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List of publications of AIIMS, New Delhi for the month of May, 2018
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1: Adhikari N, Biswas A, Bakhshi S, Khanna G, Suri V. A rare case of paediatric primary central nervous system lymphoma treated with high-dose methotrexate and rituximab-based chemoimmunotherapy and whole brain radiotherapy followed by tumour bed boost with three-dimensional conformal radiation technique. Childs Nerv Syst. 2018 Sep;34(9):1777-1783. doi: 10.1007/s00381-018-3807-9. Epub 2018 May 9. PubMed PMID: 29744624.

BACKGROUND: Primary central nervous system lymphomas (PCNSL) are rare in the paediatric population.
CLINICAL CASE: A 12-year-old boy presented to our clinic with complaints of multiple episodes of generalised tonic-clonic seizures for 1 year and gradual loss of vision in both eyes for 3 months. Baseline magnetic resonance imaging (MRI) of the brain showed a large (7.2×7 cm) enhancing soft tissue lesion in the right frontal lobe causing mass effect and midline shift. With a radiological diagnosis of supratentorial primitive neuroectodermal tumour, he underwent subtotal resection of tumour. The post-operative histopathology revealed diffuse large B cell lymphoma (DLBCL). Systemic lymphoma workup was essentially normal. He received five cycles of chemoimmunotherapy with rituximab, high-dose methotrexate (HDMTX), vincristine and procarbazine and had complete radiological response (CR). This was followed by whole brain radiotherapy (WBRT) to a dose of 36 Gy in 20 fractions and sequential tumour bed boost to a dose of 9 Gy in 5 fractions by three-dimensional conformal technique. Subsequently, he received two cycles of consolidation chemotherapy with high-dose cytarabine. At completion of treatment, 3 and 6 months thereafter, MRI brain showed CR. At last follow-up visit, 13 months from the date of diagnosis, he was disease-free and asymptomatic with the exception of dimness of vision in both eyes due to long-standing bilateral optic atrophy.
CONCLUSION: This report highlights the fact that paediatric PCNSL may be effectively treated by a combination of HDMTX and rituximab-based chemoimmunotherapy followed by consolidation with conformal WBRT and tumour bed boost. Lack of awareness of this rare entity may lead to diagnostic delay and potential ramifications as exemplified by chronic atrophic papilloedema and visual loss in the illustrative case.

DOI: 10.1007/s00381-018-3807-9
PMID: 29744624

2: Agarwal N, Gupta D. Letter to the Editor. Endoscopic endonasal versus transcranial approach to tuberculum sellae and planum sphenoidale meningiomas: unanswered questions. J Neurosurg. 2018 Aug;129(2):560-561. doi: 10.3171/2018.3.JNS18598. Epub 2018 May 25. PubMed PMID: 29799341.

3: Aggarwal B, Gupta N. Familial Hypercholesterolemia: Nip the Evil in the Bud. Indian J Pediatr. 2018 May;85(5):331-332. doi: 10.1007/s12098-018-2664-6. Epub 2018 Mar 29. PubMed PMID: 29594955.

4: Aggarwal S, Das SN. Response to the query raised by Lydia Bernardo. Oral Dis. 2018 May;24(4):674. doi: 10.1111/odi.12673. PubMed PMID: 29659135.

5: Agrawal M, Garg M, Kumar A, Singh PK, Satyarthee GD, Agrawal D, Chandra PS, Kale SS. Management of Pediatric Posttraumatic Thoracolumbar Vertebral Body Burst Fractures by Use of Single-Stage Posterior Transpedicular Approach. World Neurosurg. 2018 Sep;117:e22-e33. doi: 10.1016/j.wneu.2018.05.088. Epub 2018 May 19. PubMed PMID: 29787879.

PURPOSE: The posterior transpedicular approach (PTA) is a posterior approach that has the advantage of achieving circumferential arthrodesis by a single posterior-only approach. The purpose of this study was to analyze our experience

with PTA in the management of pediatric traumatic thoracolumbar burst fractures (TTLBFs).
METHODS: Consecutive pediatric patients (age ≤18 years) with TTLBFs treated with PTA for 6 years were included in this retrospective study. Correction of kyphotic deformity and change in neurologic status were analyzed to assess outcome. The Cobb angle and American Spinal Injury Association (ASIA) grade were used for this purpose.
RESULTS: There were 6 male and 8 female patients. Five patients had complete injury (ASIA-A), and 9 had incomplete injury. The mean Thoracolumbar Injury Classification and Severity score was 6.71. The mean preoperative Cobb angle was 14.71° and improved to -3.35° postoperatively (mean kyphosis correction -18.05°). Two of the patients experienced iatrogenic nerve root injury. There was 1 postoperative mortality due to complications unrelated to the surgery. The mean Cobb angle was -0.07° at the 32.2-month follow-up visit. Six patients experienced cage subsidence, but none required revision surgery. Postoperatively, 11 (78.5%) patients showed neurologic improvement, and none experienced deterioration. The average ASIA score improved from 2.5 to 3.78. A fusion rate of 100% (n = 12) was observed at the last follow-up visit.
CONCLUSIONS: The present study demonstrates that PTA is a feasible approach in selected pediatric patients with unstable traumatic thoracolumbar burst fractures, with results comparable with those in the adult population. This study demonstrates in detail the procedure, along with the neurologic and radiologic outcomes of this approach in the pediatric population.

