บทความที่น่าสนใจประจำเดือนมกราคม 2558

สาขาวิทยาศาสตร์สุขภาพ

Title :	[Emerging drugs for acute lung injury](#)
Author :	Daniela Impellizzeri, Giuseppe Bruschetta, Emanuela Esposito, and Salvatore Cuzzocrea
Journal :	Expert Opinion on Emerging Drugs: Posted online on January 6, 2015. (doi:10.1517/14728214.2015.1000299)
Abstract :	**Introduction**: Acute respiratory distress syndromes (ARDS) are devastating disorders of overwhelming pulmonary inflammation and hypoxemia, resulting in high morbidity and mortality. **Areas covered**: The main pharmacological treatment strategies have focused on the attempted inhibition of excessive inflammation or the manipulation of the resulting physiological derangement causing respiratory failure. Additionally, such interventions may allow reduced occurence mechanical ventilation injury. Despite promising preclinical and small clinical studies, almost all therapies have been shown to be unsuccessful in large-scale randomized controlled trials. The evidence for pharmacological treatment for ARDS is reviewed. Potential future treatments are also presented. **Expert opinion**: We suggest for future clinical trials addressing prevention and early intervention to attenuate lung injury and progression to respiratory failure
Database :	Informa Healthcare

Title :	[Copeptin as a stress marker prior and after a written examination – the CoEXAM study](#)
Author :	Sandrine A. Urwyler, Philipp Schuetz, Clara Sailer, and Mirjam Christ-Crain
Journal :	Stress: Posted online on January 8, 2015. (doi:10.3109/10253890.2014.993966)

Abstract :	The stress hormone copeptin, which is co-secreted with arginine vasopressin, increases in seriously ill patients and can predict outcome in several organic diseases. Information about the influence of psychological stress on copeptin levels is lacking, but is important for interpretation of copeptin levels in the clinical setting. The aim of this study was to evaluate the influence of psychological stress on copeptin levels. We measured copeptin levels in 25 healthy medical students before and after a written examination. The primary endpoint was change in copeptin levels from immediately prior to examination compared with after the examination. Median copeptin levels prior to the examination were significantly higher than those after its conclusion. Similar results were found for serum cortisol and salivary cortisol. Serum cortisol prior to examination was significantly higher in students with a superior examination result, compared to those with a lower score. In conclusion, psychological stress leads to a subtle increase in copeptin level and might therefore be taken into account as a confounding factor in disorders with small diagnostic copeptin range. Higher cortisol levels, but not copeptin, correlated with a better academic performance in this cohort of students.
Database :	Informa Healthcare

Title :	Type 2 diabetes as a disease of ectopic fat?
Author :	Naveed Sattar* and Jason MR Gill
Journal :	
Abstract :	Background Although obesity and diabetes commonly co-exist, the evidence base to support obesity as the major driver of type 2 diabetes mellitus (T2DM), and the mechanisms by which this occurs, are now better appreciated. Discussion This review briefly examines several sources of evidence – epidemiological, genetic, molecular, and clinical trial – to support obesity being a causal risk factor for T2DM. It also summarises the ectopic fat hypothesis for this condition, and lists several pieces of evidence to support this concept, extending from rare conditions and drug effects to sex- and ethnicity-related differences in T2DM prevalence. Ectopic liver fat

is the best-studied example of ectopic fat, but more research on pancreatic fat as a potential cause of β-cell dysfunction seems warranted. This ectopic fat concept, in turn, broadly fits with the observation that individuals of similar ages can develop diabetes at markedly different body mass indexes (BMIs). Those with risk factors leading to more rapid ectopic fat gain – for example, men (compared with women), certain ethnicities, and potentially those with a family history of diabetes, as well as others with genes linked to a reduced subcutaneous adiposity – are more likely to develop diabetes at a younger age and/or lower BMI than those without.

