

with movement suppression and tic disorders, as well as disorders belonging to obsessive-compulsive spectrum. The treatment of this disorder may be pharmacological and/or psychological. There is some evidence for the benefit of some SSRI (Selective Serotonin Reuptake Inhibitors) agents as well as for N-Acetyl-Cysteine. Various psychological treatments have been investigated and some of them have proven to be effective. These include cognitive behavioural protocols, some of which have been developed specifically for this disorder. ●

THE DISEASE OF JOB

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In 1966, Davis et al. coined the term "Job Syndrome", reporting on a new pediatric immunodeficiency disease characterized

by "cold" staphylococcal abscesses. This term is widely used in association with several immunodeficiencies with very high levels of IgE, which are also known as "Hyperimmunoglobulin E Syndromes". The assumed similarity between the biblical disease of Job and the "new" immunodeficiency was probably due to the King James' classical translation of the Bible (in 1611), wherein the disease of Job (biblically termed as "Shin") was translated as "boils". However, the biblical word "Shin" is a general term for skin disease or dermatitis, and according to the Talmud, there are 24 different skin diseases called "Shin". New scientific data states that hyper-IgE syndromes are genetic and not acquired (as was in the biblical disease of Job). Therefore, in view of the stigma associated with the name and story of Job, it is recommended to abandon the name of "Job syndrome" and refer to the immune disorders by their genetic source, such as "STAT 3 disease" or "DOCK 8 disease". ●

כרוניקה

תוצאות מבטיחות בניסוי תרכיב נגד קלמידיה



לא גרם להשפעות לוואי למעט במקום ההזרקה, וההתזה לא לא הייתה מלווה בתלונות נוספות. הממצאים הצביעו על הופעת נוגדנים בכל המחוסנות ובאף אחת מקבוצת האינבו. בקבוצה שקבלה תרכיב בליפוזומים נצפה היפוך סרולוגי מואץ יותר מאשר בקבוצת האלומיניום, וכן פרופיל מוגבר של נוגדנים בריריות, ואף תגובה חיסונית תאית קבועה יותר [Lancet infect Dis 2019;http://doi.org/10/1016/S1473-3099(19)30279-8]. איתן ישראלי

המחלה החיידקית השכיחה ביותר המועברת במגע מיני היא קלמידיה. אברהם וחב' בדקו בניסוי בשלב I בטיחות ויעילות של תרכיב נגד החיידק, המבוסס על חלבון מהונדס (CTH 522). הניסוי היה מבוקר אינבו, אקראי וכפול סמיות, בבית חולים בלונדון, ונערך ב־35 נשים בין הגילים 19-45 שנים. החלבון הוכן בשתי חלופות, בליפוזומים או בתרחיף הידרוקסיד אלומיניום. הנכללות קיבלו שלוש זריקות לשריר (85 מק"ג) בזמנים 0,1,4 חודשים, ולאחר חודש חוסנו פעמיים גם בהתזה לאף. התרכיב

כרוניקה

האם מנה אחת של תרכיב נגד פפילומה יעילה כמו שלוש מנות?



2014. נכללו בנייתוח התוצאות מעל רבע מיליון נשים: כ־50,000 שלא חוסנו, כ־175,000 שקיבלו שלוש מנות תרכיב, כ־18,000 שקיבלו שתי מנות ו־8,618 (3.4%) שקיבלו מנה אחת. הממצאים הצביעו על הפחתה משמעותית ביחס הסיכון ללקות במצבים הנ"ל בכל הקבוצות שקיבלו חיסונים בהשוואה לנשים שלא חוסנו: לגבי קבלת מנה אחת - 0.65, שתי מנות 0.61 ושלוש - 0.59. לאחר תיקון לגיל בזמן קבלת החיסון בקרב שלוש הקבוצות המחוסנות, יחס הסיכון המתוקן היה דומה בין מקבלות מנה אחת או שתיים לזה של אלה שקיבלו שלוש מנות (מנה אחת - 1.01, שתיים - 1.00). השוואה לנתונים היסטוריים בקרב נשים בגילים זהים, הצביעה על כך שהממצאים אינם כתוצאה של חיסונית עדר. המחברים מסכמים, כי מתן חיסונים נגד פפילומה במנה אחת, יפשט מאוד את המערכה נגד סרטן צוואר הרחם, יוזיל משמעותית את העלות ואף יפחית את השפעות הלוואי הנצפות בחלק מהמחוסנות Papilloma (Res 2019;8:100177 https://doi.org/10.1016/j.pvr.2019.100177). איתן ישראלי