DOI: 10.1016/j.wneu.2018.05.088
PMID: 29787879 [Indexed for MEDLINE]

6: Agrawal M, Borkar SA, Khanna G, Sharma MC, Kale SS. Pigmented Ganglioglioma of the Cerebellum: Case Report and Review. World Neurosurg. 2018 Aug;116:18-24. doi: 10.1016/j.wneu.2018.04.219. Epub 2018 May 9. Review. PubMed PMID: 29753075.

BACKGROUND: Gangliogliomas (GGs) are rare intra-axial tumors. Cerebellar seizures caused by GGs have been described only rarely. Pigmented neural cell tumors are well described in the literature but are infrequent, especially when presenting as primary neuroepithelial tumors. Only 5 cases of pigmented GG have been reported previously, including 4 in the pediatric population.
CASE DESCRIPTION: A 17-year-old female presented to us with cerebellar seizures, which resolved after tumor excision. Histopathological examination revealed a pigmented GG.
CONCLUSIONS: We present the sixth documented case of a pigmented ganglioglioma, the first such case reported in cerebellar location, associated with a rare presentation of cerebellar seizures.

DOI: 10.1016/j.wneu.2018.04.219
PMID: 29753075 [Indexed for MEDLINE]

7: Agrawal R, Garg A, Benny Malgulwar P, Sharma V, Sarkar C, Kulshreshtha R. p53 and miR-210 regulated NeuroD2, a neuronal basic helix-loop-helix transcription factor, is downregulated in glioblastoma patients and functions as a tumor suppressor under hypoxic microenvironment. Int J Cancer. 2018 May 1;142(9):1817-1828. doi: 10.1002/ijc.31209. Epub 2017 Dec 23. PubMed PMID: 29226333.

The factors involved in cell differentiation have recently garnered interest for

their role in inhibition of pathogenesis in various tumors. However, their role in glioblastoma (GBM) remains poorly understood. We analyzed The Cancer Genome Atlas (TCGA) GBM data and found significant downregulation of neurogenic differentiation factor NeuroD2 in GBM patients. Low levels of NeuroD2 were found to be correlated with poor overall survival of GBM patients in TCGA dataset as well as in our cohort. Interestingly, NeuroD2 was shown to be transcriptionally induced by p53 and post-transcriptionally targeted by hypoxia- inducible miRNA, miR-210. NeuroD2 overexpression diminished GBM aggressiveness by inhibiting cell proliferation, migration and promoting apoptosis under hypoxia. NeuroD2 overexpressing GBM cells failed to form three-dimensional (3D)-tumor spheroids and displayed reduced migration in a 3D gelatin matrix. NeuroD2 gene signature was enriched in pathways belonging to cytokine-cytokine receptor interaction, TNF-signaling, PI3K-AKT signaling, focal adhesion and ECM-receptor interaction. Overall, our study identifies a novel role of NeuroD2 as a tumor suppressor and prognostic biomarker in GBM the levels of which are tightly regulated by p53 and miR-210. Overexpressing NeuroD2 may potentially be a simple and efficient therapeutic strategy to inhibit the malignant phenotype of GBM cells.

DOI: 10.1002/ijc.31209
PMID: 29226333

8: Agrawal S, Yadav VS, Srivastava A, Kapil A, Dhawan B. Breast abscess due to Salmonella paratyphi A : Case reports with review of literature. Intractable Rare Dis Res. 2018 May;7(2):130-133. doi: 10.5582/irdr.2018.01031. PubMed PMID: 29862156; PubMed Central PMCID: PMC5982621.

Salmonella paratyphi A causes paratyphoid fever which is characterized by acute onset of fever, abdominal pain, diarrhoea, nausea and vomiting. Localized disease can occur following both overt and silent bacteremia followed by seeding of bacteria at distant sites. Salmonella species though associated with abscess formation in various organs,are rarely associated with breast abscess. We report 2 cases of breast abscess due to Salmonella enterica serotype paratyphi A. Appropriate sampling, surgery supplemented by a comprehensive microbiological work up aided in pathogen identification and appropriate antibiotic administration for a successful outcome of these patients.

