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CARDIOLOGIA

Int J Cardiol . 2020 Oct 1;316:229-235. doi: 10.1016/j.ijcard.2020.05.055. Epub 2020 May 26.

Current lipid lowering treatment and attainment of LDL targets recommended by ESC/EAS guidelines in very high-risk patients with established atherosclerotic cardiovascular disease: Insights from the START registry.

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Abstract Background: Current European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) guidelines for the management of dyslipidemias have further reduced low density lipoprotein-cholesterol (LDL-C) targets, as compared to the guidelines released in 2016. These targets are particularly restraining for patients at very high risk (VHR). **Methods:** Using the data from a nationwide, prospective registry on patients with established atherosclerotic cardiovascular disease (ASCVD), we sought to assess: 1) the contemporary use of conventional cholesterol-lowering therapies and the achievement of LDL-C goals according to previous and current ESC guidelines in subjects at VHR; 2) the proportion of VHR patients potentially eligible for proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9i) treatment. **Results:** Among the 5053 patients with data available, 4751 (94.0%) were deemed as VHR. Among these patients, the mean LDL-C levels were 62.4 ± 47.7 mg/dl at enrollment. A high dose of statin was used in 54.9%, while the association of high dose statin and ezetimibe was prescribed in 4.8% of VHR patients. A target level of LDL-C < 70 mg/dl recommended by 2016 ESC guidelines was reached by 58.1%, while a target of <55 mg/dl and LDL-C reduction $\geq 50\%$ recommended by 2019 ESC guidelines, would be reached by 3.2% of patients at VHR. Accordingly, 9.4% and 1.4% of VHR patients would be eligible for PCSK9i according to ESC guidelines and Italian regulations, respectively. **Conclusions:** In VHR patients enrolled in this large cohort of established ASCVD managed by cardiologists, the lipid management and LDL-C targets attainment is largely suboptimal.

DERMATOLOGIA

J Invest Dermatol . 2020 Sep;140(9):1691-1697. doi: 10.1016/j.jid.2019.11.023.

The Role of Autophagy in Skin Fibroblasts, Keratinocytes, Melanocytes, and Epidermal Stem Cells

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Abstract Human skin acts as a barrier to protect our bodies from UV rays and external pathogens and to prevent water loss. Phenotypes of aging, or natural aging due to chronic damage, include wrinkles and the reduction of skin thickness that occur because of a loss of skin cell function. The dysregulation of autophagy, a lysosome-related degradation pathway, can lead to cell senescence, cancer, and various human diseases due to abnormal cellular homeostasis. Here, we discuss the roles and molecular mechanisms of autophagy involved in the anti-aging effects of autophagy and the relationship between autophagy and aging in skin cells.

ENFERMEDADES RESPIRATORIAS

Chest . 2020 Sep;158(3):1268-1281. doi: 10.1016/j.chest.2020.04.036. Epub 2020 May 1.

The Use of Bronchoscopy During the Coronavirus Disease 2019 Pandemic: CHEST/AABIP Guideline and Expert Panel Report.

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Abstract Background: The coronavirus disease 2019 (COVID-19) has swept the globe and is causing significant morbidity and mortality. Given that the virus is transmitted via droplets, open airway procedures such as bronchoscopy pose a significant risk to health-care workers (HCWs). The goal of this guideline was to examine the current evidence on the role of bronchoscopy during the COVID-19 pandemic and the optimal protection of patients and HCWs. **Study design and methods:** A group of approved panelists developed key clinical questions by using the Population, Intervention, Comparator, and Outcome (PICO) format that addressed specific topics on bronchoscopy related to COVID-19 infection and transmission. MEDLINE (via PubMed) was systematically searched for relevant literature and references were screened for inclusion. Validated evaluation tools were used to assess the quality of studies and to grade the level of evidence to support each recommendation. When evidence did not exist, suggestions were developed based on consensus using the modified Delphi process. **Results:** The systematic review and critical analysis of the literature based on six PICO questions resulted in six statements: one evidence-based graded recommendation and 5 ungraded consensus-based statements. **Interpretation:** The evidence on the role of bronchoscopy during the COVID-19 pandemic is sparse. To maximize protection of patients and HCWs, bronchoscopy should be used sparingly in the evaluation and management of patients with suspected or confirmed COVID-19 infections. In an area where community transmission of COVID-19 infection is present, bronchoscopy should be deferred for nonurgent indications, and if necessary to perform, HCWs should wear personal protective equipment while performing the procedure even on asymptomatic patients.