Summary

Obesity is the major risk factor for T2DM and appears to drive tissue insulin resistance in part via gain of ectopic fat, with the best-studied organ being the liver. However, ectopic fat in the pancreas may contribute to β-cell dysfunction. In line with this observation, rapid resolution of diabetes linked to a preferential and rapid reduction in liver fat has been noted with significant caloric reduction. Whether these observations can help develop better cost-effective and sustainable lifestyle /medical interventions in patients with T2DM requires further study.

Database :	BioMed Central

Title :	Weight loss required by the severely obese to achieve clinically important differences in health-related quality of life: two-year prospective cohort study
Author :	Lindsey M Warkentin, Sumit R Majumdar, Jeffrey A Johnson, Calypse B Agborsangaya, Christian F Rueda-Clausen, Arya M Sharma, Scott W Klarenbach, Shahzeer Karmali, Daniel W Birch and Raj S Padwal
Journal :	BMC Medicine 2014, 12:175 doi:10. 1186/s12916-014-0175-5
Abstract :	Background Guidelines and experts describe 5% to 10% reductions in body weight as 'clinically important'; however, it is not clear if 5% to 10% weight reductions correspond to clinically important improvements in health-related quality of life (HRQL). Our objective was to calculate the amount of weight loss required to attain established minimal clinically important differences (MCIDs) in HRQL, measured using three validated instruments.

Methods

Data from the Alberta Population-based Prospective Evaluation of Quality of Life Outcomes and Economic Impact of Bariatric Surgery (APPLES) study, a population-based, prospective Canadian cohort including 150 wait-listed, 200 medically managed and 150 surgically treated patients were examined. Two-year changes in weight and HRQL measures (Short-Form (SF)-12 physical (PCS; MCID = 5) and mental (MCS; MCID = 5) component summary score, EQ-5D Index (MCID = 0.03) and Visual Analog Scale (VAS; MCID = 10), Impact of Weight on Quality of Life (IWQOL)-Lite total score (MCID = 12)) were calculated. Separate multivariable linear regression models were constructed within medically and surgically treated patients to determine if weight changes achieved HRQL MCIDs. Pooled analysis in all 500 patients was performed to estimate the weight reductions required to achieve the pre-defined MCID for each HRQL instrument.

Results

Mean age was 43.7 (SD 9.6) years, 88% were women, 92% were white, and mean initial body mass index was 47.9 (SD 8.1) kg/m2. In surgically treated patients (two-year weight loss = 16%), HRQL MCIDs were reached for all instruments except the SF-12 MCS. In medically managed patients (two-year weight loss = 3%), MCIDs were attained in the EQ-index but not the other instruments. In all patients, percent weight reductions to achieve MCIDs were: 23% (95% confidence interval (CI): 17.5, 32.5) for PCS, 25% (17.5, 40.2) for MCS, 9% (6.2, 15.0) for EQ-Index, 23% (17.3, 36.1) for EQ-VAS, and 17% (14.1, 20.4) for IWQOL-Lite total score.

Conclusions

Weight reductions to achieve MCIDs for most HRQL instruments are markedly higher than the conventional threshold of 5% to 10%. Surgical, but not medical treatment, consistently led to clinically important improvements in HRQL over two years.

Database :	BioMed Central

Title :	Highlights from the 2014 International Symposium on HIV & Emerging Infectious Diseases (ISHEID): from cART management to the end of the HIV pandemic
Author :	Alain Lafeuillade, Mark Wainberg, Marie-Lise Gougeon, Sabine Kinloch-de Loes, Philippe Halfon and Hervé Tissot-Dupont
Journal :	AIDS Research and Therapy 2014, 11:28 doi:10.1186/1742-6405-11-28
Abstract :	The 2014 International Symposium on HIV and Emerging Infectious Diseases (ISHEID) provided a forum for investigators to hear the latest research developments in the clinical management of HIV and HCV infections as well as HIV cure research. Combined anti-retroviral therapy (c-ART) has had a profound impact on the disease prognosis and transformed this infection into a chronic disease. However, HIV is able to persist within the infected host and the pandemic is still growing. The main 2014 ISHEID theme was, hence "Together for a world without HIV and AIDS". In this report we not only give details on this main topic but also summarize what has been discussed in the areas of HCV coinfection and present a short summary on currently emerging viral diseases.
Database :	BioMed Central

