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ORIGINAL STUDY
VIDEOTHORACOSCOPIC SYMPATHECTOMY- A SURGICAL TREATMENT FOR PRIMARY HYPERHIDROSIS

REVIEW ARTICLE
VITILIGO IN CHILDREN AND ADOLESCENTS

CASE REPORT
GENITAL BASALL CELL CARCINOMA

HISTORY OF MEDICINE
HISTORY OF DERMATOVENEREOLOGY IN SERBIA FROM 1919 – 1945: part 3

REPORT

FORTHCOMING EVENTS

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THE NOVI SAD DERMATOVENEREOLOGIC, MOULAGE COLLECTION, CLINIC OF DERMATOVENEREOLOGY, CLINICAL CENTER OF VOJVODINA, NOVI SAD, SERBIA

Videothoracoscopic sympathectomy - a standard treatment for primary hyperhidrosis at the Clinic of Thoracic Surgery in Sremska Kamenica

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Abstract

Primary hyperhidrosis affects approximately 3% of the world's population, particularly young female adults. It is defined as excessive, profuse sweating of the palms, soles, armpits and face. Conservative treament includes diverse modalities, however, surgical treatment has shown the best long-term results. The objective of this study was to assess some disease-specific epidemiological characteristics in a pre-selected group of patients seeking surgical therapy, as well as outcomes of thoracoscopic sympathectomy. The severity and impact of hypehidrosis was assessed, using Hyperhidrosis Disease Severity Scale (HDSS: patients rate the serverity of symptoms on a scale from 1 to 4). Thoracoscopic sympathectomy was performed using a double lumen endotracheal tube, via bilateral 5 mm dual port videothoracoscopic camera 0°, and an endoscopic ultrasound activated harmonic scalpel. The sympathetic chain was resected on both sides at the level of the second and the third thoracic ganglion (T2 and T3), using an ultrasound knife. The extirpated chain was also at the level T3-T4 and sent for *ex tempore* analysis. There were 162 patients undergoing thoracoscopic sympathectomy: 39.51% were males and 60.49% females; at presentation their mean age (± SD) was 30.5 (±8.3), range 16 - 58 years. Axillary hyperhidrosis occurs later than palmar-axillary-plantar ($p<0.05$). A total of 35.18% of the evaluated patients were able to name at least one member of their families who also suffered from hyperhidrosis. The most commonly affected area was palmar-axillary-plantar (30.25%). Fifty patients (30.86%) received conservative therapy before surgery. The most commonly used conservative therapy modalities included different kinds of ointments/tinctures (11.73%), botox (8.02%) and iontophoresis (2.47%). Prior to surgery, 91.36% of patients reported severe sweating (HDSS score 3 or 4). The highest mean score was given for a combination of facial-palmar-axillary-plantar hyperhidrosis (3.80±0.24). All surgeries were successfully performed, with no complications, or perioperative morbidity. The mean hospital stay was 1.28±0.68 days long. After surgery, 93.21% of patients reported mild or moderate hyperhidrosis (HDSS score 1 or 2). Compensatory sweating (lower part of the back, and abdomen) was reported by 34.57% of patients after the surgery. All patients had a 6-months long follow-up: a significant improvement in quality of life was reported by 84.56% of patients (Yates corrected χ^2 (1) = 228.42; $p=0.0000$)); due to compensatory sweating, only 4.94% and 1.85% of patients reported bad and very bad quality of life, respectively.
In conclusion, nowadays videothoracoscopic sympathectomy is a standard treatment for primary hyperhidrosis with a high success rate.

Key words

Hyperhidrosis; Sympathectomy; Thoracic Surgery, Video-Assisted

The sympathetic nervous system is a part of the autonomic nervous system which stimulates sweat production. Sympathetic innervations to upper extremities are at the level of the second and the third thoracic ganglion (T2 and T3), to armpits at T4 and T5, and to lower limbs at T2 and T7.

Excessive sweating or hyperhidrosis affects approximately 3% of the world population (1, 2), predominantly young female adults (3, 4). It is defined as excessive bilateral, mostly symmetrical sweating

pattern that does not correlate with local environment or physical activities, but results in profuse sweating of the palms, feet, armpits or face.

Hyperhidrosis may be classified as primary hyperhidrosis (idiopathic) with obscure etiology, and secondary hyperhidrosis due to certain diseases such as *diabetes mellitus*, endocrine disorders (e.g., hyperthyroidism), secretory tumors (*pheochromocytoma*, carcinoid tumors, pituitary gland tumors), tuberculosis, lymphomas, certain neurological, psychiatric, or sympathetic nervous system disorders (5).

Moreover, according to anatomic distribution, hyperhidrosis may be classified as focal and generalized. Primary or idiopathic hyperhidrosis is typically focal and limited to the armpits, palms, soles or craniofacial area. The diagnosis of primary hyperhidrosis is often based on patient's symptoms, medical history of excessive sweating, and specific clinical findings. The intensity of hyperhidrosis has not yet been precisely graded, but it may be mild, moderate and intense. Some authors have proposed the gravimetric method to precisely measure the sweat quantity by means of weighing the sweat-soaked paper, but this method is still reserved only for laboratory studies (6).

There also appears to be a genetic predisposition to primary hyperhidrosis, since 30% to 65% of patients report positive family history. An autosomal dominant mode of transmission with incomplete disease penetrance was reported (7).

Unlike functional sweating, which is due to physical exercise, fatigue or fever, primary hyperhidrosis develops as a consequence of either emotional problems or anxiety. Patients with primary hyperhidrosis have serious social problems which disturb their normal social communication. Various methods for reducing excessive sweating include: special diets (without coffee, tea, coca-cola, chocolate), diverse antiperspirants, such as over-the counter ointments/tinctures, topical aluminium chloride, medicines, drugs (oral anticholinergics), tap water ionophoresis (9), intradermal injections of botulinum toxin type A (botox) (10,11), but only surgical treatment has shown the best long-term results (12-14).

The objective of this study was to assess disease-specific epidemiological characteristics of primary focal hyperhidrosis, in preselected patients seeking surgical help, as well as outcomes of thoracoscopic sympathectomy.

Material and methods

Between January 2008 and December 2009, 162 patients with primary hyperhidrosis were evaluated at the Clinic of Thoracic Surgery, Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, Serbia, before and after thoracoscopic sympathectomy. All patients had a several-year history of excessive sweating, unresponsive to conservative treatment regimens (diet, antiperspirants, medicines, drugs).

Surgical technique

All surgeries were performed in total endotracheal anesthesia using a double lumen endotracheal tube. The patients were put into lateral decubitus position, with a rolled pillow under the top of scapula, in order to additionally extend the intercostal spaces (Figure 1). The intraoperative monitoring included: arterial blood pressure, electrocardiography, and pulse oximetry. With the lung on the operative side collapsed, the following instruments were introduced into pleural space via bilateral 5mm dual port approach (Aesculap, Tuttlingen, Germany): a videothoracoscopic camera (Telescope Aesculap 5 mm 0°, Tuttlingen, Germany) which was connected with the video data processing system (Richard Wolf 3CCD Camera System, Tuttlingen, Germany), Aesculap grasper and an ultrasonic surgical scalpel

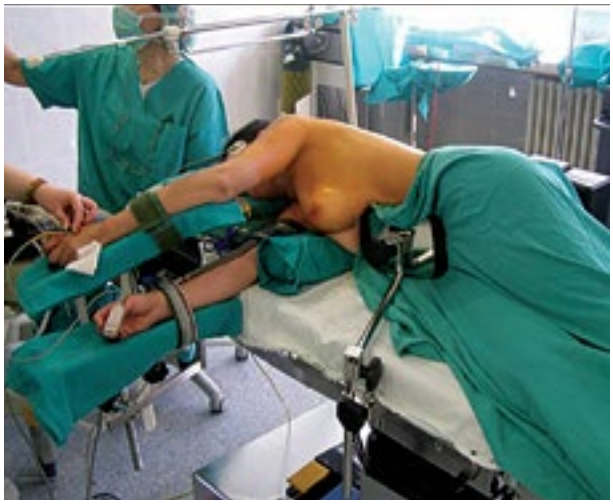

Figure 1. The patient is put into a lateral decubitus position

(Auto Sonix-Hook Probe; Auto Sonix-Ultrasonic Surgical System Tyco, International Health Care). After identification of the first rib and the sympathetic chain, the chain was cut with an ultrasonic scalpel on both sides between T2 and T3, and the 4th chain was extirpated at the level T3-T4 (Figure 2) and sent for histopathological examination *ex tempore*. The parietal pleura was resected along the body of the second and the third rib with ultrasonic scissors, starting from the costovertebral angle, in order to destroy the Kuntz fibers. The surgery ended by introducing a single thoracic drain No 16F connected to the active suction of -20cmH2O. The drain was fixed by Sofsik 0 (Tyco) and the skin suture performed by Dafilon 3.0 (B. Braun) and Vicryl 3.0 (Ethicon). The same surgical procedure was performed on the opposite side as well. After radiological verification of pulmonary parenchyma re-expansion, drains were removed two hours after surgery.

Exclusion criteria for surgery: former thoracic surgery, serious cardiac circulation or pulmonary insufficiency, pleural empyema. Exclusion criteria also included: patients suffering from secondary hyperhidrosis due to other diseases (diabetes mellitus, hyperthyroidism, carcinoid tumor, and lymphomas).

The following parameters were collected: age, sex, family history, age/period of onset (birth, childhood, puberty, later) areas primarily affected by hyperhidrosis, and previous therapy.

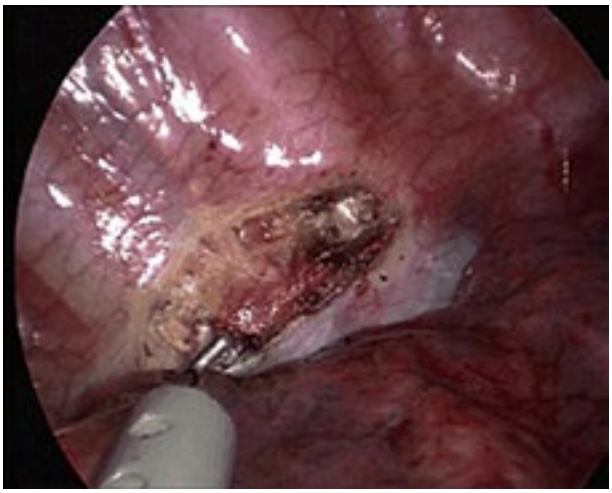

Figure 2. Sympathetic chain

Severity of disease and post-operative effects (Quality of Life Questionnaire), were graded using Hyperhidrosis Disease Severity Scale - HDSS (International Hyperhidrosis Society, www.sweathelp.org), between 1 (no symptoms) and 4 (worst symptoms) (Table 1).

Patients were asked to rate their symptoms in different areas before and after the surgery: scores between 3 and 4 indicated severe hyperhidrosis; scores between 1 and 2 indicated mild or moderate hyperhidrosis. After surgery, patients rated their symptoms again: 1-point improvement was associated with a 50% reduction in sweat production, and

Table 1. Hyperhidrosis Disease Severity Scale (International Hyperhidrosis Society)

	How would You rate the severity of your hyperhidrosis symptoms?
1	My sweating is never noticeable and never interferes with my daily activities (quality of life - excellent)
2	My sweating is tolerable, but sometimes interferes with my daily activities (quality of life - good)
3	My sweating is barely tolerable and frequently interferes with my daily activities (quality of life - bad)
4	My sweating is intolerable and always interferes with my daily activities (quality of life - very bad)

2-point improvement with 80% reduction in sweat production.

Statistical analysis Data were presented as mean ± standard deviation for continuous variables, and as frequencies while categoric data were presented percentages. Means were compared by two-sided t-test for dependent samples. Two-sided t-test was used for comparison of percentages too. Chi square test (c^2) was used to test if obtained frequencies significantly deviated from the expected, e.g. random. Two-tailed p-values less than 0.05 were considered statistically significant. Statistical analysis was performed using JMP statistical software (JMP 7, SAS Institute, Cary, NC).

Results

A total of 162 patients were evaluated. There were 64 (39.51%) males and 98 (60.49%) females, with the mean age (± SD) of 30.5 (± 8.3) years. The youngest patient was 16 years old, and the oldest 58 years old.

More than half of all patients with palmar-axillary-plantar hyperhidrosis (57.14%) and palmar-plantar hyperhidrosis (56.52%) stated that they had hyperhidrosis since early childhood, whereas 33.33% of patients with axillary hyperhidrosis and 31.25% of patients with palmar-axillary hyperhidrosis stated that their disease did not start until puberty (two-sided p=0,03). There were no sex-specific differences.

A total of 35.18% of evaluated patients were able to name at least one member of their family who also suffered from hyperhidrosis.

The most commonly affected areas were: palmar-axillary-plantar, in 49 patients (30.25%), axillary in 36 patients (22.22%), palmar-plantar in 23 patients (14.20%), palmar-axillary in 16 patients (9.88%), and palmar in 11 patients (6.79%).

There were no significent differences between males and females in regard to localization of the affected areas. However, statistically, females sweat more frequently in the palmar - axillary - plantar sites than men (two-sided p=0.06) (Table 2).