ברבות מהמדינות המתועשות, מערכות הבריאות מספקות לערות (ונערים) חיסון נגד נגיפי פפילומה, כנגד הסיכון ללקות בעתיד בסרטן צוואר הרחם. התרכיב ניתן לרוב בשלוש מנות (זמן אפס, חודש, חודשיים ושישה חודשים), ויש עדויות אפידמיולוגיות לכך שאכן התרכיב מפחית את שיעור היארעות של מצבים טרום סרטניים, שאתות באזור פי הטבעת וסרטן צוואר הרחם. בנוסף, יש תיעוד על אוכלוסיות שקיבלו שתי מנות או אפילו מנה אחת של התרכיב, עם תוצאות חיוביות של הגנה בפני סרטן. יחד עם זאת, יש דיווחים על השפעות לוואי קשות לאחר קבלת התרכיב, בעיקר בנערות, וביניהן מחלות אוטואימוניות ואף מקרי מוות. **ברטרטון** וחב' מאוסטרליה ניסו להעריך את יעילות מתן מנה בודדת של תרכיב לעומת שתיים או שלוש מנות, כנגד הופעת ניאופלזיה מדרגה CIN 2/3, אדנוקרצינומה מקומית (AIS) / סרטן, שבע שנים לאחר מתן החיסונים. החוקרים בדקו את כל רשימות הסרטן הלאומיות מול רשימות החיסונים, לנשים באוסטרליה החל מגיל 15 שנים, משנת 2007, שבה החלו בחיסונים, עד סוף שנת

Discussion: Possible explanations for these observations are provided in this article. The experience of this joint fellowship can set an example for other fellowship programs in medical areas dealing with uncommon diseases. ●

RITUXIMAB IN RHEUMATOID ARTHRITIS - THERAPEUTIC ASPECTS BASED ON 18 YEARS OF GLOBAL EXPERIENCE

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Rituximab, a monoclonal antibody against CD20 positive B cell, depletes these cells peripherally, and is a successful treatment in rheumatoid arthritis (RA). It is the second efficacious biologic to be established in the treatment of RA after TNF α blockers. Eighteen years of global experience from diverse clinical trials and from "real world" data, have demonstrated clinical efficacy in various disease scenarios and patient populations - short and long disease duration, methotrexate naïve patients and those with incomplete response to methotrexate, biologic naïve patients and those with incomplete response to previous biologics. Moreover, it has demonstrated the inhibition of radiographic progression. It seems to be most efficacious in seropositive patients. Despite vast experience, the need for concomitant traditional disease-modifying anti rheumatic drugs (DMARD), the optimal retreatment dose, and the favored retreatment interval remain somewhat uncertain. The recommended dosage is 1000 mg, administered twice, with a 2 weeks interval, although in some cases, a reduced dosage of 500 mg, administered twice may be considered. The safety profile of rituximab includes mainly infusion-related reactions, which are usually mild. A small risk of major infections has remained stable over time and repeated courses. Opportunistic infections are infrequent. Nevertheless, reactivation of hepatitis B is still a concern. Tuberculosis, malignancies, cardiovascular events and deterioration of interstitial lung disease do not appear to be increased. Since rituximab severely impairs the humoral response to vaccinations, they should be administered prior to treatment whenever possible. Rituximab has been a powerful addition to the large armamentarium for the treatment of RA. Rituximab is indicated in Israel as a second line biologic treatment for active RA. ●

DIFFUSE LOW GRADE GLIOMA: PERSONALIZED ADAPTATION OF SURGICAL RESECTION IN AN ERA OF TARGETED ONCOLOGICAL THERAPY

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Diffuse low grade glioma (DLGG) is a primary, infiltrative brain tumor which grows slowly but steadily and eventually undergoes malignant transformation into a high grade glioma. Today, it is hard to generalize the treatment approaches for DLGG. Due to different genetic and clinical variables, there is a large gap in the treatment provided to different patients. This kind of gap requires personalized adaptation of the treatment for a long period. Although there has been significant progress in the molecular characterization of DLGG, we still lack an efficient oncological targeted therapy. On the other hand, during the past two decades, there has been a significant paradigm shift in the treatment of DLGG, with the current recommendation to perform a maximal safe resection as first line treatment.