Title :	Determination of Key Parameters for a Mechanism-Based Model to Predict Doxorubicin Release from Actively Loaded Liposomes
Author :	Eva Csuhai, Sogol Kangarlou, Tian-Xiang Xiang, Andrei Ponta, Paul Bummer, Duhyung Choi and Bradley D. Anderson
Journal :	Journal of Pharmaceutical Sciences: Article first published online: 5 JAN 2015 DOI: 10.1002/jps.24307
Abstract :	Despite extensive study of liposomal drug formulations, reliable predictive models of release kinetics in vitro and in vivo are still lacking. Progress in the development of robust, predictive release models has been hindered by a lack of systematic, quantitative characterization of these complex drug delivery systems with respect to the myriad of factors that may influence drug release kinetics and the wide range of dissolution media/methods employed to monitor release. In this paper, the key processes and parameters needed to develop a complete mechanism-based model for doxorubicin release from actively loaded liposomal formulations resembling

	Doxil® are determined. Quantitative models must account for the driving force(s) [i.e., activity gradient(s) of the permeable species between the intraliposomal and external media] and the permeability-area product(s) for lipid bilayer transport. These factors are intertwined as membrane permeability-area products require knowledge of the drug species and concentrations that account for the release. The necessary information includes values for the drug pKa, identity of the permeable species and species permeability coefficients, a model to describe drug self-association and the relevant equilibrium constant(s), the bilayer/water partition coefficient of the predominant drug species under relevant pH conditions, and the solubility product (Ksp) for intraliposomal precipitates that exist in such formulations.
Database :	Wiley Online Library

Title :	A Review of the Potential Role of Nano-Enabled Drug Delivery Technologies in Amyotrophic Lateral Sclerosis: Lessons Learned from Other Neurodegenerative Disorders
Author :	Zamanzima Mazibuko, Yahya E. Choonara, Pradeep Kumar, Lisa C. Du Toit, Girish Modi, Dinesh Naidoo and Viness Pillay
Journal :	Journal of Pharmaceutical Sciences : Article first published online: 5 JAN 2015 | DOI: 10.1002/jps.24322
Abstract :	Amyotrophic lateral sclerosis (ALS) has a multitude of factors implicated in its etiology. The complex neuro-etiology and the restrictive nature of the blood–brain barrier (BBB) have significantly hindered the drug therapy of ALS. Riluzole, a moderately performing drug, is the only agent approved for treating ALS. However, several promising nanocarrier approaches are surfacing that can provide more efficient drug delivery. In addition, biologicals such as stem cells are able to carry neurotrophic factors to their target site, providing motor neurons with the benefits of both, stem cells and neurotrophic factors. This review examines the current drug delivery strategies investigated for optimally treating ALS and related neurodegenerative disorders. Examples include cerium oxide nanoparticles in Alzheimer's disease, odorranalectin, and lactoferrin-coupled PEG–PLGA nanoparticles for urocortin transportation in Parkinson's disease that can also be employed in ALS to bypass the BBB and increase drug bioavailability. A concise

	incursion into the progress (and lack thereof) made in ALS clinical trials is also discussed. Nanocarriers can potentially eliminate the challenges of poor drug bioavailability in ALS as they have been proven to cross the BBB and reach target sites while minimizing systemic side-effects. Nanocarrier-based delivery of ALS drugs is an area that requires much needed investigation.
Database :	Wiley Online Library