GASTROENTEROLOGIA

Dig Liver Dis . 2020 Sep;52(9):988-994. doi: 10.1016/j.dld.2020.07.010. Epub 2020 Jul 26.

Stimulatory effect of gastroesophageal reflux disease (GERD) on pulmonary fibroblast differentiation.

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Abstract Epidemiological studies indicate that prolonged micro-aspiration of gastric fluid is associated in gastroesophageal reflux disease with the development of chronic respiratory diseases, possibly caused by inflammation-related immunomodulation. Therefore, we sought to ascertain the effect of gastric fluid exposure on pulmonary residential cells. The expression of α -smooth muscle actin as a fibrotic marker was increased in both normal human pulmonary fibroblast cells and mouse macrophages. Gastric fluid enhanced the proliferation and migration of HFL-1 cells and stimulated the expression of inflammatory cytokines in an antibody assay.

Elevated expression of the Rho signaling pathway was noted in fibroblast cells stimulated with gastric fluid or conditioned media. These results indicate that gastric fluid alone, or the mixture of proinflammatory mediators induced by gastric fluid in the pulmonary context, can stimulate pulmonary fibroblast cell inflammation, migration, and differentiation, suggesting that a wound healing process is initiated. Subsequent aberrant repair in pulmonary residential cells may lead to pulmonary fibroblast differentiation and fibrotic progression. The results point to a stimulatory effect of chronic GERD on pulmonary fibroblast differentiation, and this may promote the development of chronic pulmonary diseases in the long term.

NEUROLOGIA

Seizure . 2020 Jul 18;81:36-42. doi: 10.1016/j.seizure.2020.07.011. Online ahead of print.

Efficacy of the ketogenic diet in patients with Dravet syndrome: A meta-analysis.

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Abstract Purpose: Dravet syndrome is an infantile epilepsy syndrome with drug resistant seizures and cognitive impairment. The aim of this meta-analysis was to summarize the findings of relevant published studies to identify the efficacy of a ketogenic diet in patients with Dravet syndrome and their compliance thereof, and to provide useful information for clinical practice. **Methods:** The PubMed, Embase, Wanfang, and CNKI databases were searched for relevant studies published up to September 25, 2019; the included studies were reviewed. Meta-analyses were performed using R software to determine the combined efficacy rates and retention rate for the ketogenic diet in patients with Dravet syndrome. **Results:** Seven studies involving 167 patients met the inclusion criteria: four were retrospective studies, and three were prospective studies. The meta-analysis revealed that 63 %, 60 %, and 47 % of responder patients achieved ≥ 50 % seizure reduction at month 3, 6, and 12, respectively. The pooled retention rate of the ketogenic diet at month 6 and month 12 was 78 % and 49 %, respectively. **Conclusions:** Our meta-analysis indicates that the ketogenic diet is a treatment option for patients with Dravet syndrome. The ketogenic diet is safe and its adverse effects are mostly acceptable. However, further investigations, especially high-quality controlled trials with large samples, are required.

PSYCHIATRIA

Psychoneuroendocrinology . 2020 Oct;120:104778. doi: 10.1016/j.psychneuen.2020.104778. Epub 2020 Jun 18.

Attachment impacts cortisol awakening response in chronically depressed individualsG

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Abstract Background: Early life experiences shape individual attachment, creating a template for regulating emotions in interpersonal situations, likely to persist across the lifespan.