DOI: 10.5582/irdr.2018.01031
PMCID: PMC5982621
PMID: 29862156

9: Al-Mallah MH, Pascual TNB, Mercuri M, Vitola JV, Karthikeyan G, Better N, Dondi M, Paez D, Einstein AJ; INCAPS Investigators Group. Impact of age on the selection of nuclear cardiology stress protocols: The INCAPS (IAEA nuclear cardiology protocols) study. Int J Cardiol. 2018 May 15;259:222-226. doi: 10.1016/j.ijcard.2018.02.060. Epub 2018 Feb 16. PubMed PMID: 29486996.

BACKGROUND: There is growing concern about radiation exposure from nuclear myocardial perfusion imaging (MPI), particularly among younger patients who are more prone to develop untoward effects of ionizing radiation, and hence US and European professional society guidelines recommend age as a consideration in weighing radiation risk from MPI. We aimed to determine how patient radiation doses from MPI vary across age groups in a large contemporary international cohort.
METHODS: Data were collected as part of a global cross-sectional study of centers performing MPI coordinated by the International Atomic Energy Agency (IAEA). Sites provided information on each MPI study completed during a single week in

March-April 2013. We compared across age groups laboratory adherence to pre-specified radiation-related best practices, radiation effective dose (ED; a whole-body measure reflecting the amount of radiation to each organ and its relative sensitivity to radiation's deleterious effects), and the proportion of patients with ED≤9 mSv, a target level specified in guidelines.
RESULTS: Among 7911 patients undergoing MPI in 308 laboratories in 65 countries, mean ED was 10.0±4.5 mSv with slightly higher exposure among younger age groups (trend p value<0.001). There was no difference in the proportion of patients with ED≤9 mSv across age groups, or in adherence to best practices based on the median age of patients in a laboratory.
CONCLUSIONS: In contemporary nuclear cardiology practice, the age of the patient appears not to impact protocol selection and radiation dose, contrary to professional society guidelines.

DOI: 10.1016/j.ijcard.2018.02.060
PMID: 29486996

10: Alhazzani AA, Kumar A, Selim M. Association between Factor V Gene Polymorphism and Risk of Ischemic Stroke: An Updated Meta-Analysis. J Stroke Cerebrovasc Dis. 2018 May;27(5):1252-1261. doi: 10.1016/j.jstrokecerebrovasdis.2017.12.006. Epub 2018 Feb 23. Review. PubMed PMID: 29478939.

BACKGROUND: Ischemic stroke is a complex, multifactorial, and polygenic disease. Reports on relationship between Factor V G1691A single nucleotide gene polymorphism and ischemic stroke have revealed inconsistent results. We conducted an updated meta-analysis to determine the role of Factor V single nucleotide gene polymorphism in ischemic stroke.
METHODS: We searched the literature using academic electronic databases that is, PubMed, Trip Data Base, EBSCO, and Google Scholar, last search up to September 2017. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated from fixed or random effects models whichever applicable using software STATA version 13 (StataCorp LP, College Station, TX).
RESULTS: Forty case-control studies met the inclusion criteria, which included 6860 cases and 18,025 controls. Altogether, 19 studies in young adults (age<or=40 years) and 17 studies were conducted in old stroke (age>40). Four studies did not report the mean age at recruitment. Significant association between Factor V G1691A gene polymorphism and risk of ischemic stroke were observed under dominant model (OR 1.40; 95% CI: 1.22 to 1.62, P value <.001). Stratified analysis suggested substantial association of Factor V gene polymorphism and risk of ischemic stroke in cases with onset at young age (OR 1.84; 95% CI: 1.47 to 2.30), but was not statistical significant in cases at old age (>40 years).
CONCLUSIONS: Factor V G1691A single nucleotide gene polymorphism was associated with risk of ischemic stroke mainly in young adults. Further research with adequately powered prospective studies in homogenous subjects are required to determine the nature of association in young stroke.

DOI: 10.1016/j.jstrokecerebrovasdis.2017.12.006
PMID: 29478939 [Indexed for MEDLINE]

11: Arora S, Damle NA, Parida GK, Singhal A, Nalli H, Dattagupta S, Bal C.

Recurrent Medullary Thyroid Carcinoma on 68Ga-Prostate-Specific Membrane Antigen PET/CT: Exploring New Theranostic Avenues. Clin Nucl Med. 2018 May;43(5):359-360. doi: 10.1097/RLU.0000000000002010. PubMed PMID: 29485449.