Table 2. The most commonly affected areas of the body (%)

Sites	Male n=64	(%)	Female n=98	(%)	Total n=162	(%)
Axillary (n=36)	15	23.44	21	21.43	36	22.22
Facial (n=7)	5	7.81	2	2.04	7	4.32
Facial+ axillary (n=10)	5	7.81	5	5.10	10	6.17
Facial + palmar + axillary + plantar (n=10)	1	1.56	9	9.18	10	6.17
Palmar (n=11)	4	6.25	7	7.14	11	6.79
Palmar + axillary (n=16)	8	12.5	8	8.16	16	9.88
Palmar + axillary + plantar (n=49)	14	21.87	35	35.71	49	30.25
Palmar + plantar (n=23)	12	18.75	11	11.22	23	14.20
Total	64	100.0	98	100	162	100.0

Previous therapies used by 50 patients (30.86%) included ointments/tinctures (11.73%), botulinum toxin injections (8.02%), iontophoresis (3.09%), antiperspirants (2.47%), drugs - tranquilizers/ sedatives (1.85%), urotropin (1.85%), acupuncture (1.23%), homeopathy (0.62%).

Nevertheless, 73.43% of male and 66.32% of female patients (two-sided p=0.35) received no previous therapy. Statistically, females used ointments/ tinctures more frequently than men (Table 3).

All 162 patients with primary hyperhidrosis, underwent bilateral thoracoscopic sympathectomy. Postoperative mortality and severe morbidity (Horner's syndrome, pneumothorax, and neuralgia) were not registered in this study. The mean hospital stay was 1.28±0.68 days.

Before surgery, 148/162 patients (91.36%) reported severe sweating (HDSS scores 3 or 4) and after surgery, 151/162 patients (93.21%) reported mild or moderate hyperhidrosis (HDSS scores 1 or 2). The highest mean score was given for the combination of facial-palmar-axillary-plantar hyperhidrosis (3.80±0.24) and for the combination of facial-axillary hyperhidrosis (3.70±0.19).

A 2-point improvement in the mean HDSS score after surgery was found in patients with: palmar-axillary-plantar hyperhidrosis (from 3.61±0.07 to 1.26±0.07), facial-plamar-axillary-plantar hyperhidrosis (from 3.80±0.24 to 1.40±0.24) and facial-axillary hyperhidrosis (from 3.70±0.19 to 1.70±0.19).

Sex-specific analysis was not performed, due to a small number of patients in specific groups.

After surgery, 34.57% of patients reported compesatory sweating on the other parts of their body (lower back, abdomen).

Table 3. Previous conservative therapy (%)

Previous conservative therapy	Male n=64	(%)	Female n=98	(%)	Total n=162	(%)
Ointments/tinctures	6	9.37	13	13.26	19	11.73
Botulinum toxin injection	5	7.81	8	8.16	13	8.02
Iontophoresis	1	1.56	4	4.08	5	3.09
Antiperspirants	1	1.56	3	3.06	4	2.47
Drugs - tranquilizers/sedatives	2	3.12	1	1.02	3	1.85
Urotropin	2	3.12	1	1.02	3	1.85
Acupuncture	0	0.0	2	2.04	2	1.23
Homeopathy	0	0.0	1	1.02	1	0.62
No previous therapy	47	73.43	65	66.32	112	69.14
Total	64	100.0	98	100.0	162	100.0

Table 4. The mean Hyperhidrosis Disease Severity Scale (HDSS) scores of sweating in different sites before and after surgery

HDSS scores Site of sweating	Before surgery (mean±SD)	After surgery (mean±SD)	P value*
Axillary (n=36)	3.42±0.73	1.72±0.85	p<0.001
Facial (n=7)	3.29±0.27	1.85±0.27	p<0.003
Facial + axillary (n=10)	3.70±0.19	1.70±0.19	p<0.001
Facial + palmar + axillary + plantar (n=10)	3.80±0.24	1.40±0.24	p<0.001
Palmar (n=11)	3.45±0.29	1.63±0.29	p<0.001
Palmar + axillary (n=16)	3.37±0.19	1.81±0.19	p<0.01
Palmar + axillary + plantar (n=49)	3.61±0.07	1.26±0.07	p<0.001
Palmar + plantar (n=23)	3.30±0.70	1.43±0.66	p<0.001

* Due to two-sided t-test for dependent samples

All patients had a six month follow-up period with regular controls. Due to compensatory swaeting on the back and abdomen, only 4.94% and 1.65% of patients reported bad or very bad quality of life, respectively. Following surgery, the majority of patients [137/162 (84.56%)] demonstrated significant improvement in quality of life (Yates corrected c^2 (1)=228.42; p=0.0000) (Table 5).

Discussion

Although it is not a major medical problem, primary hyperhidrosis significantly affects the social and psychological aspects of patients' lives, inducing their withdrawal from society (1).

More than a third of all patients affected by hyperhidrosis and included in this study were female patients, which corresponded with previous observations (3, 4, 12). The average age on presentation was 30 years in both sexes, which was in accordance with other studies (4, 12). However, our patients were not able to identify either the precise time of disease onset, nor the precise age of disease onset. That is why we decided to divide their lives into periods (birth, childhood, puberty, later). Axillary hyperhidrosis manifested later than palmar-axillary-plantar. Similar results were obtained by Kariman-Teherani et al (12).

More than a third (35.18%) of all evaluated patients in this study reported positive family history, which was in agreement with other studies, where it ranged from 30% to 65% (4, 7, 13).

The most frequent sites of excessive sweating were palmar-axillary-plantar, which was similar with previous observations (3, 4, 12). In regard to sites of affected areas, there were no significant differences between males and females. A statistical trend was found for females to sweat more frequently in the palmar-axillary-plantar sites, which was opposite to results of Kariman-Teherani et al, where women sweated significantly more frequently in the palmar-plantar areas than men, while statistical trends were

Table 5. Quality of life before and after surgery

Quality of the life	Before surgery (%)	After surgery (%)
Very good	0 (0%)	93 (57.41%)*
Good	14 (8.62%)	58 (35.80%)*
Bad	53 (32.73%)*	8 (4.94%)
Very bad	95 (58.65%)*	3 (1.85%)

*Statistically significant (Yates corrected c^2 (1)=228.42; p=0.0000)

found for armpits in women and palmar-axillary-plantar sites in men (12).

There were 50 patients (30.86%) who indicated that they had used one or more therapies prior to surgery. Most frequently used (in 11.73% of patients) were ointments and tinctures. This was probably due to the fact that ointments and tinctures could be easily obtained and did not require special consultation. Women used these products more frequently than men, which was in accordance with the previous study (12).

Patients included in our study were preselected patients with severe focal primary hyperhidrosis. Since the vast majority of them (91.36%) had HDSS scores 3 or 4, all of them underwent bilateral thoracoscopic sympathectomy. Thus, the objective of this paper was also to review early postoperative results and a 6-month follow-up of patients undergoing videothoracoscopic sympathectomy. After surgery, 93.21% of patients reported mild or moderate hyperhidrosis, and 84.56% reported a significant improvement in quality of life. These data were similar to other studies (14, 15, 21), emphasizing the effectiveness of thoracoscopic sympathectomy in the treatment of primary focal hyperhidrosis.

The first surgical treatment of hyperhidrosis was reported at the end of the 19th and the beginning of the 20th century. After video-assisted thoracoscopic surgery was introduced into the standard thoracic surgery practice in the 90s of the 20th century, as well as the latest technological advances, thoracoscopic sympathectomy has become the standard treatment for primary hyperhidrosis. Open surgical techniques (posterior, supraclavicular, transthoracic or transaxillary approaches) are nowadays almost completely abandoned. They were substituted by minimally invasive procedures, such as videothoracoscopic sympathectomy or percutaneous radiofrequency ablation (15, 17). The advantages of this minimally invasive surgical procedure include: excellent visualization of the sympathetic chain, facilitating the surgical procedure itself, a significant reduction of hospital stay, reduction in analgesic medications, as well as extraordinary postoperative results. According to the literature data, after bilateral thoracoscopic sympathectomy for palmar hyperhidrosis, outstanding therapeutic results have been achieved in over 99% of cases. Favorable effects are immediately evident, and the patient usually wakes up from anesthesia with dry and warm palms. In cases with facial blushing and facial and axillary hyperhidrosis, successful results were reported in 95% of cases (18).

There was no postoperative mortality and severe morbidity (Horner's syndrome, pneumothorax, and neuralgia) in any of the 162 patients with primary hyperhidrosis who underwent thoracoscopic sympathectomy. The mean hospital stay was 1.28±0.68-days. According to the literature data, complications occur in less than 1% of cases: Horner's syndrome, unsuccessful sympathectomy due to unresected Kuntz's fibers, pneumothorax, bleeding,

postoperative neuralgia, esophageal injury (19, 20). In most cases complications depend on the surgeon's experience and skills. Thus, careless cutting of the first thoracic ganglion (T1) may result in Horner's syndrome, while unresected Kuntz's fibers, can results in unsuccessful sympathectomy. Recently, it has been reported that symptoms of compensatory sweating may be prevented by keeping the second thoracic ganglion (T2) unresected (21). Clipping has been proposed (in order to replace electrocauter or ultrasound knife), since it may be easily removed in case of excessive compensatory sweating or Horner's syndrome (16).

After surgery, 34.57% of patients reported compesatory sweating on other parts of the body (lower back, abdomen), but after six months of follow-up, only 4.94% and 1.65% of patients reported bad, or very bad quality of life, respectively. Compensatory sweating is undesirable, but fairly common side effect of sympathetic nerve surgery, and with negative impact on the quality of life after surgery. This phenomenon significantly depends on the environment, such as the air temperature and humidity. About 40% of patients may also develop a transitory excessive saliva secretion. Although the reported compensatory sweating rate ranges from 30% to 65% (22-24), it is mostly a transient, well tolerated side effect, thus the vast majority of patients express high satisfaction with the results of this surgery with respect to alleviation of their primary symptoms (20,25-27).

In conclusion, thoracoscopic sympathectomy is a standard procedure for the treatment of primary focal hyperhidrosis, associated with a high success rate.

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Videotorakoskopska simpatektomija – standarna hirurška metoda za lečenje primarne hiperhidroze na Klinici za grudnu hirurgiju u Sremskoj Kamenici

Sažetak

Uvod: Primarna hiperhidroza prisutna je kod približno 3% svetske populacije. Definiše se kao prekomerno i nekontrolisano znojenje dlanova, pazušnih jama i lica. Konzervativna terapija obuhvata uporebu raznih antiperspiranata, lekova, jontoforeze, injekcije botulinum toksina tip A (botoks) ali je hirurška terapija jedina pokazala najbolje trajne rezultate.

Cilj: Ispitivanje je imalo za cilj da prikaže neke epidemiološke karakteristike pacijenata sa primarnom fokalnom hiperhidrozom i terapijske efekte torakoskopske simpatektomije.

Materijal i metode: Ispitivanje je obuhvatilo 162 osobe kod kojih je urađena torakoskopska simpatektomija zbog primarne fokalne hiperhidroze na Klinici za grudnu hirurgiju Instituta za plućne bolesti Vojvodine u Sremskoj Kamenici, u periodu između januara 2008. i decembra 2009. godine. Popunjavanjem upitnika (International Hyperhidosis Society, www.sweathelp.org), pre i posle operacije, pacijenti su ocenili stepen svojih tegoba na zahvaćenim delovima tela HDSS - *Hyperhidrosis Disease Severity Scale* skorom 1 do 4 (eng. skala za ocenu težine hiperhidroze). Sve operacije su izvedene u lateralnom dekubitusu, pomoću dvolumenskog endotrahelanog tubusa, putem dve petomilimetarske radne porte, uz videotorakoskopsku kameru i endoskopsku ultrazvučnu kuku, presecanjem simpatičkog lanca između drugog (T2) i trećeg torakalnog gangliona (T3) i ekstirpacijom simpatičkog lanca između trećeg i četvrtog torakalnog gangliona (T3-T4). Ekstirpirani materijal je poslat na *ex tempore* patohistološku verifikaciju. Ultrazvučnim makazama vršena je lateralna resekcija parijetalne pleure po telima drugog i trećeg rebra počev od kostovertebralnog ugla, u dužini od 4-5 cm, čime se omogućilo presecanje Kuntzovih nerava (koji premošćuju drugi i treći grudni ganglion).

Rezultati: U istraživanje je uključeno 64 (39,51%) osoba muškog pola i 98 (60,49%) osoba ženskog pola, prosečne starosti (u momentu kada su se javili na operaciju) 30,5±8,3 godina. S obzirom da pacijenti nisu mogli da navedu tačnu godinu života u kojoj je bolest počela, mi smo početak bolesti vezali za pojedine faze života (rođenje, detinjstvo, pubertet, kasniji period života) za koje smo mogli dobiti podatke. Tako je više od polovine (57,14%) pacijenata sa palmarnom-aksilarnom-plantarnom hiperhidrozom i palmarnom-plantarnom hiperhidrozom (56,52%) tvrdilo da je njihova bolest započela u ranom detinjstvu, dok je 33,33% svih pacijenata sa aksilarnom hiperhidrozom i 31,25% pacijenata sa palmarnom-aksilarnom hiperhidrozom tvrdilo da njihova bolest nije počela pre puberteta (*two-saided* p=0,03). Obolele srodnike je navelo 35,18% pacijenata. Najčešće lokalizacije zahvaćene prekomernim znojenjem bile su: palmarno-aksilarno-plantarna (30,25%), aksilarna (22,22%) i palmarno-plantarna 14,20%. Pedeset pacijenata (30,86%) je pre operacije koristilo neku

konzervativnu terapiju. Najčešće korišćene terapije bile se: različite kreme (11,73%), botoks injekcije (8,02%) i jontoforeza (2,47%). Pre operacije, 148/162 obolelih (91,36%) ocenilo je svoje znojenje teškim (HDSS skor 3-4). Sve operacije su izvedene uspešno bez komplikacija i perioperativnog morbiditeta. Prosečno trajanje hospitalizacije iznosilo je 1,28±0,68 dana. Posle operacije 151/162 obolelih (93,21%) ocenilo je svoje znojenje kao blago ili umereno (HDSS skor 1-2). Nakon operacije kod 34,57% pacijenata javilo se prolazno kompenzatorno znojenje (donji deo leđa i stomak).

