hazard ratio of 0.3 (95% CI=0.18-0.51, p<0.0001). The progression-free survival curves separated early and remained separated, in favour of the dabrafenib group. At data cutoff, 57% patients in the dabrafenib group and 22% in the dacarbazine group remained on treatment, while 44% of the dacarbazine group crossed over to dabrafenib. Treatment-related adverse events occurred in 53% of the dabrafenib group and 44% in the dacarbazine group. The most common ones included cutaneous hyperkeratosis, papillomas, palmoplantar erythrodysaesthesia, pyrexia, fatigue, headache and arthralgia. However, severe phototoxic or hyperkeratotic skin reactions, non-melanotic skin cancer and other adverse reactions were uncommon and occurred in less than 10% of patients in both groups.

The authors concluded that dabrafenib is a promising treatment which significantly improved progression-free survival compared with dacarbazine in BRAF V600E mutated stage IV melanoma patients with good performance status. However, the generalisability to those with CNS metastases, organ dysfunction, poor performance status, previously treated patients and non-white populations was unknown.

## Improved survival with MEK inhibition in BRAF-mutated melanoma

Flaherty K, Robert C, Hersey P, Nathan P, Garbe C, Milhem M, et al.
New Eng J Med 2012;367:107-14.

Selective BRAF-inhibitor therapy improves survival in patients with BRAF-mutated advanced melanoma. They have been shown to improve survival compared to conventional chemotherapy, but the responses were short-lived. The mechanism of resistance of melanoma cells seemed to have involved MAP kinase-pathway upstream of MEK. MEK inhibitors and BRAF inhibitors have showed growth inhibition and cell-death in tumours bearing BRAF mutations. Trametinib is an orally available selective inhibitor of MEK1 and MEK2 which was previously shown in phase 1 and 2 trials to have induced tumour regression and disease stabilisation in melanoma with BRAF V600E and V600K mutation.

A phase-3 open-label, randomised trial involving 322 patients was carried out to assess whether trametinib was better than standard chemotherapy in treatment of metastatic melanoma. Patients of age 18 or above, stage IIIC or IV BRAF V600E or V600K mutation-positive melanoma were recruited. Exclusion criteria included poor performance status, organ dysfunction and previous use of BRAF or MEK inhibitors or ipilimumab. Patients with stable brain metastasis were allowed to enroll. They were randomly assigned (2:1) to receive trametinib (2 mg, orally) or chemotherapy, dacarbazine (1000 mg/$m^2$ intravenously every 3 weeks), or paclitaxel (175 mg/$m^2$ every 3 weeks). Treatment was continued until disease progression, death, or treatment withdrawal, with cross over to trametinib allowed if disease progression was confirmed. The baseline demographics were well-balanced between the two groups with a median age of 54 (chemotherapy group) and 55 (trametinib group) years.

Median progression-free survival was 4.8 months in trametinib group and 1.5 months in chemotherapy group, with a hazard ratio of 0.45 (95% CI=0.33 to 0.63, p<0.001). The progression-free survival curves separated early and remained separated, in favour of the trametinib group. At data cutoff, 47% of chemotherapy group crossed over to trametinib. Six-month overall survival rate was 81% in the trametinib group and 67% in the chemotherapy group despite cross over (hazard ratio for death 0.54, 95% CI=0.32-0.92, P=0.01).

Treatment-related adverse events occurred in 57% of the trametinib group and 37% in the

chemotherapy group. Common toxic effects of trametinib were papulopustular eruption, acneiform dermatitis, diarrhoea, peripheral oedema and rarely, asymptomatic reversible reduction in ejection fraction, central serous retinopathy and retinal vein occlusion. They were managed with dose interruption and reduction. There were no cases of non-melanoma skin cancer reported.

The authors concluded that trametinib improved rates of progression-free and overall survival among patients with BRAF V600E and V600K mutated metastatic melanoma. Further studies of combination treatment with BRAF and MEK inhibitors to combat the issue of resistance in melanoma are currently underway.

## Known and potential new risk factors for skin cancer in European populations: a multicentre case-control study

de Vries E, Trakatelli M, Kalabalikis D, Ferrandiz L, Ruiz-de-Casas A, Moreno-Ramirez D, et al.
Br J Dermatol 2012;167:1-13.

This multicentre hospital-based case–control study was performed in eight European countries to investigate the environmental characteristics associated with skin cancer risk. Data from these dermatological centres were collected from patients with recently diagnosed squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and cutaneous malignant melanoma (CMM) to compare with healthy controls. Patients recently diagnosed with SCC, BCC or CMM and 18 years of age or older were included. Exposures were assessed by the questionnaire which was developed by EPIDERM team to include common skin cancer risk factors and frequent use of certain drugs or food items known to increase cutaneous photosensitivity.

In total, 409 patients with SCC, 602 with BCC and 360 with CMM compared with the 1550 control persons were included. Ciprofloxacin was associated with a reduced risk of BCC (OR=0.33, 95% CI=0.16-0.71) and similarly with reduced risk of SCC (OR=0.34, 95% CI=0.14-0.85), while use of thiazide diuretics was modestly associated with increased risk of BCC (OR=2.04, 95% CI=1.13-3.69) and SCC (OR=1.66, 95% CI=1.16-2.37) respectively. Consumption of pomegranate which contains large amounts of antioxidants was associated with reduced risk of BCC and SCC. On the other hand, recent stressful events were associated with an increased risk, especially of CMM. A sun-sensitive skin type and dermatologists reported photoaging had a statistically significantly increased risk of all types of skin cancer and presence of common naevi had a statistically significantly increased risk of CMM and BCC. The authors therefore concluded that the role of some new potential protective factors and potential risk factors such as stress, consumption of certain foods and medications warrants further study.