The prostate-specific membrane antigen (PSMA) is highly expressed in prostate cancer cells. Few other malignancies have shown expression of PSMA. We present a case of 35-year-old man with medullary thyroid carcinoma, post total thyroidectomy and bilateral neck dissection, now presenting with rising calcitonin levels (doubling time 9 months) and local neck recurrence with negative I-MIBG scan. We decided to perform Ga-PSMA-HBED-CC PET/CT scan to assess PSMA expression and explore the therapeutic option in view of rising serum calcitonin. It revealed intense PSMA uptake in the soft tissue mass in left thyroid bed and cervical lymph nodes.

DOI: 10.1097/RLU.0000000000002010
PMID: 29485449 [Indexed for MEDLINE]

12: Arora S, Damle NA, Passah A, Yadav MP, Ballal S, Aggarwal V, Gupta Y, Kumar P, Tripathi M, Bal C. Incidental Detection of Parathyroid Adenoma on Somatostatin Receptor PET/CT and Incremental RoleÂ of (18)F-Fluorocholine PET/CT in MEN1 Syndrome. Nucl Med Mol Imaging. 2018 Jun;52(3):238-242. doi: 10.1007/s13139-018-0520-2. Epub 2018 May 2. PubMed PMID: 29942404; PubMed Central PMCID: PMC5995772.

Multiple endocrine neoplasia type 1 (MEN1) syndrome is characterized by combined occurrence of tumors of endocrine glands including the parathyroid, the pancreatic islet cells, and the anterior pituitary gland. Parathyroid involvement is the most common manifestation and usually the first clinical involvement in MEN1 syndrome, followed by gastroentero-pancreatic neuroendocrine tumors (NETs). Here we present a case where the patient initially presented with metastatic gastric NET and a single parathyroid adenoma was detected incidentally on 68Ga-DOTANOC PET/CT done as part of post 177Lu-DOTATATE therapy (PRRT) follow-up. Further 18F-fluorocholine PET/CT showed four adenomas for which the patient subsequently underwent subtotal parathyroidectomy.

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PMCID: PMC5995772 [Available on 2019-06-01]
PMID: 29942404

Conflict of interest statement: Compliance with Ethical StandardsSaurabh Arora, Nishikant Avinash Damle, Averilicia Passah, Madhav Prasad Yadav, Sanjana Ballal, Vivek Aggarwal, Yashdeep Gupta, Praveen Kumar, Madhavi Tripathi, and Chandrasekhar Bal declare that they have no conflict of interest.All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.Informed consent was obtained from all individual participants included in the study.

13: Ashraf S, Kudo H, Rao J, Kikuchi A, Widmeier E, Lawson JA, Tan W, Hermle T, Warejko JK, Shril S, Airik M, Jobst-Schwan T, Lovric S, Braun DA, Gee HY, Schapiro D, Majmundar AJ, Sadowski CE, Pabst WL, Daga A, van der Ven AT, Schmidt JM, Low BC, Gupta AB, Tripathi BK, Wong J, Campbell K, Metcalfe K, Schanze D, Niihori T, Kaito H, Nozu K, Tsukaguchi H, Tanaka R, Hamahira K, Kobayashi Y, Takizawa T, Funayama R, Nakayama K, Aoki Y, Kumagai N, Iijima K, Fehrenbach H, Kari JA, El Desoky S, Jalalah S, Bogdanovic R, StajiÄ‡ N, Zappel H, Rakhmetova A, Wassmer SR, Jungraithmayr T, Strehlau J, Kumar AS, Bagga A, Soliman NA, Mane SM, Kaufman L, Lowy DR, Jairajpuri MA, Lifton RP, Pei Y, Zenker M, Kure S,

Hildebrandt F. Mutations in six nephrosis genes delineate a pathogenic pathway amenable to treatment. Nat Commun. 2018 May 17;9(1):1960. doi: 10.1038/s41467-018-04193-w. PubMed PMID: 29773874; PubMed Central PMCID: PMC5958119.

No efficient treatment exists for nephrotic syndrome (NS), a frequent cause of chronic kidney disease. Here we show mutations in six different genes (MAGI2, TNS2, DLC1, CDK20, ITSN1, ITSN2) as causing NS in 17 families with partially treatment-sensitive NS (pTSNS). These proteins interact and we delineate their roles in Rho-like small GTPase (RLSG) activity, and demonstrate deficiency for mutants of pTSNS patients. We find that CDK20 regulates DLC1. Knockdown of MAGI2, DLC1, or CDK20 in cultured podocytes reduces migration rate. Treatment with dexamethasone abolishes RhoA activation by knockdown of DLC1 or CDK20 indicating that steroid treatment in patients with pTSNS and mutations in these genes is mediated by this RLSG module. Furthermore, we discover ITSN1 and ITSN2 as podocytic guanine nucleotide exchange factors for Cdc42. We generate Itsn2-L knockout mice that recapitulate the mild NS phenotype. We, thus, define a functional network of RhoA regulation, thereby revealing potential therapeutic targets.