Svi pacijenti su praćeni tokom šest meseci. Samo 4,94% operisanih pacijenata imalo je loš a 1,85% veoma loš kvalitet života usled kompenzatornog znojenja u predelu donjeg dela leđa i trbuha, dok je 84,56% imalo značajno poboljšanje kvaliteta života u odnosu na period pre operacije (*Yates corrected* c^2 (1)=228,42; p=0,0000).

Zaključak: Videotorakoskopska simpatektomija predstavlja standardnu metodu u lečenju obolelih od primarne hiperhidroze, koja pruža visok stepen bezbednosti i efikasnosti.

Ključne reči

Hiperhidroza; Simpatektomija; Video-asistirana torakalna hirurgija

Vitiligo in Children and Adolescents: a Lliterature Review

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Abstract

Vitiligo is an acquired, often hereditary skin depigmentation disorder, characterized by discrete, well-circumscribed, chalk-white macules or patches. It affects all age groups, but in more than half of the patients it occurs before the age of twenty, when self-image is being formed and social acceptance is of great importance. Although similar to the disease in adults, vitiligo in children and adolescents does have differences in epidemiology, association with other endocrine and/or autoimmune disorders, and treatment. This is a review of vitiligo in the pediatric population, emphasizing key differences with vitiligo in adults. According to the literature reports, we suggest that children and adolescents with vitiligo, especially non-segmental type, should perform annual screening for thyroid dysfunction, particularly for parameters of autoimmune thyroiditis.

Key words

Vitiligo; Child; Adolescent

Vitiligo is an acquired, presumably a hereditary autoimmune skin disorder characterized by progressive, well-circumscribed milky white patches affecting the skin and/or mucosal membranes (1, 2).

Epidemiology

Vitiligo affects individuals of all races worldwide. It is estimated that it affects around 1 – 2% of the world population. Vitiligo is primarily a disease of the young. It affects all age groups, but half of them are under the age of 20 (1 - 8). Epidemiology of childhood vitiligo is similar to that in adults, but there are some specificities of vitiligo in children. Unlike in adults, where it affects both genders equally, childhood vitiligo is more frequent in girls (9). Only 8% of adults with vitiligo have a positive family history, whereas it is positive in 12 – 35% of affected children (5, 7 - 9).

Generalized vitiligo is the most common type, both in children and in adults. It has been reported that from 33% to 78% of children with vitiligo are affected by a generalized type of the disease (4 - 9)

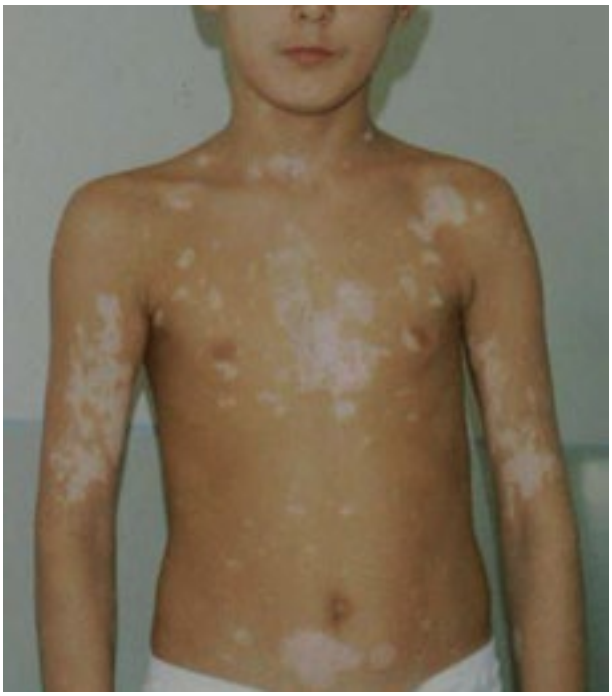

Figure 1. Generalized vitiligo in a 12-year-old boy

(Figure 1). The second most frequent type is focal vitiligo (14.4% - 34.6%). Segmental vitiligo is significantly more frequent in children than in adults. It has a prevalence of 20% in children, but only 5% in adults. Acrofacial (7.6%) and universal vitiligo (0.4%) are rarely found in children (4 - 9).

Etiology and Pathogenesis

The etiology and pathogenesis of vitiligo are not fully understood. It has been known that genetic factors play a certain role in the development of vitiligo (3, 4, 10). In patients with non-segmental vitiligo and positive family history of vitiligo, the disease occurs at a younger age (at the age of 24.8 years on the average), whereas in patients without positive family history it occurs at the age of 42.2 years (11). Recent research shows that there are two possible modes of inheriting vitiligo, both associated with the age of vitiligo development (12). In patients with an early onset of vitiligo (under the age of 30 years), it is caused by dominant mode of inheritance, with incomplete penetration. However, in patients affected by vitiligo after the age of 30, a predisposition to vitiligo is resulting from a recessive genotype and exposure to certain environmental triggers (13, 14). Very early onset of vitiligo (under the age of 7) has also been established in children with a positive family history of vitiligo (15). There is clear evidence that certain HLA haplotypes are strongly associated with positive vitiligo family history, time of onset, severity of the disease, and ethnic background (13, 14). There are several theories of vitiligo pathogenesis: autoimmune, oxidative stress theory, and neurogenic theory (1 - 4).

Autoimmune theory

Autoimmune theory of vitiligo has been best supported by clinical and basic investigations (1, 3, 13 - 15). Some researches show that increased incidence of autoimmune thyroiditis in vitiligo patients is genetically determined. Autoimmune susceptibility locus on chromosome 1 (AIS1) is thought to provoke autoimmune reactions, especially in vitiligo associated with other genes (for example the major histocompatibility complex – MHC, located in the short arm of chromosome 6), and combined with exposure to external or internal factors, it may mediate the development of Hashimoto's thyroiditis (HT) (16, 17). It is common knowledge that genes located on chromosome 17p13 contribute to the development of certain autoimmune diseases: generalized vitiligo, autoimmune thyroiditis, insulin-dependent diabetes mellitus, rheumatoid arthritis, psoriasis, pernicious anemia, systemic lupus erythematosus and Addison's disease. According to recent research of NALP1 protein, it is a gene which plays a major role in the regulation of intracellular innate immunity. DNA sequence variants in the NALP1 region are associated with the increased risk for the development of generalized vitiligo (Figures 2 and 3), and/or other

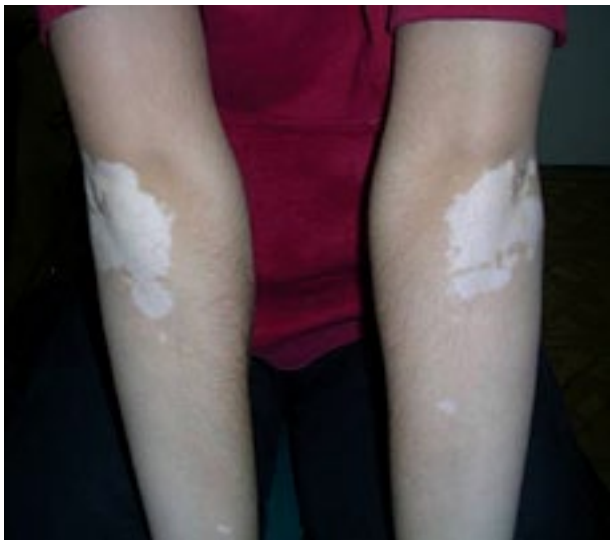

Figure 2. Generalized vitiligo in a 15-year-old girl

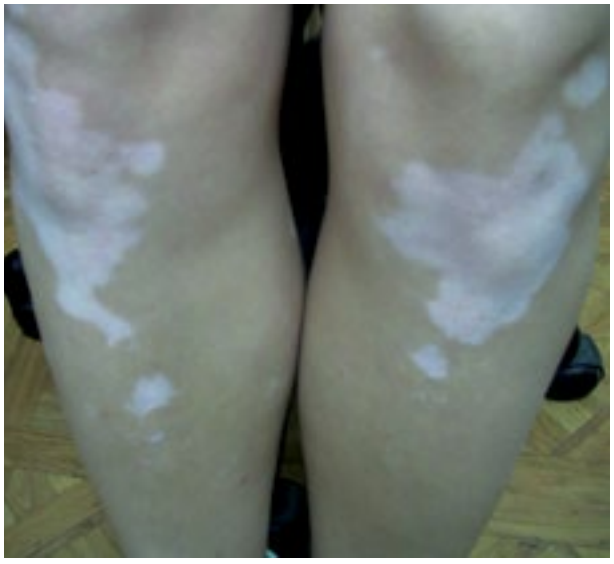

Figure 3. Generalized vitiligo in a 15-year-old girl

associated autoimmune diseases, such as autoimmune thyroiditis (18). It is estimated that autoimmune mechanisms have a key role in the development of non-segmental vitiligo (1 - 3) (Figure 4).

Oxidative stress theory

In the melanocytes of active vitiligo there is an increase of antioxidants, as well as a deficiency of antioxidant enzyme systems, consequently causing oxidative damage in the melanocytes, being the basis of oxidative stress theory (3, 19 - 22).

Neurogenic theory

Development of segmental vitiligo can best be explained by neurogenic theory, which explains lesions to be the result of abnormal release of neurochemical mediators inhibiting melanogenesis, or having toxic effects causing melanocytes destruction (23 - 25). Segmental vitiligo is extremely rarely associated with autoimmune diseases (26, 27) (Figure 5).

Coexistence with endocrine and/or autoimmune diseases

Adult patients with vitiligo are at higher risk for developing a number of endocrine and/or autoimmune diseases, including thyroid gland diseases (mostly Hashimoto's thyroiditis), insulin-dependent diabetes mellitus, pernicious anemia, Addison's disease, autoimmune polyglandular deficiency syndrome, rheumatoid arthritis and alopecia areata. Vitiligo may develop prior, concurrently or after the occurrence of endocrine and/or autoimmune diseases (1, 3, 28). Epidemiological studies, including a large number of children with vitiligo, have not shown an increased risk of above-mentioned diseases (9, 29 - 33). Unlike adults, children and adolescents with non-segmental vitiligo develop more frequently only Hashimoto's thyroiditis (34 - 36) (Figure 6). Given the fact that vitiligo often precedes Hashimoto's thyroiditis, early diagnosis of HT is possible. Therefore, children

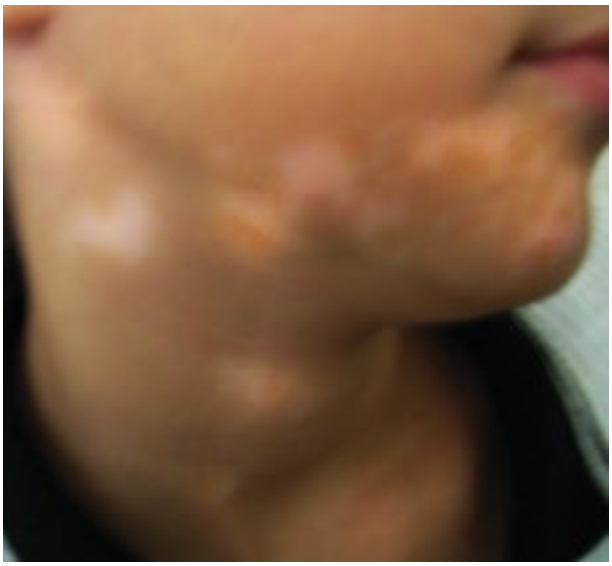

Figure 5. Segmental vitiligo in a 9-year-old girl

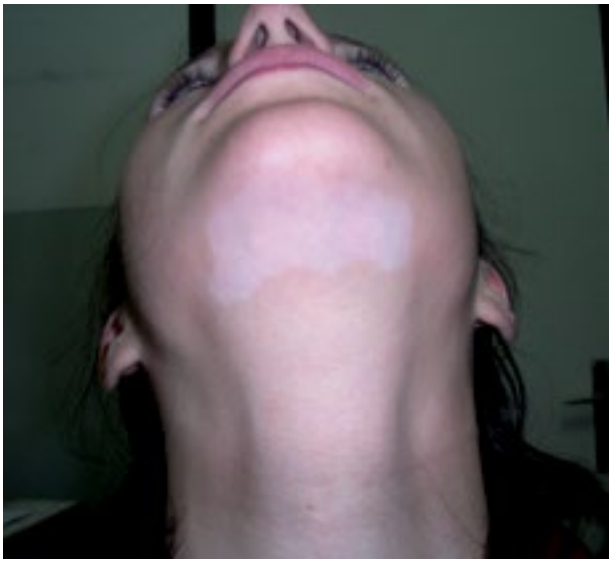

Figure 4. Focal vitiligo in a 17-year-old female patient

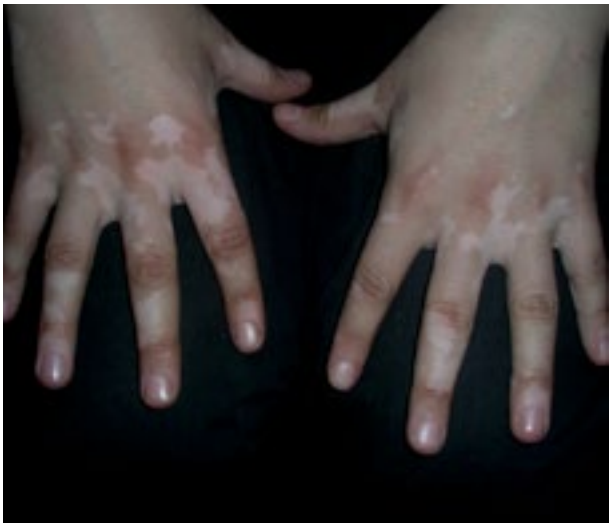

Figure 6. Initial lesions of vitiligo in a 16-year-old adolescent with Hashimoto thyroiditis

and adolescents with non-segmental vitiligo should undergo testing for: thyroid peroxidase antibodies (TPO-Ab), thyroglobulin antibodies (Tg-Ab), and thyroid-stimulating hormone (TSH) once a year (34 - 36).