Title :	Adenoviral vectors as novel vaccines for influenza
Author :	Lynda Coughlan, Caitlin Mullarkey and Sarah Gilbert
Journal :	Journal of Pharmacy and Pharmacology: Article first published online: 5 JAN 2015 | DOI: 10.1111/jphp.12350
Abstract :	Objectives Influenza is a viral respiratory disease causing seasonal epidemics, with significant annual illness and mortality. Emerging viruses can pose a major pandemic threat if they acquire the capacity for sustained human-to-human transmission. Vaccination reduces influenza-associated mortality and is critical in minimising the burden on the healthcare system. However, current vaccines are not always effective in at-risk populations and fail to induce long-lasting protective immunity against a range of viruses. Key findings The development of 'universal' influenza vaccines, which induce heterosubtypic immunity capable of reducing disease severity, limiting viral shedding or protecting against influenza subtypes with pandemic potential, has gained interest in the research community. To date, approaches have focused on inducing immune responses to conserved epitopes within the stem of haemagglutinin, targeting the ectodomain of influenza M2e or by stimulating cellular immunity to conserved internal antigens, nucleoprotein or matrix protein 1. Summary Adenoviral vectors are potent inducers of T-cell and antibody responses and have demonstrated safety in clinical applications, making them an excellent choice of

	vector for delivery of vaccine antigens. In order to circumvent pre-existing immunity in humans, serotypes from non-human primates have recently been investigated. We will discuss the pre-clinical development of these novel vectors and their advancement to clinical trials.
Database :	Wiley Online Library

Title :	The effects of serum apolipoprotein E genetic variants and concentration on serum lipid parameters in haemodialysis patients
Author :	Kai Wang, Pei Wang, Yingjin Qiao, Xiaoqing Lu, Xin Wang and Zhangsuo Liu
Journal :	Journal of Pharmacy and Pharmacology: Article first published online: 5 JAN 2015 | DOI: 10.1111/jphp.12356
Abstract :	Objectives Many epidemiological studies demonstrate that the apolipoprotein E gene (ApoE) is an important candidate gene for playing key roles in the development of haemodialysis (HD). The purpose of this study is to evaluate the effects of ApoE genetic variants and concentration on serum lipid parameters in HD. Methods A total of 288 HD patients and 292 healthy controls were enrolled in this case–control study. The genotypes of ApoE genetic variants were investigated through the created restriction site-polymerase chain reaction and DNA-sequencing methods. Key findings Our data indicated that the levels of triglyceride, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, apolipoprotein A-I (ApoA-I), ApoB, ApoE, lipoprotein (a) (Lp(a)) of mutant genotypes in ApoE c.61G > A and c.761T > A genetic variants were different from those subjects with wild genotype in HD patients and healthy controls. Conclusions These preliminary results from this study suggest that the ApoE genetic variants and

	concentration could affect the serum lipid parameters in HD and could be risk factors for evaluating HD.
Database :	Wiley Online Library

Title :	[Assessing outcomes of alcohol-related brain damage (ARBD): What should we be measuring?](#)
Author :	Lindsay Horton, et al.
Journal :	Drugs: education, prevention, and policy: Posted online on January 5, 2015. (doi:10.3109/09687637.2014.991278)
Abstract :	The recent move towards outcomes-focused assessment in health and social care has made it important to identify which outcomes are relevant to alcohol-related brain damage (ARBD). Clinical outcomes' guidance for ARBD is currently absent from policy documentation. Thus, the aim of this review is to evaluate the current evidence base to determine recommendations for the measurement of ARBD outcomes. A total of 71 separate references were identified through a systematic online database and hand search. The screening and exclusion strategy left seven articles to be included in this review. The findings indicate that research into ARBD has focussed on a number of outcome domains, including the type of accommodation and provision of support, drinking status, employment status, the number of deaths, mental health and psychiatric symptoms, activities of daily living, social functioning and cognitive functioning. The identified outcomes suggest that practitioners should focus on a comprehensive range of clinical outcomes for ARBD service users. Nevertheless, the paucity of the existing evidence base makes it difficult to make clinical recommendations for the measurement of ARBD outcomes. Further research is necessary to shed light on long-term outcomes for people with ARBD and to increase the strength of the evidence in this area.
Database :	Informa Healthcare