DOI: 10.1038/s41467-018-04193-w
PMCID: PMC5958119
PMID: 29773874

14: Babu BV, Sharma Y, Kusuma YS, Sivakami M, Lal DK, Marimuthu P, Geddam JB, Khanna A, Agarwal M, Sudhakar G, Sengupta P, Borhade A, Khan Z, Kerketta AS, Brogen A. Internal migrants' experiences with and perceptions of frontline health workers: A nationwide study in 13 Indian cities. Int J Health Plann Manage. 2018 May 9. doi: 10.1002/hpm.2538. [Epub ahead of print] PubMed PMID: 29744933.

The role of frontline health workers is crucial in strengthening primary health care in India. This paper reports on the extent of services provided by frontline health workers in migrants' experiences and perceptions of these services in 13 Indian cities. Cluster random sampling was used to sample 51 055 households for a quantitative survey through interviewer-administered questionnaires. Information was sought on the receipt of health workers' services for general health care overall (from the head/other adult member of the household) and maternal and immunization services in particular (from mothers of children <2 years old). Purposively, 240 key informants and 290 recently delivered mothers were selected for qualitative interviews. Only 31% of the total respondents were aware of the visits of frontline health workers, and 20% of households reported visits to their locality during past month. In 4 cities, approximately 90% of households never saw health workers in their locality. Only 20% of women and 22% of children received antenatal care and vaccination cards from frontline health workers. Qualitative data confirm that the frontline health workers' visits were not regular and that health workers limited their services to antenatal care and childhood immunization. It was further noted that health workers saw the migrants as"outsiders." These findings warrant developing migrant-specific health-care services that consider their vulnerability and living conditions. The present study has implications for India's National Urban Health Mission, which envisions addressing the health care needs of the urban population with a focus on the urban poor.

DOI: 10.1002/hpm.2538
PMID: 29744933

15: Bahrani K, Singh MB, Bhatia R, Prasad K, Vibha D, Shukla G, Vishnubhatla S, Patterson V. A response to S. Basu (2017). Seizure. 2018 May;58:164. doi: 10.1016/j.seizure.2018.01.004. Epub 2018 Jan 5. PubMed PMID: 29336983.

16: Balhara YPS, Verma K, Bhargava R. Screen time and screen addiction: Beyond gaming, social media and pornography- A case report. Asian J Psychiatr. 2018 Jun;35:77-78. doi: 10.1016/j.ajp.2018.05.020. Epub 2018 May 26. PubMed PMID: 29803121.

17: Bauddha NK, Jadon RS, Mondal S, Vikram NK, Sood R. Progressive disseminated histoplasmosis in an immunocompetent adult: A case report. Intractable Rare Dis Res. 2018 May;7(2):126-129. doi: 10.5582/irdr.2018.01022. PubMed PMID: 29862155; PubMed Central PMCID: PMC5982620.

Histoplasmosis is a systemic fungal infection caused by Histoplasma capsulatum which occurs endemically in some parts of the world like North and Central America particularly in Mississippi and Ohio River valleys, but is uncommon in India. Progressive disseminated form of histoplasmosis (PDH) usually occurs in the immune-compromised hosts especially in HIV positive population. In PDH any organ can be involved like lung, liver, spleen, brain, adrenals etc. Involvement of oral cavity and buccal mucosa in PDH is common but pharyngeal involvement is rare. We here report a case of progressive disseminated histoplasmsosis with pharyngeal involvement in an immunocompetent male from non-endemic area. This case presented to us with history of long duration fever and we found the etiology by giving due significance to a trivial symptom and thorough evaluation of the same. Etiology was found as disseminated histoplasmosis, which is not a common disease. We treated him initially with amphotericin-B then subsequently with itraconazole for one year. He recovered fully over the period of one year with the given treatment. This case report emphasizes that disseminated histoplasmosis should be considered one differential diagnosis in case of long duration of fever, even in an immunocompetent patient. It also emphasizes that in evaluation of a case of long duration of fever, even a trivial symptom is very crucial, which may direct towards the diagnosis.