Differential diagnosis

There may be difficulties in differential diagnosis of childhood vitiligo related to other diseases associated with hypopigmentation such as: pityriasis alba, tinea versicolor alba, postinflammatory hypopigmentation, piebaldism, morphea, leprosy and so on. In order to obtain correct diagnosis of vitiligo, it is necessary to know types of inheritance as well as characteristic signs and symptoms of the above-mentioned diseases (8, 37).

Treatment

Treatment of vitiligo should start with an agreement between the dermatologist and the patient, after treatment options and their efficacy are explained. The treatment option depends on the age of the patient and type of vitiligo (1, 2, 38, 39). Children and adolescents experience the disease differently, depending on their age, locality and severity of lesion distribution, as well as on their personal abilities and reactions of their family and social environment. If the disease has a negative effect on their overall appearance, affecting their self-esteem, they should seek psychological help (40 - 42). All patients suffering from vitiligo should avoid sun exposure and use photoprotection (1, 2).

Phototherapy

Phototherapy includes PUVA (Psoralen + UVA light) therapy, KUVA (Khellin + UVA light) therapy, UVB narrow-band therapy and laser phototherapy (4, 8).

Local PUVA therapy

Local PUVA therapy is recommended for the treatment of non-segmental vitiligo. However, its efficacy is limited to 50 – 60%; recurrences are frequent, as well as adverse effects such as burns and hyperpigmentation (39). This treatment modality is recommended to children with vitiligo affecting less than 20% of body surface, and in whom local therapy has not been successful (5, 6).

Local KUVA therapy

Local KUVA (Khellin + UVA light) therapy exhibits significantly less side effects, while its efficacy is similar (44%) to PUVA therapy (53%) (43).

Systemic PUVA therapy

Systemic PUVA therapy**,** due to its late adverse effects, should be used only in adolescents, particularly in those with 20 – 30% of body surface affected by vitiligo (8). The therapeutic efficacy is rather high (around 70%), but the treatment lasts from 12 to 18 months, twice a week, which requires high motivation and commitment of parents and children (5).

Narrow-band UBV therapy

Narrow-band UBV (311 nm) phototherapy, used both in active and stable generalized vitiligo in adults (efficacy of 63%), has also proven effective in studies including a limited number of children (efficacy of 53%). The cosmetic effects are more acceptable than with PUVA therapy, due to less hyperpigmentation of the surrounding skin (44 - 46). Further investigations concerning its efficacy and possible adverse reactions in children are necessary (8).

Laser therapy

Excimer laser phototherapy (308 nm) has proven successful in localized vitiligo in adults (efficacy of 53%), with less adverse effects in regard to PUVA therapy, but further investigations are needed concerning its safety in children (47, 48).

Local therapy

Corticosteroid therapy

Local corticosteroid therapy has proven efficient in 53% of adults and not more than 64% of children with vitiligo (4, 5, 8). If vitiligo lesions affect the trunk and extremities, local corticosteroid therapy with moderate potency is recommended, whereas low potency corticosteroids are used for facial lesions. The therapy should last at least 3 to 4 months, while better results are obtained in dark-skinned children. Unfortunately, local adverse effects are limiting this mode of treatment in children (4). Segmental vitiligo does not respond to local corticosteroid therapy.

Other local therapy modalities

Other local therapy modalities have limited effects when used as monotherapy, so these agents are mainly used in combination therapy of vitiligo (10). However, they have not been approved for vitiligo therapy by Food and Drug Administration (FDA) in the United States (8).

Melagenine is a human placental extract, which has shown to be effective in the vitiligo therapy in children with lesions affecting the scalp, exhibiting least adverse effects (49).

Calcineurin inhibitors (Pimecrolimus, Tacrolimus) are macrolide immunomodulators which were isolated from *Streptomyces tsukubaensis* in Japan. They are used as an alternative to local corticosteroid therapy, with significantly less adverse effects on sensitive skin regions (face, groin, perigenital region). Successful application of tacrolimus has been reported both in adults and children (efficacy of 41.3%) (50 - 52). Lepe and associates reported that monotherapy using pimecrolimus and tacrolimus showed efficient only in 25% of children with vitiligo (**52**). Tacrolimus has shown good therapeutic results in segmental vitiligo as well (53). According to one study report, tacrolimus caused local hypertrichosis (54). Further investigations on the efficacy and safety of calcineurin inhibitors in the therapy of childhood vitiligo are still necessary (8).

A combination of catalase enzymes and superoxide dismutase, a melon *(Cucumis melo)* extract, decreases the production of hydrogen peroxide by keratinocytes in vitiligo lesions. Topical use of gel containing this extract proved to be successful in 23.5% of vitiligo patients. Combined with narrow-band UVB phototherapy, repigmentation was achieved in 35.5% of patients with vitiligo, without any reported side effects (55).

Calcipotriol is a vitamin D analogue which induces melanogenesis through an unknown mechanism involving melanocytes 1-alpha-25 dihydroxy vitamin D3 receptors. It has been successfully used in the therapy of childhood vitiligo. Its most common side effect is local irritation (56). In a study including 18 children with vitiligo, complete repigmentation was reported in 10 (56%) after local application of calcipotriol (57). Significantly better results were achieved when it was combined with local corticosteroids (58).

Surgical therapy

Surgical therapy is indicated as a therapy of choice for patients with segmental vitiligo, but only in adolescents and adults (1, 2, 3, 10). The most common procedures include: ***epidermal grafting using the tops of suction, autologous skin grafting, and miniature punch grafting*** (1 - 3). *Autologous* ***skin*** *grafting* is popular in the management of focal and stable generalized vitiligo with an efficacy of 87% and 95%, respectively (38). This procedure is highly complicated and requires general anesthesia. Treatment results are better in the young, especially when combined with PUVA therapy, so it is recommended to adolescents with segmental vitiligo (8). Gupta and Kumar were successful in the treatment of vitiligo in adolescents, using *epidermal grafting and tops of suction*, combined with postsurgical phototherapy (59). Other surgical procedures, such as tattooing vitiligo lesions, are recommended only in focal vitiligo (60).

Depigmentation

Depigmentation of the remaining pigmented skin islands using monobenzyl ether of hydroquinone and 4-methoxyphenol cream is indicated only in adult patients with extensive vitiligo (loss of pigment over 40% of body surface), and universal vitiligo (1 - 4, 7, 8).

Cosmetic camouflage

Cosmetic camouflage products are inexpensive, easy to use and have no adverse effects (61). However, their use in children is limited, because most of these products are not water-proof and may be removed during play. On the other hand, some resistant products give no acceptable match for the surrounding, normally pigmented skin (5).

Conclusion

Vitiligo causes significant psychological and emotional distress in children and adolescents (5, 40 - 42). We can conclude that there are important differences in the epidemiology, comorbidity with other diseases, and therapy of vitiligo in children and adults. Results of recent research of vitiligo in children and adolescents point to the necessity of screening for thyroid dysfunction, especially for autoimmune thyroiditis (34 - 36). Phototherapy and local use of corticosteroids,

most commonly used in the management of vitiligo in adults, are less successful in children (8). Further clinical investigations are necessary to find efficient therapeutic procedures adjusted to the treatment of childhood vitiligo (8).

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Abbreviations

AIS - autoimmune susceptibility
FDA- Food and Drug Administration
HT - Hashimoto's thyroiditis
KUVA- khellin + UVA therapy
PUVA - psoralen + UVA
Tg-Ab - thyroglobulin antibodies
TPO –Ab – thyroid peroxidase antibodies
TSH - thyroid-stimulating hormone

Vitiligo kod dece i omladine - pregled literature

Sažetak

Uvod: Vitiligo je stečeno oboljenje, najverovatnije autoimune prirode, ponekad sa jasnom naslednom komponentom, koje se karakteriše progresivnim, jasno ograničenim, mlečnobelim mrljama na koži i/ili sluzokožama (1,2).
Epidemiologija: Vitiligo je prvenstveno bolest mladih, kod polovine svih obolelih javlja se pre 20 godine života. Epidemiologija vitiliga kod dece je slična kao kod odraslih sa vitiligom, ali za razliku od odraslih sa vitiligom, gde je učestalost javljanja kod oba pola približno ista, kod dece se vitiligo češće javlja kod devojčica. U porodičnoj anamnezi

obolele srodnike ima 12 do 35% obolele dece, za razliku od oko 8% odraslih bolesnika sa vitiligom.
Generalizovani vitiligo je najčešći tip vitiliga i kod dece i kod odraslih. Navodi se da 33% do 78% dece sa vitiligom ima generalizovani oblik bolesti, 14,4% do 34,6% ima fokalni vitiligo dok se segmentni vitiligo značajno češće javlja kod dece nego kod odraslih. Prevalenca segmentnog vitiliga kod dece iznosi oko 20%, a kod odraslih svega 5%. Akrofacijalni (7,6%) i univerzalni vitiligo (0,4%) se ređe viđaju kod dece.
Etiologija i patogeneza: Poznato je da genetski faktori imaju izvesnu ulogu u nastanku vitiliga. Kod bolesnika sa ranim početkom vitiliga (pre 30 godine), vitiligo je uslovljen dominantnim načinom nasleđivanja, sa nekompletnom penetracijom. Međutim, kod bolesnika sa kasnim početkom vitiliga (posle 30 godine), predispozicija za vitiligo je rezultat recesivnog genotipa i uticaja spoljašnje okoline. Raniji početak vitiliga (do 7 godine) utvrđen je i kod dece sa vitiligom i pozitivnom porodičnom anamnezom za vitiligo.
Kao moguće teorije patogeneze vitiliga navode se: autoimuna, teorija oksidativnog stresa i neurogena teorija. Autoimuna teorija ima najčvršću podlogu u kliničkim i bazičnim istraživanjima. Neka istraživanja pokazuju da je povećana učestalost autoimunog tireoiditisa kod pacijenata sa vitiligom genetski determinisana. Lokus AIS1 (eng. ***a***uto***i***mmune ***s***usceptibility) na hromozomu 1, odgovoran je za sklonost ka autoimunom reagovanju, naročito za vitiligo, a uz sadejstvo različitih spoljašnjih ili unutrašnjih faktora, može posredovati u nastanku Hashimoto tireoiditisa. Poznato je takođe da geni na hromozomu 17p13 doprinose nastanku određenih automunih bolesti npr.generalizovanog vitiliga i autoimunog tireoiditisa. Novija istraživanja opisuju NALP1 protein, kao produkt gena koji reguliše intaktnost imunog sistema. Promene u nizu DNA u oblasti NALP1, udružene su sa povećanim rizikom za nastanak generalizovanog vitiliga i/ili drugih združenih autoimunih bolesti, kao što je autoimuni tireoiditis. Smatra se da autoimuni mehanizmi imaju ključnu ulogu za nastanak nesegmentnog vitiliga. U melanocitima aktivnog vitiliga ustanovljeno je povećanje oksidanata kao i deficit antioksidantnih enzimskih sistema, sa posledičnim oksidativnim oštećenjem melanocita, na čemu se bazira teorija oksidativnog stresa. Nastanak segmentnog vitiliga najbolje se može objasniti neurogenom teorijom, prema kojoj se iz nervnih završetaka oslobađaju neurohemijski medijatori, koji inhibišu melanogenezu ili imaju toksično dejstvo na melanocite uništavajući ih. Segmentni vitiligo je izuzetno retko udružen sa autoimunim bolestima.
Udruženost sa endokrinim i/ili autoimunim oboljenjima: Vitiligo se može javiti pre, istovremeno ili posle nastanka endokrinih i/ili autoimunih bolesti. Epidemiološke studije, rađene na velikom broju dece sa vitiligom, nisu pokazale povećan rizik oboljevanja od navedenih oboljenja. Za razliku od odraslih, kod dece i adolescenata sa nesegmentnim vitiligom dokazana je povećana učestalost isključivo Hashimoto tireoiditisa. S obzirom da vitiligo najčešće prethodi pojavi tireoiditisa, predlaže se da se kod dece i adolescenata sa nesegmentnim vitiligom jednom godišnje uradi skrining na tireoperoksidazna, tireoglobulinska antitela i tireostimulišući hormon.
Diferencijalna dijagnoza: Kod dece mogu postojati diferencijalno dijagnostičke poteškoće u odnosu na druge bolesti koje su praćene hipopigmentacijom, kao što su: pityriasis alba, tinea versicolor varietas alba, postinflamatorne hipopigmentacije, pijebaldizam, morfea, lepra i druge.
Terapija: Izbor terapijske opcije zavisi od uzrasta bolesnika i tipa vitiliga. Kod svih obolelih od vitiliga neophodna je primena mera zaštite od sunčevog zračenja i korišćenje fotoprotektivnih sredstava.
Lokalna primena PUVA (psoralen + UVA zraci) terapije se preporučuje za lečenje nesegmentnog vitiliga, ali je efikasnost ograničena na 50-60% i česti su recidivi vitiliga, kao i neželjeni efekti u vidu opekotina i hiperpigmentacija. Ovaj vid terapije se preporučuje kod dece kod koje vitiligo zahvata manje od 20% površine tela i kod kojih nije bila uspešna lokalna terapija.