Our aspirations to preserve the high function abilities of these relatively young patients for a long period (median overall survival of 15 years), together with the intention to postpone the malignant transformation as late as possible, have led to increases in the prevalence of awake craniotomies for DLGG. In this surgical technique, the resection of the tumor is as wide as possible, according to its functional boundaries (and not its radiological - anatomical ones). This kind of resection allows us to preserve the functioning abilities of the patients while making a wide resection. This resection can be performed with full adaptation to the patient's will, as well as for the tumor's characteristics. The long-term treatment of patients with DLGG requires us to perform personalized adaptation in any therapeutic junction and in any case where the delicate balance between function of the patient and his oncological status needs to be preserved. This study reviews the different options for personalized treatment in DLGG and emphasize the importance of awake surgeries in these cases. ●

EXCORIATION (SKIN-PICKING) DISORDER

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Excoriation (Skin-Picking) disorder is a clinically recognized condition which was recently included in the Diagnostic and Statistical manual of the American Psychiatric Association (DSM) - fifth edition, as OCD (obsessive compulsive disorder) related disorder. The disorder's official status has been achieved due to its high frequency and unique clinical picture involving both mental and physical impairment. In this article, we would like to present a concise review of the literature together with an illustrative case.

Epidemiological surveys show a prevalence of 3% to 5% for the general population, with heterogeneous gender and age distribution. In recent years the disorder has been categorized under the family of BFRB's (Body Focused Repetitive Behaviours). However, there are some elements associated

ASSOCIATION OF OBESITY, SMOKING AND SOCIOECONOMIC STRATA WITH THE FIBROMYALGIA SYNDROME

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Background: Obesity is a worldwide epidemic with devastating impacts on the public's health. There are several indications that obesity might also be involved in the pathogenesis of chronic pain syndromes such as fibromyalgia.

Aim: This study aimed to examine a possible association between BMI levels, smoking and socio-economic status and the existence of fibromyalgia.

Methods: Patients who were diagnosed with fibromyalgia were compared to population-based controls, matched in age and gender (by a ratio of 1:5). Body mass indices, smoking status and socioeconomic strata were retrieved from computerized medical records of the Clalit Health Services database. Body mass index was classified in WHO categories of underweight, normal, overweight and obese (<18.5, 18.5–<25, 25.0–<30, ≥30.0 kg/m²); x², t-tests, and logistic regression models were used to compare the study groups and assess the association between obesity and fibromyalgia.

Results: The study included 14,296 patients with fibromyalgia and 71,324 controls. Among patients with fibromyalgia the average BMI [body mass index] was higher than that of the controls 29.1±6.2 vs. 28.0±6.01, p<0.001) with every increment of 1 unit of the BMI score, there was an increment of 2.7% of the odds of having coexistent fibromyalgia. The chances of having fibromyalgia was 56% higher among subjects with obesity compared to individuals of normal weight. The data revealed that patients with fibromyalgia smoke more and belong to lower socioeconomic levels.

Conclusions: Our findings demonstrate that obesity is significantly associated with a higher proportion of fibromyalgia. This finding underlines the role that obesity plays in inflammation and chronic pain. ●

FIBROMYALGIA, OBESITY AND ALL THAT LIES IN BETWEEN

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Chronic pain is an issue of increasing health concern, with a negative impact on suffering patients, their families, and

society since it is contributing to high health care costs and loss of productivity. Fibromyalgia is one of the most common causes of chronic pain, especially in women, and is associated with several comorbidities, leading to both increased levels of distress as well as decreased function.

Obesity is another chronic disease, with increasing prevalence around the world, associated with increasing morbidity and mortality. In their study published in the present issue of Harefuah, Blokh Kerpel et al found a strong link between these two epidemics – fibromyalgia and obesity. This association contributes to our understanding regarding the epidemiology and pathogenesis of fibromyalgia.

Obesity also negatively affects the course of fibromyalgia. Obese patients with fibromyalgia experience more pain, are more depressive, have reduced mobility and function and use more medications. Moreover, feasibility and efficacy of treatment interventions is challenging, especially in terms of physical activity - the mainstream of fibromyalgia treatment - which is severely reduced in obese patients. Optimal treatment for obese patients with fibromyalgia must address these issues. ●

A REPORT ON THE PRACTICALITIES OF THE JOINT FELLOWSHIP IN PEDIATRIC RHEUMATOLOGY IN ISRAEL

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Background: The field of pediatric rheumatology was only recently recognized in Israel as a sub-specialty. To enable a fellowship program in this field comprising mainly uncommon diseases, the Meir and Shaare Zedek medical centers were authorized to implement a joint fellowship program, in which the trainees split their time between the two medical centers.