DOI: 10.5582/irdr.2018.01022
PMCID: PMC5982620
PMID: 29862155

18: Beveridge LA, Khan F, Struthers AD, Armitage J, Barchetta I, Bressendorff I, Cavallo MG, Clarke R, Dalan R, Dreyer G, Gepner AD, Forouhi NG, Harris RA, Hitman GA, Larsen T, Khadgawat R, Marckmann P, Mose FH, Pilz S, Scholze A, Shargorodsky M, Sokol SI, Stricker H, Zoccali C, Witham MD. Effect of Vitamin D Supplementation on Markers of Vascular Function: A Systematic Review and Individual Participant Meta-Analysis. J Am Heart Assoc. 2018 May 30;7(11). pii: e008273. doi: 10.1161/JAHA.117.008273. Review. PubMed PMID: 29848497; PubMed Central PMCID: PMC6015391.

BACKGROUND: Low 25-hydroxyvitamin D levels are associated with an increased risk of cardiovascular events, but the effect of vitamin D supplementation on markers of vascular function associated with major adverse cardiovascular events is unclear.
METHODS AND RESULTS: We conducted a systematic review and individual participant meta-analysis to examine the effect of vitamin D supplementation on flow-mediated dilatation of the brachial artery, pulse wave velocity, augmentation index, central blood pressure, microvascular function, and reactive hyperemia index. MEDLINE, CINAHL, EMBASE, Cochrane Central Register of Controlled Trials, and http://www.ClinicalTrials.gov were searched until the end of 2016 without

language restrictions. Placebo-controlled randomized trials of at least 4 weeks duration were included. Individual participant data were sought from investigators on included trials. Trial-level meta-analysis was performed using random-effects models; individual participant meta-analyses used a 2-stage analytic strategy, examining effects in prespecified subgroups. 31 trials (2751 participants) were included; 29 trials (2641 participants) contributed data to trial-level meta-analysis, and 24 trials (2051 participants) contributed to individual-participant analyses. Vitamin D3 daily dose equivalents ranged from 900 to 5000 IU; duration was 4 weeks to 12 months. Trial-level meta-analysis showed no significant effect of supplementation on macrovascular measures (flow-mediated dilatation, 0.37% [95% confidence interval, -0.23 to 0.97]; carotid-femoral pulse wave velocity, 0.00 m/s [95% confidence interval, -0.36 to 0.37]); similar results were obtained from individual participant data. Microvascular function showed a modest improvement in trial-level data only. No consistent benefit was observed in subgroup analyses or between different vitamin D analogues.
CONCLUSIONS: Vitamin D supplementation had no significant effect on most markers of vascular function in this analysis.

DOI: 10.1161/JAHA.117.008273
PMCID: PMC6015391
PMID: 29848497

19: Bhasin D, Gupta SK, Arava S, Kothari SS. Eosinophilia to endomyocardial fibrosis: Documentation of a case. Ann Pediatr Cardiol. 2018 May-Aug;11(2):207-210. doi: 10.4103/apc.APC_143_17. PubMed PMID: 29922022; PubMed Central PMCID: PMC5963239.

Endomyocardial fibrosis (EMF) is an important cause of restrictive cardiomyopathy in tropical countries. The etiopathogenesis of EMF remains obscure. The role of eosinophilia in the etiopathogenesis of EMF has been debated extensively, but remains unproven. Accordingly, we present a case wherein a patient with documented eosinophilia and heart failure at the age of three-and-a-half years presented with endomyocardial fibrosis at the age of nine years. Such documentation is important to highlight the central role of eosinophils in the pathogenesis of EMF.

DOI: 10.4103/apc.APC_143_17
PMCID: PMC5963239
PMID: 29922022

Conflict of interest statement: There are no conflicts of interest.

20: Bijalwan A, Patel BP, Marieswaran M, Kalyanasundaram D. Volumetric locking free 3D finite element for modelling of anisotropic visco-hyperelastic behaviour of anterior cruciate ligament. J Biomech. 2018 May 17;73:1-8. doi: 10.1016/j.jbiomech.2018.03.016. Epub 2018 Mar 16. PubMed PMID: 29599040.

Solids such as polymers, soft biological tissues display visco-hyperelastic, isochoric and finite deformation behaviour. The incompressibility constraint imposed severe restriction on the displacement field results in volumetric locking. Many techniques have been developed to address the issue such as reduced integration, mixed formulation, B-Bar and F-Bar methods, each of them with their own merits and demerits. In this work, we have developed a 3D finite element (hereby referred as J-Bar method) to counter volumetric locking in

visco-hyperelastic solids. To validate the proposed J-Bar method, rheological characteristics of the human anterior cruciate ligament (ACL) were predicted and compared with the experimental results.

DOI: 10.1016/j.jbiomech.2018.03.016
PMID: 29599040

21: Biswal S, Barhwal KK, Das D, Dhingra R, Dhingra N, Nag TC, Hota SK. Salidroside mediated stabilization of Bcl -x(L) prevents mitophagy in CA3 hippocampal neurons during hypoxia. Neurobiol Dis. 2018 Aug;116:39-52. doi: 10.1016/j.nbd.2018.04.019. Epub 2018 May 1. PubMed PMID: 29723606.