Lokalna primena KUVA terapije (khellin + UVA zraci) ima znatno manje neželjenih efekata, a efikasnost je slična (44%) kao kod sistemske PUVA terapije (53%).

Sistemska primena PUVA terapije je zbog svojih kasnih neželjenih efekata ograničena na uzrast adolescenata kod kojih vitiligo zahvata više od 20-30% površine tela. Terapijska efikasnost je visoka (oko 71%), ali lečenje traje 12 do 18 meseci, dva puta nedeljno.

Fototerapija UVB zracima uskog spektra (311 nm), koja se primenjuje kod aktivnog ali i stabilnog generalizovanog vitiliga kod odraslih (efikasnost 63%), se pokazala uspešnom (efikasnost 53%) i u studijama sa ograničenim brojem dece. Kozmetski efekat je bolji nego kod PUVA terapije, jer je manje izražena hiperpigmentacija okolne kože.

Fokusirana laserska fototerapija (308 nm) se pokazala uspešnom kod lokalizovanog vitiliga u odraslih (efikasnost 53%), sa manje neželjenih efekata od PUVA terapije, ali su neophodna dalja ispitivanja o bezbednosti primene kod dece.

Lokalna kortikosteroidna terapija se pokazala uspešnom kod 53% odraslih i najviše 64% dece sa vitiligom. Lečenje treba sprovoditi najmanje 3 do 4 meseca, a bolji rezultati se postižu u tamnoputе dece. Segmentni vitiligo ne raeguje na lokalnu terapiju kortikosteroidima.

Drugi vidovi lokalne terapije imaju ograničeno dejstvo kao monoterapija, pa se navedeni lekovi uglavnom koriste u kombinovanoj terapiji vitiliga. Međutim, oni nisu prihvaćeni za terapiju vitiliga, od strane FDA (engl. *Food and Drug Administration*) u USA: melagenin koji predstavlja ekstrakt humane placente, se pokazao uspešnim u terapiji vitiliga poglavine kod dece, uz minimalne neželjene efekte; kalcineurin inhibitori (pimekrolimus, takrolimus) se mogu koristiti u područjima osetlijve kože (lice, prepone, perigenitalna regija). Uspešna primena takrolimusa je opisana i u odraslih i u dece (efikasnost do 41,3%), kao i u lečenju segmentnog vitiliga. Može se razviti lokalna hipertrihoza na mestu aplikacije takrolimusa; kombinacija enzima katalaze i superoksid dizmutaze ekstraktovanih iz posebne vrste dinje *(Cucumis melo),* smanjuje proizvodnju hidrogen peroksida od strane keratinocita u lezijama vitiliga. Opisana je uspešna lokalna primena ovog ekstrakta, u obliku gela, u 23,5% obolelih od vitiliga, u kombinaciji sa UVB zracima uskog spektra, repigmentacija je postignuta u 35,3% pacijenata sa vitiligom, pri čemu nisu zabeleženi neželjeni efekti; kalcipotriol stimuliše melanogenezu nepoznatim mehanizmom delujući na 1- alfa- 25 dihidroksi- vitamin D3 receptore melanocita. Sa uspehom (kompletnu repigmentaciju u 56%) je korišćen u terapiji vitiliga kod dece, a kao neželjeni efekat se navodi lokalna iritacija. Znatno bolji rezultati su postignuti u kombinaciji sa lokalnom primenom kortikosteroida.

Hirurško lečenje je terapija izbora za segmentni vitiligo ali isključivo kod adolescenata i odraslih osoba. Najznačajnije metode su: presađivanje epiderma dobijenog sukcijom, metoda autolognog kožnog grafta, i metoda minitransplantacije *punch* biopsijama. Metoda autolognog kožnog grafta se pokazala uspešnom kod fokalnog i stabilnog generalizovanog vitiliga. Efikasnost je između 87% i 95%. Postupak je veoma komplikovan i podrazumeva opštu anesteziju. Uspešnije je kod mlađih, naročito u kombinaciji sa PUVA terapijom, pa se savetuje adolescentima sa segmentnim vitiligom. Opisani slučajevi uspešnog lečenja vitiliga kod adolescenata, metodom presađivanja epiderma dobijenog sukcijom, uz naknadnu fototerapiju. Primena tetovaže vitiligo lezija, se preporučuju samo kod fokalnog vitiliga.

Depigmentacija malobrojnih, preostalih pigmentovanih delova kože, upotrebom monobenzil etar hidrokvinona i 4-metoksi-fenola u vidu krema, primenjuje kod ekstenzivnog (gde vitiligo zahvata više od 40% površine tela) i univerzalnog vitiliga i to isključivo kod odraslih osoba.

Kozmetička kamuflažna sredstva su relativno jeftina, laka za upotrebu i nemaju neželjenih efekata. Njihova upotreba kod dece je ograničena stoga što većina ovih preparata nije vodootporna i lako se mogu skinuti tokom dečje igre.

Zaključak**:** Možemo zaključiti da postoje značajne

razlike u epidemiologiji, udruženosti sa drugim oboljenjima i terapiji vitiliga kod dece i odraslih. Rezultati najnovijih istraživanja vitiliga kod dece i adolescenata ukazuju na potrebu skrininga na tireoidnu disfunkciju, posebno na autoimuni tireoiditis. Fototerapija i lokalna primena kortikosteroida, predstavljaju terapijske modalitete koji se najčešće koriste u lečenju vitiliga kod odraslih, ali se njihova primena pokazala manje uspešnom u lečenju vitiliga kod dece.

Ključne reči

Vitiligo; deca; adolescenti

LA ROCHE-POSAY
LABORATOIRE DERMATOLOGIQUE

LIPIKAR BAUME AP

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Balzam za telo koji koži vraća lipide. Deluje protiv iritacije i svraba.
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Namenjena izuzetno suvoj i koži sklonoj atopiji beba, dece i odraslih.

La Roche-Posay brine o Vašoj koži,
i zato vam ekskluzivno nudi negu
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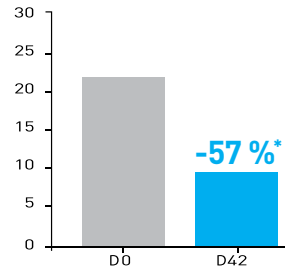
po ceni 2070 DIN
u svim ovlašćenim apotekama.*

* Cena je informativna i može odstupati zavisno od pravilnika cena apoteke.

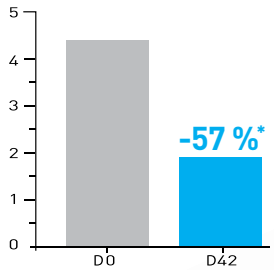
Značajno smanjenje SCORAD indeksa i svraba

SMANJEN SCORAD INDEKS
(atopijski dermatitis)
Rezultat: 0 do 103



*p<0,001

SMANJEN SVRAB
Rezultat: 0 do 10



VISOKA KONCETRACIJA AKTIVNIH SASTOJAKA

→ NIACINAMID
→ KARITE MASLAC
→ GLICEROL
→ ULJE KANOLE

BEZ MIRISA / BEZ PARABENA

VISOKA TOLERANCIJA

Brzo upijajuća tekstura, koja pospešuje redovnu upotrebu i omogućava oblačenje odmah nakon nanošenja.

Ekskluzivni polimer omogućava visoku koncetraciju aktivnih sastojaka, koji koži vraćaju lipide, u teksturi koja se brzo upija.

Formula O/V
Nemasna, nelepljiva tekstura

Protokol:
Multicentrično ispitivanje (5 centara) sproveo je u Kanadi prof. Bissonette na 73 pacijenta (uzrasta od 3 do 12 godina) koji boluju od blagog do umerenog atopijskog dermatitisa (SCORAD ≤ 30). Dva nanošenja dnevno.
Procena tolerancije i efikasnosti (SCORAD) 42. dana u poređenju sa nultim danom

La Roche-Posay. Posvećen dermatologiji.

Genital superficial basall cell carcinoma - a case report

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UDC 616.5:616.66]-006.6

Abstract

Basal cell carcinoma (BCC) is the most common type of skin cancer in the Caucasian population. However, BCC of the genitalia is extremely rare. To the best of our knowledge, only 30 patients with BCC of the genitalia have been reported in the literature so far. BCC usually occurs in individuals over the age of 50, on sun-exposed areas of the body, and it is more prevalent in females. Superficial BCCs account for approximately 10% of BCC, and are commonly found on the trunk or limbs. This is a report on a 55-year-old male patient with penile BCC, and a literature review on this condition. The patient presented with asymptomatic skin lesions in the genital area which progressed during the last 15 years. Before admission, the patient received: antimycotics, antiviral, antibacterial and corticosteroid therapy, but without any improvement. Examination of the proximal penile skin revealed a sharply marked, smooth and shiny erythematous plaque of about 3.3 x 2 cm, with whitish squamae in the central zone. The histopathology finding revealed a superficial BCC and total excision was recommended. Treatment of the superficial BCC depends on its size and location. It includes surgical removal with possible reconstruction, radiotherapy, application of immunomodulators, local chemotherapy and local retinoid therapy. Although this is an extremely rare type of BCC, it is important to keep in mind that it may affect body areas seldom exposed to direct sunlight.

Key words

Carcinoma, Basal Cell; Genital Neoplasms, Male; Penile Neoplasms

Basal cell carcinoma (BCC) is the most common non-melanoma skin cancer in Caucasian population (1). BCCs frequently occur on sun-exposed areas of the body, and they are slow growing, locally invasive and rarely metastasize. However, on rare occasion these tumors may occur in areas of the body seldom exposed to the sun (2). Superficial BCCs account for approximately 10% of BCC, and are commonly found on the trunk or limbs (3). Ultraviolet light exposure may be an important etiologic factor for BCCs located on sun-exposed areas (1). Occurrence of BCCs on sun-protected areas raises the possibility of other, etiologic factors, not clearly defined yet (1, 4). The likelihood of developing BCC increases with age, and BCC is rarely found in patients under than 40 years of age (1).

Case report

We report a case of a 55-year-old uncircumcised male patient with asymptomatic, slowly progressive, atrophic plaque on the proximal part of the penile skin (Figure 1 and 2). The patient believed that the lesion first appeared 15 years before admittance. It was misdiagnosed and treated with topical corticosteroids, antifungal, antiviral and antibacterial agents, without any improvement. He

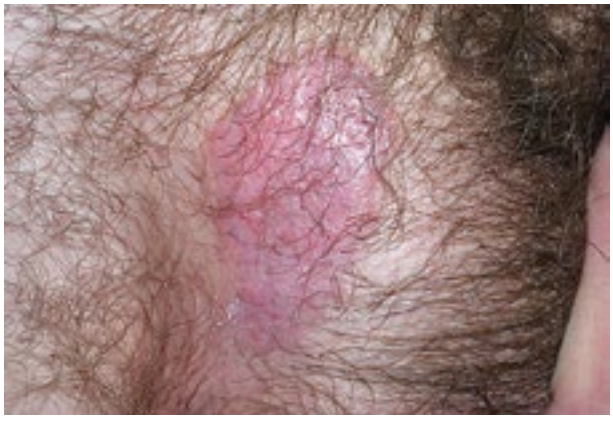

Figure 1. Erythematous plaque on the proximal penile skin

denied sun-bathing and radiation exposure. He had no history of other skin diseases, arsenic exposure or getting sunburned. His personal and family histories were negative for skin cancer. At the time of physical examination, the patient presented with a 3.3 x 2 cm atrophic plaque on the proximal part of the penile skin, without lymphadenopathy or abnormalities in the complete blood count (CBC), serum and urinanalysis. He had Fitzpatrick type II skin with no signs of excessive sun damage. Examination of the entire skin revealed no other lesions suspicious for malignancy. The biopsy showed a discontinuous layer of tumor cells connected to the epidermal basal cell layer, extending down into the papillary dermis (Figure 3). The diagnosis of superficial BCC was established and a surgical excision was recommended.