Objectives: This article presents the unique experience as a trainee in the joint fellowship program in pediatric rheumatology, while relating to the different characteristics of these centers, patient populations and variable disease exposure.

Methods: Assessment of the extent of clinical and procedural exposure was achieved by comparing the exposure data of the fellow during the first two years of the joint fellowship to the published data derived from questionnaires answered by 44 fellows in the United States.

Results: All requirements for successfully completing the Israeli fellowship program were fulfilled, but also those of the North American and European programs. We have shown that the extent of both clinical and procedural exposure is high in the joint fellowship program. We also show the differences in the variety of diseases seen in both centers.

while male patients develop significantly more structural damage compared to females in general.

Aim: To examine statistical correlation between mSASSS and serum levels of testosterone in males suffering from AS.

Methods: Twenty males with AS known for at least 5 years (average disease duration 12.8 years) and aged between 25 to 40 years donated 5 ml of peripheral blood for serum testosterone assay, and underwent X-ray films of cervical and lumbar spine. The mSASSS was calculated and correlation with serum testosterone levels was examined using Pearson correlation test.

Results: The mSASSS values of patients included in the final analysis ranged from 0-14 units and testosterone levels ranged from 8.4-25.5 nmol/L. No significant correlation was found between mSASSS values and testosterone levels in this cohort.

Conclusion: This study did not find statistical correlation between mSASSS and serum levels of testosterone in males suffering from AS. ●

PREMEDICATION WITH CORTICOSTEROIDS PRIOR TO IV INFLIXIMAB - A COMPARISON BETWEEN INFLAMMATORY BOWEL DISEASE (IBD) AND RHEUMATIC PATIENTS

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Introduction: Infliximab is a protein with an anti TNF- α activity which is given in an intra-venous manner to treat inflammatory bowel disease and inflammatory joint disease. This treatment may cause infusion reaction events, but this may be prevented using treatment with pre-medication.

Objectives: To assess the incidence of infusion reaction in patients with inflammatory bowel disease and patients with rheumatic disease who are treated with Infliximab, with or without corticosteroid premedication respectively. To determine whether premedication with corticosteroids decreases the incidence of infusion reactions.

Patients and methods: We conducted a retrospective cohort study at the Soroka Medical Center that includes records from 92 patients treated with Infliximab: Group A includes 70 inflammatory joint disease patients who were not treated with hydrocortisone premedication and, group B includes 22 inflammatory bowel disease patients who were treated with hydrocortisone premedication. Incidence and severity of infusion reaction were assessed.

Results: The incidence of infusion reactions in the group which did not receive premedication was 26.1% (18/69), while in the group receiving premedication the incidence was 13.6% (3/22). Results are not statistically significant but reflect a

trend. Most reactions occurred in the second treatment and most were of medium severity.

Conclusion: The results seem to reflect a positive trend favoring the use of premedication with hydrocortisone before Infliximab infusion, especially given the minor side-effects of this treatment. ●

IS THERE A CORRELATION BETWEEN CARRIAGE OF AN MEFV MUTATION AND GOUT?

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Introduction: Gout is an inflammatory condition mediated by Interleukin-1-beta (IL-1 β). A mutation in the MEFV gene (the gene related to Familial Mediterranean fever) may cause an elevation in IL-1 β , and is associated with a variety of inflammatory conditions. Reports in the literature are inconsistent as to whether a mutated MEFV gene is related to the phenotype of gout.

Study objectives: To assess whether a carriage state of a mutation in the MEFV gene correlates with the expression and severity of gout.

Methods: A total of 73 patients, 50 with gout and 23 with hyperuricemia were examined for an MEFV mutation. Carriage rate was compared between hyperuricemic and gout patients, and disease activity measures were compared between MEFV mutation carriers and non-carriers.

Results: We did not find a statistically significant difference in the carriage rate of an MEFV mutation between gout patients and hyperuricemic patients without gout, nor did we find a correlation between MEFV mutation carriage and gout severity.