Chronic hypoxic stress results in deposition of lipofuscin granules in the CA3 region of hippocampal neurons which contributes to neurodegeneration and accelerated neuronal aging. Oxidative stress and mitophagy during hypoxia are crucial to cause aggregation of these lipofuscin granules in hypoxic neurons. Salidroside, a glucoside derivative of β-Tyrosol, has been reported to protect hypoxic neurons through maintenance of mitochondrial activity. The present study is aimed at investigating the potential of Salidroside in preventing mitophagy during chronic hypoxia and identification of the molecular targets and underlying signaling mechanisms. In-silico analysis for interaction of salidroside with Bcl-xL was carried out using VLife MDS software. The prophylactic efficacy of Salidroside for amelioration of global hypoxia induced neuronal aging was studied in adult male Sprague-Dawley rats exposed to hypobaric hypoxia simulating an altitude of 7600 m for 21 days. Salidroside was supplemented at a daily dose of 25 mg kg-1b.w. p.o. during hypoxic exposure. Ultra-structural and immune-histological studies were conducted to study lipofuscin aggregation and mitophagy. In-silico findings on salidroside mediated stabilization of Bcl-xL were validated by investigating its effect on downstream signaling molecules involved in mitophagy. Administration of Salidroside reduced deposition of lipofuscin in hypoxic CA3 hippocampal neurons and prevented mitophagy. Salidroside stabilizes Bcl-xL in hypoxic neurons resulting in inhibition of PGAM5 phosphatase activity and maintenance of FUNDC1 in phosphorylated state. Salidroside mediated inhibition of pFUNDC1 dephosphorylation prevents FUNDC1-LC3 II interaction which is crucial for mitophagy. The present study demonstrates potential of Salidroside in preventing lipofuscin deposition during chronic hypoxic stress.

DOI: 10.1016/j.nbd.2018.04.019
PMID: 29723606

22: Chandan S, Shukla G, Gupta A, Srivastava A, Vibha D, Prasad K. Acute-onset Restless legs syndrome in acute neurological conditions-a prospective study on patients with the Guillain-Barre syndrome and acute stroke. Acta Neurol Scand. 2018 May;137(5):488-499. doi: 10.1111/ane.12890. Epub 2018 Jan 22. PubMed PMID: 29359321.

OBJECTIVES: While the Restless legs syndrome (RLS) is usually recognized as a chronic condition, it has often been diagnosed among patients with acute neurological illnesses, in which limb discomfort is reported. This study was conducted to determine how many among these, actually have acute-onset RLS, and also to evaluate characteristics of this subgroup of patients with Guillain-Barre syndrome (GBS) and stroke developing acute-onset RLS.
METHODS: Consecutive patients diagnosed with GBS and eligible stroke patients,

admitted to our Neurology services over a 1-year period, were enrolled. They were evaluated for symptoms of RLS based on IRLSSG consensus criteria and the AIIMS RLS Questionnaire for Indian patients (ARQIP).
RESULTS: Forty adults with GBS and 58 with stroke were included. A total of 10 of the 40 (25%) patients with GBS developed definite acute RLS, which was mostly monophasic. Seven (70%) of these had demyelinating type of GBS, a significant association with acute RLS (P = .024). Six of the 58 stroke patients (10%) developed definite acute-onset, often persistent RLS. Subcortical location showed significant association with increased risk of developing acute RLS (P < .001). All patients diagnosed with acute-onset RLS had an immediate and good response to dopamine agonists.
CONCLUSION: This is the first study showing that acute-onset RLS is common, affecting nearly 25% of patients with GBS and 10% patients with acute stroke. Recognizing and treating it can majorly contribute toward symptom relief and early improvement in the quality of life for this population.

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PMID: 29359321 [Indexed for MEDLINE]

23: Claeys C, Zaman K, Dbaibo G, Li P, Izu A, Kosalaraksa P, Rivera L, Acosta B, Arroba Basanta ML, Aziz A, Cabanero MA, Chandrashekaran V, Corsaro B, Cousin L, Diaz A, Diez-Domingo J, Dinleyici EC, Faust SN, Friel D, Garcia-Sicilia J, Gomez-Go GD, Antoinette Gonzales ML, Hughes SM, Jackowska T, Kant S, Lucero M, Malvaux L, Mares Bermudez J, Martinon-Torres F, Miranda M, Montellano M, Peix Sambola MA, Prymula R, Puthanakit T, Ruzkova R, Sadowska-Krawczenko I, Salamanca de la Cueva I, Sokal E, Soni J, Szymanski H, Ulied A, Schuind A, Jain VK, Innis BL; Flu4VEC Study Group. Prevention of vaccine-matched and mismatched influenza in children aged 6-35 months: a multinational randomised trial across five influenza seasons. Lancet Child Adolesc Health. 2018 May;2(5):338-349. doi: 10.1016/S2352-4642(18)30062-2. Epub 2018 Mar 5. PubMed PMID: 30169267.