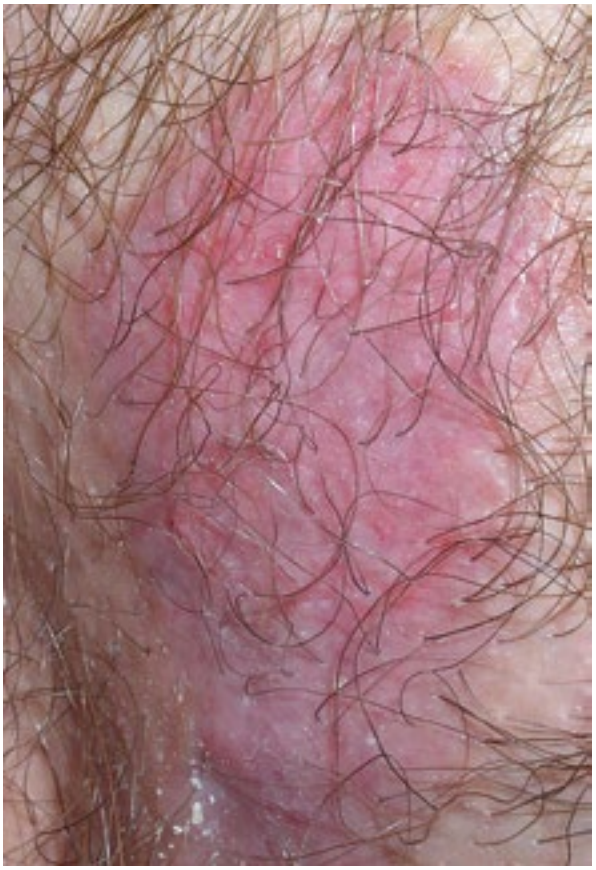

Figure 2. Erythematous shiny plaque with elevated borders

Discussion

BCC is a subtype of nonmelanoma skin cancer, with an increasing incidence worldwide and it is the most common cutaneous malignancy in humans (1). Although BCC most frequently develops on the head and neck, approximately 20% of BCCs occur in sun-protected areas (2). BCC, particularly superficial BCC, arising on the genitalia, as found in our patient, is extremely rare (5). Superficial BCC commonly presents as erythematous maculo-papular lesion or thin plaque, and it may be difficult to differentiate it clinically from benign inflammatory lesions, extramammary Paget's disease, actinic keratosis or spinocellular carcinoma in situ (1, 3). The mean age at diagnosis is 57 years.

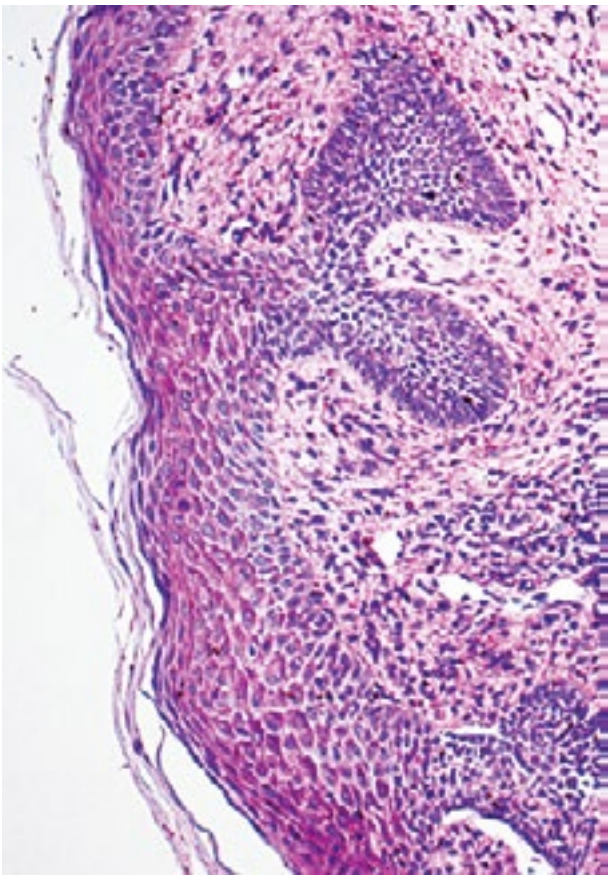

Figure 3. Discontinuous layer of tumor cells connected to the epidermal basal cell layer, extending down into the papillary dermis (HE x 50)

There is strong evidence that ultraviolet light plays a central role in the molecular pathogenesis of non-melanoma skin cancer development (1). Apart from this, exposure to arsenic, present in drinking water or in medications, increases the risk of BCC (6). Our patient denied prolonged sun exposure, radiation exposure or arsenic intake. Neglected tumors can lead to significant local destruction and even disfigurement. That is why early diagnosis and

adequate treatment are nessecary in order to prevent relapse and metastasis (7). The most common sites of metastasis are the lymph nodes, lungs, and bones.

The diameter of lesions varies from a few millimeters to several centimeters. The growth pattern is primarily horizontal, but these tumors can be deeply invasive with induration, ulceration and nodule formation.

Our patient had a representative histopathology of superficial BCCs: buds of tumor attached to epidermis, extending down into the papillary dermis. Clear peripheral palisading were also present (Figure 3).

The first line treatment is usually surgical excision, as recommended to our patient, but numerous alternatives (3) such as immunomodulators (8), topical chemotherapeutic agents (8) and photodynamic therapy (9) are available. Combination of several therapeutic modalities improves the overall treatment efficacy, minimizing adverse effects and maximizing cosmetic results.

Conclusion

BCC, especially genital superficial BCC, is extremely rare. To the best of our knowledge, about 30 cases of genital BCC have been reported in the literature so far. We believe that it is important to increase awareness of physicians relating to this rare clinical presentation of non-melanoma skin cancer, since early diagnosis and adequate treatment are essential to prevent both recurrence and metastasis.

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Abbreviations

BCC – Basal Cell Carcinoma
CBC – Complete Blood Count

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Bazocelularni karcinom kože u genitalnoj regiji - prikaz slučaja

Sažetak

Uvod: Epithelioma basocellulare (EB) najčešći je maligni tumor kože kod čoveka bele rase. Karakterišu ga spor rast i dobra prognoza. Tumor je lokalno invazivan, retko metastazira i pojavljuje se isključivo na zonama gde postoje folikuli dlake. Značajnu ulogu u etiopatogenezi ima izlaganje UV zracima. Incidencija EB je značajno porasla tokom poslednjih nekoliko godina. Najčešća lokalizacija Epithelioma basocellulare superficiale (EBS) jesu trup (zadnja strana) i vrat. EBS se najčešće javlja pre pedesete godine života, češći je kod žena.
Prikaz slučaja: Prikazujemo pacijenta u dobu od 55 godina sa anamnestičkim podatkom o asimptomatskoj promeni na koži u genitalnoj regiji koja se polako povećava tokom poslednjih petnaestak godina. Pre pregleda u ambulanti IDV lečen je antimikoticima, antivirusnim, antibakterijskim i kortikosteroidnim preparatima za lokalnu primenu – bez uspeha. Pregledom je na koži proksimalnog dela korpusa penisa ustanovljeno prisustvo glatkog, sjajnog eritematoznog plaka promera 3,3 x 2 cm sa naglašenim rubom i beličastom skvamom u centralnoj zoni.
HP pregledom isečka uzetog sa promene postavljena je dijagnoza EBS. Savetovana je ekscizija in toto.

Lečenje EBS zavisi od lokalizacije i veličine promene. Dostupne metode su hirurško uklanjanje sa eventalnom rekonstrukcijom, radioterapija, upotreba imunomodulatora, hemioterapeutika za lokalnu primenu i sintetskih retinoida za lokalnu primenu.
Komentar: Lokalizacija EB u genitalnoj regiji, posebno EBS je veoma retka. Na osnovu naših saznanja, do sada je u svetu obavljeno manje od 30 pacijenata sa BCC u genitalnoj regiji. S obzirom da se radi o retkoj formi EB, neophodno je da se skrene pažnja kliničarima na mogućnost razvoja karcinoma kože na delovima tela koji nisu direktno izloženi sunčevim zracima.

Ključne reči

Bazocelularni karcinom; genitalni tumori muškaraca; tumori penisa

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History of dermatology and venereology in Serbia – part IV/3: Dermatovenereology in Serbia from 1919 – 1945, part 3

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Abstract

The seven years' war (1912 – 1918) and epidemics of infectious diseases, led to a great loss of lives and medical corps of Serbia. As already stated, venereal and skin diseases were spreading in the postwar period that can be seen from medical reports of dermatovenereology institutions. They contain appropriate pathologies and some specific conditions under which they developed. In dermatovenereal pathology, venereal diseases were still dominating. In the *Outpatient Clinic for Skin and Venereal Diseases,* 10.000 patients were examined during the period from 1919 to 1921, venereal diseases accounted for 73.13%, whereas skin diseases accounted for 26.87% of all established diagnoses. A similar distribution existed at the territory of Serbia (Belgrade excluded) in 1931: venereal diseases accounted for 73.4%, and skin diseases for 26.6%; moreover, in Belgrade, the situation was even more drastic: venereal diseases accounted for 84.7%, and skin diseases for 15.3%. However, in the student population, the distribution was reversed: 43% and 57%, respectively. In regard to venereal diseases, in the series from 1919 to 1921, non-endemic syphilis was the most common disease, if serologically positive cases (latent syphilis) were added up to the clinically manifested cases. In the same series of patients, syphilis was staged as follows: syphilis I in 10%, syphilis II in 29.3%, syphilis III in 1.7%, tabes dorsalis in 0.8%, and latent syphilis in 56% of patients. In regions with endemic syphilis, from 1921 to 1925, the distribution was as follows: syphilis I in 4%, syphilis II in 49.8%, syphilis III in 18.3%, hereditary syphilis in 1.3%, and latent syphilis in 26.5% of patients. In patients suffering from gonorrhea, balanitis was found in 4.5%, and arthritis in 0.43% of cases. Generally, spreading of prostitution had a significant role, and its abolition was an important preventive action. In regard to skin diseases, in the above-mentioned series of patients, treated at the *Outpatient Clinic for Skin and Venereal Diseases* (1919 – 1921), scabies was the commonest skin disease (26.7%), eczemas were the second most common (21.8%), followed by pyococcal diseases (20.4%), while fungal diseases (4.5%) and skin tuberculosis (1.9%) were considerably less frequent.
This is the final report about the foundation of modern dermatovenereology in Serbia.

Key words

History of Medicine; History, 20th Century; Dermatology; Venereology; Serbia

The seven years' war (1912 – 1918) and epidemics of infectious diseases, led to a great loss of lives and medical corps of Serbia. As already stated, venereal and skin diseases were spreading in the postwar period that can be seen from medical reports of dermatovenereology institutions. They contain appropriate pathologies and some specific conditions under which they developed.

Dermatovenereology diseases

During the third and fourth decades of the 20th century, venereal diseases still prevailed in regard to skin diseases. According to the report of Đ. Đorđević, in the newly opened *Outpatient Clinic for Skin and Venereal Diseases* (OCSVD) in Belgrade, from July 16, 1919 to May 15, 1921, 10.000 patients were examined for the first time: venereal diseases were

established in 7.313 (73.13%), and dermatoses in 2.687 (26.87%) patients. Although detailed analysis of this report showed that given statistics were not quite accurate, globally, they were still indicative (1). Ten years later, in 1931, in the territory which roughly corresponded to today's Serbia (Belgrade excluded), 7.136 dermatovenereological patients underwent outpatient examination, and similar results were obtained: 73.4% of patients suffered from venereal diseases, and 26.6% had dermatoses (2). In the same year, in the OCSVD in Belgrade, venereal diseases accounted for 84.7%, and dermatoses for 15.3% of diseases (2). It is clear that venereal diseases markedly prevailed over dermatological. However, it seems that the situation was different in the young population: during the academic year 1938/39, 43% of students suffered from venereal diseases, and 57% had dermatoses (3).

Venereal Diseases

According to the above-mentioned report of the OCSVD (1919 – 1921), clinical and laboratory findings verified 4.777 patients with venereal diseases: syphilis (SY) in 1.929 patients (40.3%), gonorrhea (GO) in 1.838 (38.5%), Ulcus molle (UM) in 582 (12.2%) patients, whereas 428 (9%) patients presented with suspected changes or other venereal diseases. According to specified numbers and percentages, the number of patients with GO and SY was almost the same. The author of this report, Prof. Dr. Đ. Đorđević, considered this conclusion incorrect and he stated his reasons. Out of the total number of examined patients (10.000), 2.536 patients presented without clinical symptoms of venereal diseases. However, as they took the Wassermann test, which proved to be positive in a great number of patients, according to Đ. Đorđević, they should have been included in the group of patients with (latent) syphilis. Apart from this, there were 256 cases with the following diagnoses: erosion, phimosis, edema and so on, which mostly belonged to the SY group, in the opinion of Đ. Đorđević (1). Hence, SY was significantly more frequent than GO. Đ. Đorđević, a leading dermatovenereologist, included conditions, under which they had to work at that time, into his conclusion (which is probably correct) and they are as follows: postwar period, the service just began with organized work; recording of laboratory results was improvised and insufficient. In our opinion, basically, his conclusions were realistic.

In the group of students from Belgrade (academic year 1938/39) the situation was once again different than in general population: GO accounted for 65%, SY for 7%, and other venereal diseases for 28% of diseases (3).

Syphilis

According to V. Mihailović, from 1923 to 1927, SY remained at a high level in general population: in 10.000 inhabitants it accounted from 16.4% to 25.8%, with an irregular and uneven increase in the number of patients (4). It is hard to explain such a high incidence, because some basic data are missing, although given by an experienced dermatovenereologist. However, they cannot be rejected, because 20 years later, when eradication of SY started, the average percentage of infection for all the investigated parts of Serbia was 5.32%, although in some endemic regions of the North-East Serbia it was over 30% (5). Certain types of SY outside the endemic regions were found in the above-mentioned series of OCSVD (1919-1921): SY I was found in 10%, SY II in 29.3%, SY III in 1.7%, congenital SY in 1.9%, tabes dorsalis in 0.8%, and latent SY in 56.3% (1). In the North-East Serbia, region with endemic syphilis, from 1921 to 1925, out of the total number of outpatients and hospitalized persons, there were 1.757 infected patients: SY I in 4%, SY II in 49.8%, SY III in 18.3%, hereditary SY in 1.3%, and latent SY in 26.5% of patients. Such a small percentage of hereditary syphilis is unrealistic, due to the fact that only children above the age of two were examined (6). A low percentage of SY I was observed in both groups, especially in endemic regions, which is probably the consequence of discrete, hidden and spontaneously resolved lesions, due to which patients rarely sought medical treatment. SY II had a significantly higher incidence in both groups, especially endemic SY – being the consequence of untreated primary stage, and the fact that patients with SY II often sought medical help. Late SY in the non-endemic type is characterized by high percentage of latent syphilis, whereas SY III and latent SY were more frequent in the endemic type. These results have only an approximate value, which was inevitable in the postwar period. In 1929, due to a number of

problems associated with venereal diseases the Third Yugoslav Dermatovenereology Congress made a decision to seek a new law against venereal diseases from the *Ministry of Social Policy and Public Health* (4).