Research has shown that individual attachment creates vulnerability for depression, and also impacts the Hypothalamic-Pituitary-Adrenal (HPA) axis. Still, the relationship between attachment and the HPA axis in depressed individuals is unclear. Cortisol awakening response (CAR) has been recently investigated as a possibly useful physiological marker related to attachment insecurity and depression risk. However, research exploring the relationship between the CAR and attachment in individuals with chronic depression in either the presence or the absence of comorbid anxiety is lacking.

The purpose of the current study was to fill this gap, by comparing the CAR in individuals with chronic depression with/without comorbid anxieties and controls. In addition, we also wanted to explore the relationship between attachment and the CAR in this group and to explore their predictive role for later depression severity. Methods: Individuals experiencing a current depressive episode at least six months in length (cMDD; n = 63) and healthy controls (HC; n = 57) were enrolled in the study (total n = 120). Participants completed a structured clinical diagnostic interview (SCID-I) as well as measures of depression severity (Beck Depression Inventory-II (BDI-II) and Hamilton Rating Scale for Depression) and attachment dimensions (Experiences in Close Relationships scale; ECR) at baseline. In addition, participants provided salivary samples at four time points (i.e. 0 (S1), 30, 45 and 60 min) following awakening on two consecutive days. S1 cortisol, the area under the curve with respect to ground (AUCg) and increase (AUCi) were calculated based on the average values across both days. The HC and cMDD groups were compared on all measures. The CAR for individuals with cMDD alone (n = 14) and individuals with cMDD with two or more comorbid anxiety disorders (cMDD \geq 2Anx; n = 30) were also compared. A subset of participants (n = 59) agreed to return for follow up one year later. Participants returning for follow up repeated the BDI-II and ECR. No salivary samples were collected at follow-up. Results: The cMDD group had significantly lower S1 cortisol and AUCg compared to the HC group (both $p \leq 0.02$). cMDD and cMDD \geq 2Anx groups did not differ in their CAR. Regression analyses revealed that depression severity and the attachment interaction term was associated with lower S1 and AUCg cortisol ($p < 0.01$). Greater attachment avoidance was positively associated with S1 cortisol ($p = 0.02$), while mean awakening time on sample days was negatively associated with S1 cortisol. We also found a significant interaction between the attachment dimensions such that at low levels of attachment anxiety, attachment avoidance had a positive relationship with S1 cortisol and AUCg. The opposite relationship existed when attachment anxiety was high. Higher baseline BDI-II score and higher baseline attachment anxiety were predictive of higher scores on the BDI-II one-year later (both $p < 0.05$). Conclusions: The current findings bring evidence that depression severity is associated with blunting of the CAR irrespective of the comorbid status with anxiety disorders. In addition, attachment avoidance may protect against the CAR blunting in individuals with low attachment anxiety. However, individuals with high attachment anxiety and avoidance might have additional CAR blunting. Attachment anxiety might be a good predictor of future depression severity.

PEDIATRIA Y NEONATOLOGIA

An Pediatr (Barc) . 2020 Sep;93(3):206.e1-206.e8. doi: 10.1016/j.anpedi.2020.05.004. Epub 2020 Jun 27.

[Diagnosis and treatment of acute tonsillopharyngitis. Consensus document update] [Article in Spanish] .

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Abstract An update of the Spanish consensus document on the diagnosis and treatment of acute tonsillopharyngitis is presented. Clinical scores should not be used to prescribe antibiotics, unless microbiological tests are not available or there is a child at risk of rheumatic fever.