Conclusion: Further large-scale studies should be conducted in order to determine a possible correlation between MEFV mutation carriage and gout. ●

CRYGLOBULINEMIA AND ENDOCARDITIS AS A PRESENTATION OF COXIELLA BURNETII (Q-FEVER) INFECTION

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An infection with *Coxiella burnetii* (Q FEVER) can be manifested as an autoimmune or rheumatologic disease as it was presented in our patient, showing cryoglobulinemia and massive destruction of the aortic valve.

In the differential diagnosis we must consider an infection with *Coxiella burnetii* which may change the course of the disease and may cause life-threatening manifestations. ●

TRANSGENDER ENDOCRINOLOGY

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Clinical encounters with transgender people seeking hormonal treatment for gender reaffirmation, provide an opportunity, besides engagement in the endocrine dilemmas, to challenge the binary pattern of thinking and reveal many fascinating and complex matters of transgender medicine: human, philosophical and political. The current review of the subject is presented by an endocrinologist engaged in hormonal treatment of transgender people. ●

RHEUMATOLOGY IN ISRAEL – THE PLATINUM ERA

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For years patients with rheumatic diseases were managed by internists, orthopedics and rehabilitation clinics. The first rheumatology clinic in Israel was opened in 1965. The founders of rheumatology were rheumatologists who were trained in Europe and North America. Only in 1988, rheumatology was recognized as a subspecialty of internal medicine, and in 2012 pediatric rheumatology was recognized as a separate sub-specialty. There are 166 certified rheumatologists in Israel who are members of the Israeli Society of Rheumatology (ISR).

The goal of the ISR is to provide an organized platform for education and scientific exchange in rheumatology through the provision of high quality education for all health care providers in the field of rheumatology, bi-annual scientific meetings dedicated to the advancement of clinical and basic science research, and the promotion of best clinical practice in the delivery of care for patients with rheumatologic disorders. In addition, the ISR promotes the introduction of new drugs and technologies, representing the rheumatology patients' best interests as well as collaboration with rheumatology patients' advocacy groups. ●

THE EMERGENCE OF RHEUMATOID ARTHRITIS AT THE AGE OF OVER 60 – A COMPARISON OF CLINICAL MANIFESTATIONS AND ACCESS TO TREATMENT PATTERN COMPARED TO YOUNGER PATIENTS

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Introduction: The aging process of rheumatoid arthritis (RA) requires re-assessment of diagnostic and treatment approaches in patients who developed RA at 60-69 years (EORA-Elderly-Onset RA), 70 years and older (LORA-Late Onset RA) compared with CORA patients - Common Onset RA (35 - 50 years).

Methods: Comparing data of CORA, EORA and LORA patients: gender, nationality; swollen and tender joints (out of 28 joints), Disease Activity Score (DAS28), inflammatory markers, rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (ACPA); treatment with corticosteroids and disease modifying anti rheumatic drugs (DMARDs).

Results: Patients' files were examined: CORA (39, 33.5%), EORA (37, 30.8%) and LORA (44, 36.7%). No differences were observed between swollen and tender joints, inflammatory markers, DAS28, RF, and ACPA. Methotrexate was introduced in 94.9% of CORA patients versus EORA (77.3%) and LORA (78.4%); 88.6% LORA-patients received corticosteroids versus 69.2% CORA; 43.2% of LORA patients and 92.3% CORA received synthetic disease-modifying antirheumatic drugs (DMARDs); 43.6% CORA versus 16.2% EORA and 9.3% LORA patients received biologics.

Conclusions: No clinical and laboratory differences were found between CORA, EORA, and LORA groups. EORA and LORA patients received less synthetic and biological DMARDs. It is necessary to change the attitude to EORA and LORA and to promote advanced optimal treatments. Prospective studies on the efficacy and safety of novel drugs in EORA and LORA patients are needed. ●

SPINAL SYNDESMOPHYTE SCORE DOES NOT CORRELATE WITH SERUM TESTOSTERONE LEVEL IN MALE PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a chronic progressive inflammatory rheumatic disease primarily involving sacroiliac joints and spine. Structural damage, caused by AS, manifests with development of vertebral syndesmophytes and can be calculated as units of modified Spinal Ankylosing Spondylitis Syndesmophyte Score (mSASSS). The rate of growth of spinal syndesmophytes differs among individual AS patients,