Gonorrhea and Ulcus Molle

In the series of the OCSVD (1919 - 1921), there are no data on types of GO (acute, sub-acute, chronic), but 83 cases (4.5%) of epididymitis and 8 cases (0.43%) of arthritis are reported. The author pointed out that the number of infected women was small; the symptoms were often overlooked, and women sought gynecological services after a longer period of time (1). Ulcus molle also appeared as Ulcus mixtum, but there are no statistical data about it (1). It could be argued that in these diseases questions asked could be more important than the data obtained.

In organizing a network of dermatovenereological health institutions, with introduction of current diagnostic, therapeutic and education measures, prevention of venereal diseases remained the central activity of these services, as well as of research studies, up to the era of antibiotics. These activities were also part of the programs of national congresses; at the II Yugoslav Dermatovenereology Congress, the three main topics dealt with syphilis (7); at the III Congress, three topics were about venereal, and two about skin diseases (4).

Prostitution

As prostitution was spreading during the war, in order to control venereal diseases, in 1926 the OCSVD issued *"Temporary Measures for the Prevention of Venereal Diseases"*, based on which brothels were closed, prostitution was no longer regulated by the police, but by health institutions, and medical check-ups and personal booklets were mandatory for prostitutes. Hidden prostitution was also controlled, because it caused infections in almost 80% of cases. In the period from March 1, 1919 to October 1, 1921, 408 women were under health control. Out of this number, 222 were exiled or departed on their own, and 96 were released. However, during the 3-year follow-up**,** from 408 women, only one was healthy and all the rest were infected and received treatment on regular basis (1). Legalization of prostitution used to have opponents earlier as well, but it was finally accepted (8), while prostitution was considered primarily as a social, not a medical or police problem (9). It was finally abolished by bringing the *Law on Eradication of Venereal Diseases* in 1934 (8).

Skin Diseases

The already mentioned report of the OCSVD (1919 - 1921), includes a great variety of dermatological diagnoses (out of 10.000 patients, there were 2.687 with skin diseases). The most common was scabies, accounting for 26.7% (1), which remained a problem in the future as well, so in 1936, in the frame of the *Municipal Disinfection Institute* in Belgrade, a *Section for the Treatment and Eradication of Scabies* was founded. Six thousand examinations were performed by this Section, and there were 1.401 infected individuals (10). Dermatitis and eczema (21.8%) were the second most common skin diseases, followed by pyococcal diseases (20.4%) (1). Fungal diseases (4.5%) were unexpectedly rare (1), but in 1938 M. Kićevac insisted on a systemic fight against venereal diseases, as well as against the initial stages of carcinomas, and mycotic diseases (11). Skin tuberculosis was also rare (1.9%), particularly in relation to tuberculosis of other organs (1). Pemphigus vulgaris, dermatitis herpetiformis, lupus erythematodes and other diseases were reported only as individual cases. It seems that pellagra was quite common, because in 1926, a decision was made to treat patients with pellagra free of charge, regardless of their social status (2).

Based on the participation of Serbian dermatovenereologists in the work of the Serbian Medical Society and meetings abroad, as well as on data available in the Clinical Library, which still keeps substantial textbooks and journals from the last decades of the nineteenth and first decades of the twentieth centuries, and based on the analysis of the Belgrade moulage collection (13), it is evident that Serbian dermatovenereology followed development of the profession in the world.

Conclusion

This is the final report about the foundation of modern dermatovenereology in Serbia. In the limited scope of this paper, it was impossible to deal with all the analyses, so we chose to deal with important

facts which pointed to the complexity of organization of our sanitary service. This process has proved that during the last twenty years, between the two world wars, dermatovenereology in Serbia has overcome hard times which were imposed in its long, turbulent history, and accepted current medical thought, created in the course of almost two centuries.

Finally, we wish to say that in this type of work mistakes are inevitable, either because of incomplete, lost or contradictory data, due to inaccessible or under-researched sources, or because of incorrect assessment, which may be objective, but also subjective. That is why we have always had in mind the thought of Iwan Bloch: The history should always be written from the beginning (14).

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Abbreviations

GO –Gonorrhea
SY – Syphilis
UM – Ulcus Molle
OCSVD – Outpatient Clinic for Skin and Venereal Diseases

Istorija dermatologije i venerologije u Srbiji - IV/1-3: Dermatovenerologija u Srbiji u periodu 1919 - 1945.

Sažetak

Zakonodavstvo i organizacija dermatovenerološke službe: Posle Prvog svetskog rata Srbija je ostala opustošena i razrušena, a organizacija zdravstvene službe bila je uništena. Organizacija i reorganizacija zdravstvene službe počela je borbom protiv zaraznih bolesti koje su se širile. Otvaranje specijalističkih zdravstvenih ustanova bio je jedan od prvih zadataka. Zdravstvene ustanove: Već 1920. godine otvorena je *Ambulanta za kožne i venerične bolesti* sa šefom prof. dr Đorđem Đorđevićem. On je 1922. godine osnovao *Kliniku za kožne i venerične bolesti* i bio njen prvi direktor. *Opštinska ambulanta za kožne i venerične bolesti* osnovana je 1928. a 1938. Godine uz novu zgradu dobila je savremenu organizaciju službe. *Kožnoveneričnо odeljenje Opšte vojne bolnice* u Beogradu, otvoreno 1909. radilo je do Prvog svetskog rata, kada je *Opšta vojna bolnica*, pod austrijskom okupacijom, postala *Das K. und K Reservspital Brško*. Posle rata, Odeljenje nastavlja s radom do početka II svetskog rata. Od 1941. do 1944. godine ponovo

okupatorska vlast koristi Glavnu vojnu bolnicu za svoje potrebe. *Odeljenje za kožne i venerične bolesti* (100 kreveta) pri *Opštoj državnoj bolnici* (ODB), kao i samostalnu *Državnu ambulantu* za besplatno lečenje veneričnih bolesnika u Novom Sadu, osnovao je 1921. godine dr Jovan Nenadović, prvi Srbin dermatovenerolog u Vojvodini. On je rukovodio obema ustanovama. Napominjemo da je 1909. godine bila otvorena u Novom Sadu *Gradska bolnica* sa *Dermatovenerološkim odeljenjem*, ali posle Prvog svetskog rata oboleli od kožnih i veneričnih bolesti nisu imali gde da se leče.

Prva *Organizaciona jedinica za venerične bolesti* u Nišu osnovana je 1912. godine; *Venerično odeljenje* sa *Ambulantom* nastalo je 1921. godine; njime je rukovodio dr Petar Davidović. *Kožno-venerično odeljenje* pri Opštoj državnoj bolnici u Nišu otvoreno je 1927. godine, od kojeg će posle osnivanja Medicinskog fakulteta u Nišu (1960. godine), postati nastavna baza. Prvi šef Odeljenja bio je dr Petar Zurin, dermatovenerolog. Dermatovenerološko odeljenje Vojne bolnice u Nišu osnovano je 1920. godine. Na inicijativu prof. dr Đorđa. Đorđevića, 1921. godine u Srbiji su radile kompletne ambulante u Nišu, Petrovcu, Užicu, Boljevačkom srezu, Subotici, Velikom Bečkereku i Mitrovici. Već 1923. godine u bolnicama opšteg tipa postojalo je 14 veneričnih i jedno kožno-venerično odeljenje, u Subotici. Uočljivo je da su odeljenja nazivana *venerična*, kao što su i lekari specijalisti nazivani *venerolozi*, što još jednom pokazuje da su venerične bolesti i dalje bile glavni dermatovenerološki problem.

Lekari: Posle Prvog svetskog rata u organizaciji zdravstvene službe, pored nedovoljnog broja bolnica, postojao je i nedovoljan broj lekara. Oba problema bila su neposredno povezana sa dermatovenerologijom. Za razvoj dermatovenerologije kao savremene discipline, najznačajniji doprinos dali su prof. dr Đorđe Đorđević, koji je bio prvi direktor *Klinike za kožne i venerične bolesti*, u Beogradu (1922-1935), i njegov najbliži saradnik i naslednik prof. dr Milan Kićevac (1935-1940). U timskom radu, oni su koncipirali zakonske propise, organizovali suzbijanje veneričnih bolesti i prostitucije i postavili temelje stručnoj i naučnoj dermatovenerologiji u Srbiji.

Prof. dr Đorđe Đorđević je 1922. godine bio glavni osnivač dve institucije značajne za srpsku dermatovenerologiju – *Klinike za kožne i venerične bolesti* (KKVB), čiji je bio direktor, i *Katedre za dermatovenerologiju,* kao prvi nastavnik dermatovenerologije na *Medicinskom fakultetu* u Beogradu. Prof. dr Đorđe Đorđević je 1927. godine učestvovao i u osnivanju *Dermatovenerološke sekcije Srpskog lekarskog društva,* a iste godine, on i njegov saradnik i naslednik – prof. dr Milan Kićevac, bili su glavni organizatori *Udruženja Dermatovenerologa Jugoslavije.* Sa ovim udruženjem, sva ostala regionalna dermatovenerološka društva u zemlji uvedena su u *Sveslovensko dermatološko društvo*. Prof. dr Đorđe Đorđević je zajedno sa prof. dr Milanom Kićevcem organizovao Prvi, Drugi i Treći jugoslovenski dermatovenerološki kongres (1927, 1928. i 1929.), a 1931. godine i Drugi kongres Sveslovenskog dermatološkog društva.

Dr Vojislav Mihailović (1879-1949), značajno ime za srpsku dermatovenerologiju, bio je šef na *Kožno-veneričnom odeljenju Opšte državne bolnice* u Beogradu. Radovi i knjige dr Vojislava Mihailovića iz istorije dermatovenerologije i opšte medicine imali su veliki uticaj na srpsku dermatovenerologiju.

Eksperimentalnom dermatovenerologijom bavio se doc. dr Sava Bugarski (1897-1945), koji je bio đak prof. Kićevca a kasnije i direktor na *Klinici za kožne i venerične bolesti* u Beogradu (1940-1945).

Dr Jovan Nenadović (1875-1952), jedan od najuglednijih lekara u Novom Sadu, učestvovao je u osnivanju i radu *Dermatovenerološke sekcije Srpskog lekarskog društva* i bio njen doživotni počasni predsednik.

U periodu između dva svetska rata, među najznačajnijim lekarima zaslužnim za razvoj dermatovenerologije u okviru vojnog saniteta bili su načelnici Dermatovenerološkog odeljenja Opšte vojne bonice u Beogradu: major, kasnije sanitetski brigadni general, dr Božidar Janković i sanitetski brigadni general dr Milivoje Pantić. Eminentni lekari vojnog saniteta, kao što je bio dr Petar Davidović, dali su značajan doprinos radu civilnih dermatovenerooloških ustanova tog vremena.

Sedmogodišnji rat (1912-1918) i epidemije zaraznih bolesti dovele su do velikih ljudskih i materijalnih gubitaka u sanitetu Srbije. Zarazne bolesti su se proširile, uključujući i venerične bolesti, pa je bilo nephodno time otpočeti organizovanje i reorganizovanje sanitetske službe.

Dermatovenerološke bolesti: U dermatovenerološkoj patologiji i dalje su dominirale venerične bolesti. U Ambulanti za kožne i venerične bolesti, u periodu 1919-1921. godine venerične bolesti su bile zastupljene sa 73,13%, a kožne sa 26,87%. Sličan odnos postojao je i 1931. godine na teritoriji Srbije (bez Beograda): 73,4% prema 26,6%, kao i u Beogradu: 84,7% u odnosu na 15,3%. U studentskoj populaciji (1938-1939) odnos je bio obrnut, 57% prema 43%.
Od venеričnih bolesti, prema navedenoj seriji iz perioda 1919-1921. godine, sifilis je bio najčešće oboljenje, ako se klinički manifestnim slučajevima dodaju serološki pozitivni slučajevi (latentni sifilis). U istoj seriji pojava sifilisa prema stadijumima bila je: sifilis I kod 10%, sifilis II kod 29,3%, sifilis III kod 1,7%, *tabes dorsalis* kod 0,8% i latentni sifilis kod 56% obolelih. U krajevima sa endemskim sifilisom, u periodu 1921-1925. godine registrovan je: sifilis I kod 4%, sifilis II kod 49,8%, sifilis III kod 18,3%, hereditarni sifilis kod 1,3% i latentni sifilis kod 26,5% obolelih. Kod obolelih od gonoreje, balanitis je nađen u 4,3%, a artritis u 0,43 slučajeva.
U navedenoj seriji, u Ambulanti za kožne i venerične bolesti (1919-1921) među kožnim bolestima najčešči je bio skabijes (26,7%), potom ekcemi (21,8%), piokokna oboljenja (20,4%), dok su gljivična oboljenja (4,5%) i tuberkuloza kože (1,9%) bili znatno ređi.
Zaključak: Ovim završavamo izlaganje o postavljanju temelja dermatovenerologije u Srbiji. U tekstu ograničenog obima nije bilo moguće davati analize, već samo bitne činjenice koje su ukazivale na kompleksnost organizacije naše sanitetske službe. Ovaj proces je pokazao da je dermatovenerologija u Srbiji u toku poslednjih dvadeset godina premostila razorne ratne periode kroz koje je prolazila u svojoj dugoj, turbulentnoj istoriji i usvojila savremenu medicinsku misao, stvaranu u toku gotovo dva veka. Na kraju bismo istakli da su u ovakvom poslu neizbežni nedostaci, bilo zbog nepotpunih, izgubljenih ili kontradiktornih podataka, bilo zbog nepristupačnih ili nedovoljno istraženih izvora, bilo zbog nepravilne procene, koja može biti objektivna, ali i subjektivna. Zato smo imali i imamo uvek na umu misao Ivana Bloha (Iwan Bloch): „Istorija se uvek piše iznova“.