There is no score better than those set out in the previous consensus. Microbiological tests are recommended in proposed cases, regardless of the result of the scores. Penicillin is the treatment of choice, prescribed twice a day for 10 days. Amoxicillin is the first alternative, prescribed once or twice a day for the same time. First-generation cephalosporins are the treatment of choice in children with non-immediate reaction to penicillin or amoxicillin. Josamycin and midecamycin are the best options for children with immediate penicillin allergic reactions, when non-beta-lactam antibiotics should be used. In microbiological treatment failure, and in streptococcal carriers, the treatments proposed in the previous consensus are still applicable

GINECOLOGÍA OBSTETRICIA

Eur J Obstet Gynecol Reprod Biol . 2020 Sep;252:490-501. doi: 10.1016/j.ejogrb.2020.07.034. Epub 2020 Jul 22.

Maternal and neonatal characteristics and outcomes among COVID-19 infected women: An updated systematic review and meta-analysis.

Pallavi Dubey 1 , Sireesha Y Reddy 1 , Sharron Manuel 1 , Alok K Dwivedi 2

Abstract Objective: Coronavirus disease 2019 (COVID-19) has become a global pandemic and may adversely affect pregnancy outcomes. We estimated the adverse maternal and neonatal characteristics and outcomes among COVID-19 infected women and determined heterogeneity in the estimates and associated factors. **Study designs:** PubMed search was performed of confirmed COVID-19 pregnant cases and related outcomes were ascertained prior to July 8, 2020, in this systematic review and meta-analysis. Studies reporting premature birth, low birth weight, COVID-19 infection in neonates, or mode of delivery status were included in the study. Two investigators independently performed searches, assessed quality of eligible studies as per the Cochrane handbook recommendations, extracted and reported data according to PRISMA guidelines. Pooled proportions of maternal and neonatal outcomes were estimated using meta-analyses for studies with varying sample sizes while a systematic review with descriptive data analysis was performed for case report studies. Maternal and neonatal outcomes included C-section, premature birth, low birth weight, adverse pregnancy events and COVID transmission in neonates. **Results:** A total of 790 COVID-19 positive females and 548 neonates from 61 studies were analyzed. The rates of C-section, premature birth, low birth weight, and adverse pregnancy events were estimated as 72 %, 23 %, 7 %, and 27 % respectively. In the heterogeneity analysis, the rate of C-section was substantially higher in Chinese studies (91 %) compared to the US (40 %) or European (38 %) studies. The rates of preterm birth and adverse pregnancy events were also lowest in the US studies (12 %, 15 %) compared to Chinese (17 %, 21 %), and European studies (19 %, 19 %). In case reports, the rates of C-section, preterm birth, and low birth weight were estimated as 69 %, 56 %, and 35 %, respectively. Adverse pregnancy outcomes were associated with infection acquired at early gestational ages, more symptomatic presentation, myalgia symptom at presentation, and use of oxygen support therapy. **Conclusions:** Adverse pregnancy outcomes were prevalent in COVID-19 infected females and varied by location, type, and size of the studies. Regular screening and early detection of COVID-19 in pregnant women may provide more favorable outcomes.

ENDOCRINOLOGIA Y METABOLISMO

Trends Endocrinol Metab . 2020 Sep;31(9):642-654. doi: 10.1016/j.tem.2020.04.005. Epub 2020 May 13.

Insulin and Growth Hormone Balance: Implications for Obesity.

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Abstract Disruption of endocrine hormonal balance (i.e., increased levels of insulin, and reduced levels of growth hormone, GH) often occurs in pre-obesity and obesity. Using distinct intracellular signaling pathways to control cell and body metabolism, GH and insulin also regulate each other's secretion to maintain overall metabolic homeostasis. Therefore, a comprehensive understanding of insulin and GH balance is essential for understanding endocrine hormonal contributions to energy storage and utilization. In this review we summarize the actions of, and interactions between, insulin and GH at the cellular level, and highlight the association between the insulin/GH ratio and energy metabolism, as well as fat accumulation. Use of the [insulin]:[GH] ratio as a biomarker for predicting the development of obesity is proposed.

NUTRICION

Clin Nutr . 2020 Sep;39(9):2702-2710. doi: 10.1016/j.clnu.2019.12.020. Epub 2019 Dec 23.

Effects of phytosterols supplementation on blood pressure: A systematic review and meta-analysis.

Ehsan Ghaedi 1 , Sahar Foshati 2 , Rahele Ziaei 2 , Sara Beigrezaei 3 , Hamed Kord-Varkaneh 4 , Abed Ghavami 5 , Maryam Miraghajani 6

Abstract Several reports have indicated a positive effect of phytosterols on blood pressure (BP), nevertheless these findings have been controversial. Therefore, a systematic review and meta-analysis of randomized controlled trials (RCTs) was aimed to investigate the effects of phytosterol supplementation on BP. An online search was carried out in PubMed, Scopus, ISI Web of Science, Cochrane library and Google Scholar up to May 2019. Weighted Mean difference (WMD) with 95% confidence intervals (CIs) were calculated using a fixed-effects model. The present meta-analysis of 19 RCTs showed that supplementation with phytosterols can decrease both systolic BP (WMD: -1.55 mmHg, 95% CI: -2.67 to -0.42, $p = 0.007$) and diastolic BP (WMD: -0.84 mmHg, 95% CI: -1.60 to -0.08, $p = 0.03$). Dose-response analysis revealed that phytosterol intake change SBP significantly based on treatment dose in nonlinear fashion. Subgroup analysis based on duration showed a significant effect of phytosterol on SBP and DBP in subsets of <12 weeks. In addition, a significant effect of phytosterol was observed in dosage of ≥ 2000 mg for SBP and <2000 mg for DBP. Based on current findings supplementation with phytosterol may be a beneficial adjuvant therapy in hypertensive patients as well as a complementary preventive option in prehypertensive and normotensive individuals. However, this issue is still open and requires further investigation in future studies.

Modic changes - An evidence-based, narrative review on its patho-physiology, clinical significance and role in chronic low back pain Vibhu.

Krishnan Viswanathan 1 , Ajoy Prasad Shetty 1 , S Rajasekaran 1 2

Abstract Objective: Lumbar degenerative spinal ailments are the most important causes for chronic low back pain. Modic changes (MC) are vertebral bone marrow signal intensity changes seen on MRI, commonly in association with degenerative disc disease (DDD). Despite being widely studied, majority of issues concerning MC are still controversial. The current narrative, evidence-based review comprehensively discusses the various aspects related to MC. **Literature search:** An elaborate search was made using keywords "Modic changes", "lumbar Modic changes", "Modic changes in lumbar spine", and "vertebral Endplate Spinal Changes", on pubmed and google (scholar.google.com) databases on the 3rd of March 2020. We identified crucial questions regarding Modic changes and included relevant articles pertaining to these topics for this narrative review. **Results:** The initial search using the keywords "Modic changes", "lumbar Modic changes", "Modic changes in lumbar spine", and "vertebral Endplate Spinal Changes" on pubmed yielded a total of 568, 412, 394 and 216 articles on "pubmed" database, respectively. A similar search using the aforementioned keywords yielded a total of 3650, 3548, 3726 and 21570 articles on "google scholar" database. The initial screening involved exclusion of duplicate articles, articles unrelated to MC, animal or other non-clinical studies, and articles in non-English literature based on abstracts or the titles of articles. This initial screening resulted in the identification of 405 articles. Full manuscripts were obtained for all these selected articles and thoroughly scrutinised at the second stage of article selection. All articles not concerning Modic changes, not pertaining to concerned questions, articles concerning other degenerative phenomena, articles discussing cervical or thoracic MC, case reports or animal studies, articles in non-English language and duplicate articles were excluded. Review articles, randomised controlled trials and level 1 studies were given preference. Overall, 69 articles were included in this review. **Conclusion:** Modic change (MC) is a dynamic phenomenon and its true etiology is still not definitely known. Disc/end plate injury, occult discitis and autoimmune reactions seem to trigger an inflammatory cascade, which leads to their development. Male sex, older age, diabetes mellitus, genetic factors, smoking, obesity, spinal deformities, higher occupational loads and DDD are known risk factors. There is no conclusive evidence on the causative role of MC in chronic low back pain (LBP) or any influence on the long term outcome in patients with LBP or lumbar disc herniations (LDH). Patients with MC have been reported to have less satisfactory outcome following conservative treatment or discectomy, although the evidence is still unclear.