Ključne reči

Istorija medicine; istorija 20. veka; dermatologija; venerologija; Srbija

Erratum

Published in Volume 1 Number 3, pp. 123-7.
The paper by Lalević – Vasić contains the following error:
• Page 124 the first column line 14 from below - Erratum: “In 1895, this privilege was exercised by all patients with sexually transmitted diseases, as well as by railway ”guardians” and low-paid railway staff”. Corrigendum: “In 1895, this privilege also applied to all sexually transmitted diseases, railway ”guardians” and low-paid railway staff as well”.

A Report on the 19th Congress of the European Academy of Dermatology and Venereology, Gothenburg, Sweden, 2010

The 19th Congress of the European Academy of Dermatology and Venereology (EADV) was held in Gothenburg, Sweden, from 6th to 10th October, 2010. It was the first time the EADV was hosted in Sweden, where dermatology and venereology have a more than 100 year old tradition. Gothenburg is the second largest city in Sweden, and it is the largest port in Scandinavia.

The meeting venue of the 19th EADV Congress was the Swedish Exhibition and Congress Centre. Nine eminent professors of dermatology from Germany, Sweden, United Kingdom, Denmark, Austria and Switzerland were invited to present plenary lectures. Attendees of the Congress had the opportunity to listen to the following lectures: „Multiresistant Bacteria: Are They Important in Dermatology?" by U. Jappe, „Dermatology and the Environment" by J. Larsson, „Sun, Vitamin D and the Skin" by B. Diffey, „Skin Cancer in Organ Transplant Recipients" by E. Stockfleth, „Pharmacogenomics" by R. Warren, „The Importance of Patient Compliance in Treatment Outcome" by J. Serup, „Evolving Strategies in STI Prevention" by A. Stary, „An Overview of Stem Cells in Dermatology" by Y. Barrandon, and „Molecularly Targeted Treatments in Skin Cancer" by A. Hauschild. There were 51 symposia with various topics that covered most of the dermatovenereology. For this report we selected the following: Treatment of Skin Disorders in Pregnancy, Advances in the Management of HIV Infection/AIDS, Atopic Dermatitis in Children, Adverse Cutaneous Drug Reactions, Management of Cutaneous Lymphoma, New Imaging Methods in Dermatology, Viruses and the Skin, Update on the Management of Melanoma, Esthetic Procedures for Medical Skin Diseases, Straightening Out Hair Problems, New Strategies for the Biologic Therapy of Psoriasis, Fragrance Allergy and Urticaria.

Besides plenary lectures and symposia, the program also included of workshops, courses on very hot topics for both office and hospital-based dermatologists and venereologists. Also, "What's New" lectures and satellite symposia provided up-to-date information. The Congress motto was "Making waves in dermatology".

Figure 1. "Making Waves in Dermatology" motto of the 19th Congress of the EADV in Gothenburg, 2010

Figure 2. Our participants / Some of our participants at the 19th Congress of the EADV in Gothenburg, 2010: Nevenka Urošević, Ljiljana Trklja, Anica Radulović, Zoran Golušin, Ljiljana Medenica, Dušan Škiljević i Đorđije Karadaglić

During the 19th EADV Congress, presentations of two ongoing campaigns were held: the Euro-Melanoma as a pan-European prevention campaign against skin cancer, and the EADV – europrevention 2010 campaign "*healthy skin@work*".

The Euro-Melanoma day gives an opportunity to general public to have a free-of-charge screening of their moles by a dermatologist, one day each year. Its main aim is to provide everyone interested information on skin cancer prevention, early diagnosis and treatment. The campaign has been organized in Serbia since 2008.

The EADV–europrevention 2010 campaign "*healthy skin@work*" started in 2010. It is scientifically guided by the European Initiative for the Prevention of Occupational Skin Diseases (EPOS), which is a network of - so far - 70 experts from more than 50 dermatological centers in 23 European countries. The campaign aims to disseminate experience and make recent achievements in dermatological prevention available to every European citizen. Professions affected by occupational skin diseases are increasingly getting aware of the disease burden and that dermatology can offer a solution. In 2010, the European Commission has granted funding for a research project "Safe Hair". Apart from other things, it includes teaching hairdressers, as the number 1 profession at high risk from occupational skin diseases, to make an adequate skin protection and skin care as a habit in the trade.

Prof. Dr Miloš Nikolić, a dermatologist from Serbia, was a co-chair in the symposium "Diagnosis and menagement of vasculitis". He spoke about "ANCA-associated autoimmune diseases induced by antithyroid drugs: comparison with ANCA vasculitis". In this symposium, Dr. Dušan Škiljević gave a lecture "Acute hemorrhagic edema of infancy". There were 23 poster presentations from Serbia.

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FORTHCOMING EVENTS

Dermatology and Venereology Events 2010-2011

DATE	MEETINGS, CONGRESSES, SYMPOSIA	ABSTRACT SUBMISSION DEADLINE	MORE INFORMATION AT
4-7 September, 2010	16th Meeting of the European Society for Pigment Cell Research, Hinxton Cambridge, UK	31 May, 2010	www.registration.hinxton.wellcome.ac.uk
9-11 September, 2010	40th Annual ESDR Meeting (European Society for Dermatological Research), Helsinki, Finland	14 May, 2010	www.esdr2010.org
15-18 September, 2010	10th Congress of the European Society of Contact Dermatitis, Strasbourg, France	March, 2010	www.escd-gerda2010.com
23-25 September, 2010	25th IUSTI (International Union against Sexually Transmitted Infections) – Europe Conference, Tbilisi, Georgia	31 May, 2010	www.iusti2010-tbilisi.ge
23-26 September, 2010	31st Annual Meeting of the ISDS (International Society for Dermatologic Surgery)	No abstract submission	www.isdsworld.com
6-10 October, 2010	19th EADV Congress Gothenburg, Sweden	3 March, 2010	www.eadvgothenburg2010.org
15-17 October, 2010	6th EMAA (European Masters in Aesthetic and Anti-aging Medicine), Paris, France	30 May, 2010	www.euromedicom.com
21-23 October, 2010	XXXI Symposium of the International Society of Dermato-pathology, Barcelona, Spain	25 August, 2010	www.isdpbarcelona2010.net
29 October – 01 November, 2010	Xth ADI (Ionic Dermatological Association) International Congress, Floriana, Malta	27 August, 2010	www.malta2010.net
4-7 November, 2010	1st World Congress on Controversies in Plastic Surgery and Dermatology, Barcelona, Spain	4 August, 2010	www.comtecmed.com/coplasdy/2010
12-13 November, 2010	XV Belgrade Dermatological Days, Department of Dermatology, Military Medical Academy, Belgrade, Serbia	1 September, 2010	www.udvs.org
9-11 December, 2010	COSMODERM XIV – The International Aesthetic Dermatology Congress of ESCAD, Dresden, Germany	15 June, 2010	www.cosmoderm2010.de
14-17 April, 2011	8th EADV Spring Symposium Carlsbad, Czech Republic	Under construction	www.eadv.org
24-29 May, 2011	22nd World Congress of Dermatology, Seoul, Korea	31 October, 2010	www.wcd2011.org
7-10 September, 2011	41st Annual ESDR Meeting (European Society for Dermatological Research) , Barcelona, Spain	Under construction	www.esdr.org
15-17 September, 2011	2nd 5-Continent-Congress for Lasers and Aesthetic Medicine, Cannes, France	31 March, 2011	www.5-cc.com
20-24 October, 2011	20th Congress of the European Academy of Dermatology and Venereology, Lisbon, Portugal	Under construction	www.eadv.org

Prepared by: Dr. Tatjana Roš, Clinic of Dermatovenereology Diseases, Clinical Center of Vojvodina, Novi Sad, Serbia

AUTHOR GUIDELINES

Serbian Journal of Dermatology and Venereology is a journal of the *Serbian Association of Dermatologists and Venereologists*. The journal is published in English, but abstracts will also be published in Serbian language. The journal is published quarterly, and intended to provide rapid publication of papers in the field of dermatology and venereology. Manuscripts are welcome from all countries in the following categories: editorials, original studies, review articles, professional articles, case reports, and history of medicine.

Categories of Manuscripts

1. Editorials *(limited to 5 pages) generally provide commentary and analyses concerning topics of current interest in the field of dermatology and venereology. Editorials are commonly written by one author, by invitation.*

2. Original studies *(limited to 12 pages) should contain innovative research, supported by randomized trials, diagnostic tests, outcome studies, cost-effectiveness analysis and surveys with high response rate.*

3. Review articles *(limited to 10 pages) should provide systemic critical assessment of literature and other data sources.*

4. Professional articles *(limited to 8 pages) should provide a link between the theory and practice, as well as detailed discussion or medical research and practice.*

5. Case reports *(limited to 6 pages) should be new, interesting and rare cases with clinical significance.*

6. History of medicine *(limited to 10 pages) articles should be concerned with all aspects of health, illness and medical treatment in the past.*

The journal also publishes book reviews, congress reports, as well as reports on local and international activities, editorial board announcements, letters to the editor, novelties in medicine, questions and answers, and "In Memoriam". All submitted manuscripts will undergo review by the editor-in-chief, blind review by members of the manuscript review panel or members of the Editorial Board. Manuscripts submitted to this journal must not be under simultaneous consideration by any other publisher. Any materials submitted will NOT BE RETURNED to the author/s.

All manuscripts should be submitted to the **Editor in Chief: Prof. Dr. Marina Jovanović***, Clinic of Dermatovenereologic Diseases, Clinical Center of Vojvodina, Hajduk Veljkova 1-3, Novi Sad, Serbia, by mail to: serbjdermatol@open.telekom.rs.*

Manuscripts for submission must be prepared according to the guidelines adopted by the International Committee of Medical Journal Editors (www.icmje.org). Please consult the latest version of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals.

1. Manuscript Preparation Guidelines

The manuscript should be written in English, typed in double spacing throughout on A4 paper, on one side only; Use Times New Roman, font size 12, with 30 lines and 60 characters per line. Articles must be written clearly, concisely and in correct English. Accepted manuscripts in need of editing will be returned after editing to the corresponding author for approval. When preparing their manuscripts, authors should follow the instructions given in the *Categories of Manuscript:* the number of pages is limited (including tables, figures, graphs, pictures and so on to 4 (four)), and all the pages must be numbered at the bottom center of the page.

For manuscript preparation, please follow these instructions:

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The title page should include the following information:

- The title of the article, which should be informative, without abbreviations and as short as possible;

- A running title (limited to 30 characters);

- Authors' names and institutional affiliations;

- The name, mailing address, telephone and fax numbers, and email of the corresponding author responsible for correspondence about the manuscript. Furthermore, authors may use a footnote for acknowledgements, information and so on.

1.2. Abstracts

A structured abstract in English *(limited to 150 words) should follow the title page. The abstract should*

provide the context or background for the study, as well as the purpose, basic procedures, main findings and principal conclusions. Authors should avoid using abbreviations.

- An **abstract in Serbian language**, *(limited to 150 words) should follow the second page. It should contain a briefing on the purpose of the study, methods, results and conclusions, and should not contain abbreviations.*

1.3. A list of abbreviations

Use only standard abbreviations, because use of non-standard abbreviations can be confusing to readers. Avoid abbreviations in the title, abstract and in the conclusion. A list of abbreviations and full terms for which they stand for should be provided on a separate page. All measurements of length, height, weight, and volume should be reported in the metric units of the International System of Units – SI, available at http://www.bipm.fr/en/si/.

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Manuscripts must be accompanied by a cover letter, which should include a date of submission, statement that the manuscript has been read and approved by all the authors and that the authorship requirements have been met. It should also include the name, address, and telephone number of the corresponding author, who is responsible for communicating with other authors about revisions and final approval of the proofs. The original copy of the cover letter, signed by all authors, should be enclosed with the manuscript.

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Tables *should capture information concisely and precisely. Including data in tables, rather than in the text, reduces the length of the article itself.*

- Submit tables in separate files, not included in the manuscript. Tables are to be double spaced and numbered sequentially, with Arabic numbers (Table 1, Table 2, etc.), in order of text citation. Each column, including the first, must have a heading. Provide a brief title for each table. Put all explanatory matter in footnotes, including any nonstandard abbreviations used in the table.

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3. References

References in the text, tables and legends should be identified by Arabic numerals in parentheses. Number references consecutively in the order in which they are first mentioned in the text. The *Vancouver System* of referencing should be used. List each author's last name and initials; full first names are not included. List all authors, but if the number exceeds six, give the first six followed by „et al." National journals, which are not indexed in *Index Medicus*, should be abbreviated according to the style in the *List of Abbreviated Titles of Yugoslav Serial Publications* available on http://vbsw.vbs.rs. For further information please visit www.ICMJE.org.

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