OTORRINOLARINGOLOGIA

Otolaryngol Clin North Am . 2020 Oct;53(5):897-904. doi: 10.1016/j.otc.2020.05.019. Epub 2020 Jul 20.

Sinus Headache: Differential Diagnosis and an Evidence-Based Approach.

Raymond Kim 1 , Zara M Patel 2

Abstract The diagnosis "sinus headache" has been reclassified as "headache attributed to disorder of the nose or paranasal sinuses" by the International Headache Society, but the term is still commonly used by patients and primary care doctors alike. Rhinologic symptoms and headache disorders are common, and they may coexist without a causative relationship. Patients may undergo unnecessary medical interventions because of inadequate understanding of the classifications and management of various headache disorders. Otolaryngologists frequently treat patients with these complaints, and a systematic approach to the differential diagnosis and utilization of a multidisciplinary approach are critical in providing optimal patient care.

UROLOGIA

J Pediatr Urol . 2020 Aug;16(4):464.e1-464.e6. doi: 10.1016/j.jpuro.2020.05.162. Epub 2020 May 31.

Sexual function and health status in adult patients with Congenital Adrenal Hyperplasia.

Barbara Dobrowolska-Glazar 1 , Ireneusz Honkisz 2 , Janusz Sulislawski 2 , Katarzyna Tyrawa 3 , Michal Wolnicki 2 , Rafal Chrzan 2

Abstract Introduction: Congenital Adrenal Hyperplasia (CAH) is the most common reason for undifferentiated genital appearance in new-borns. Psychosexual outcome in women with CAH has been rarely evaluated, but it seems to be one of the most important factors determining the indications for the surgical treatment of CAH. **Objective:** This is to assess sexual function and the health status (HS) in adult females with CAH who had feminizing genitoplasty in childhood. **Material and method:** The protocol was approved by the Ethical Committee, and the hospital database was searched for patients with CAH who had genitoplasty between 1975 and 2000. 57 adult patients were identified, and 9 (18%) patients agreed to participate in the study. Mean age at operation was 5.4 years, and mean follow-up duration was 10.9 years. The Female Sexual Function Index (FSFI) was used to evaluate sexual function, and the 36-item Short Form Health Survey (SF-36) was used to evaluate their health status (HS). A FSFI score < 26,55 was classified as Female Sexual Dysfunction (FSD). The control group consisted of 10 adult female volunteers of comparable age, without any oncological or chronic diseases. Fisher's exact test was used for statistical analysis. **Results:** All patients in the CAH group had female gender identity. One was homosexual, and one reported not having any sexual activity. In the control group, all patients had female gender identity. All were heterosexual and one reported not having any sexual activity. The sexual function in five domains and total score were similar in both groups. More pain was reported in the CAH group as compared with the control group, and it was statistically significant. In the CAH group, 5/9 patients had FSD. In the control group, 4/10 patients had FSD. The difference was statistically insignificant ($p = 0.66$). Mean SF-36 score in the CAH group was 47.1 points, while it was 46.7 points in the control group. The testosterone level in all CAH patients was within the normal range (0.13-1.1 ng/ml).

The 17-OH progesterone level was above normal range in 5/9 (55.6%) patients with CAH. All women in the CAH group were hormonally treated. In the control group, all patients had a normal testosterone level (0.15-0.68 ng/ml); the 17-OH progesterone level was in normal range in this group. Discussion: We compared our results with the literature data, which used the same questionnaires as in our study. Conclusions: Health status and sexual function in the traceable CAH patients didn't differ from the control group.



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