BACKGROUND: Despite the importance of vaccinating children younger than 5 years, few studies evaluating vaccine prevention of influenza have been reported in this age group. We evaluated efficacy of an inactivated quadrivalent influenza vaccine (IIV4) in children aged 6-35 months.
METHODS: In this phase 3, observer-blinded, multinational trial, healthy children from 13 countries in Europe, Central America, and Asia were recruited in five independent cohorts, each in a different influenza season. Participants were randomly assigned (1:1) to either IIV4 (15 μg haemagglutinin antigen per strain per 0·5 mL dose; a single dose on day 0 for vaccine-primed children, and two doses, on days 0 and 28, for vaccine-unprimed children) or to one or two doses of a non-influenza control vaccine. Primary endpoints were moderate-to-severe influenza or all influenza (irrespective of disease severity) confirmed by RT-PCR on nasal swabs. Cultured isolates were further characterised as antigenically matched or mismatched to vaccine strains. Efficacy was assessed in the per-protocol cohort and total vaccinated cohort (time-to-event analysis), and safety was assessed in the total vaccinated cohort.
FINDINGS: Between Oct 1, 2011, and Dec 31, 2014, 12 018 children were recruited into the total vaccinated cohort (6006 children in the IIV4 group and 6012 children in the control group). 356 (6%) children in the IIV4 group and 693 (12%) children in the control group had at least one case of RT-PCR-confirmed influenza. Of these 1049 influenza strains, 138 (13%) were A/H1N1, 529 (50%) were A/H3N2, 69 (7%) were B/Victoria, and 316 (30%) were B/Yamagata. Overall, 539 (64%) of 848 antigenically characterised isolates were vaccine-mismatched (16 [15%] of 105 for A/H1N1; 368 [97%] of 378 for A/H3N2; 54 [86%] of 63 for B/Victoria; 101 [33%] of 302 for B/Yamagata). Vaccine efficacy was 63% (97·5% CI

52-72) against moderate-to-severe influenza and 50% (42-57) against all influenza in the per-protocol cohort, and 64% (53-73) against moderate-to-severe influenza and 50% (42-57) against all influenza in the total vaccinated cohort. There were no clinically meaningful safety differences between IIV4 and control.
INTERPRETATION: IIV4 prevented influenza A and B in children aged 6-35 months despite high levels of vaccine mismatch. Vaccine efficacy was highest against moderate-to-severe disease, which is the most clinically important endpoint associated with greatest burden.
FUNDING: GlaxoSmithKline Biologicals SA.

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24: Devnani B, Kumar R, Pathy S, Phulware RH, Mathur S, Kumar L. Cutaneous metastases from neuroendocrine carcinoma of the cervix-An unusual metastatic lesion from an uncommon malignancy. Curr Probl Cancer. 2018 May 23. pii: S0147-0272(18)30076-X. doi: 10.1016/j.currproblcancer.2018.04.004. [Epub ahead of print] PubMed PMID: 29937242.

Neuroendocrine carcinoma (NEC) is an uncommon and aggressive type of small cell cervical cancer. NECs mostly arise from gastro-entero-pancreatic tract and the lung, but rarely from other organs like cervix. NEC of the cervix is a rare malignancy and constitutes 0.9%-1.5% of cervical tumors. NECs of cervix are common in perimenopausal females and present with abnormal vaginal bleeding and mimic squamous cell cancers, usually with no distinguishing features. On Immunohistochemistry, presence of chromogranin, synaptophysin, and CD-56 is necessary to make a diagnosis of small cell carcinoma. These tumors are notorious for local as well as distant relapses in comparison to their squamous and adenocarcinoma counterpart. NECs are characterized by highly aggressive clinical behavior and carry a poor prognosis. They commonly metastases to lung, liver, brain, and bones even in early stages of the disease. Metastasis to skin is a rare occurrence. We herein report a case of a NEC of the uterine cervix with multiple cutaneous metastases. After the initial diagnosis of NEC of cervix, the patient received concurrent chemoradiation followed by intracavitary brachytherapy. On subsequent follow-up, the patient developed multiple cutaneous metastasis along with liver metastases. This case is reported in view of rarity of the case with skin metastases. To the best of our knowledge, only 3 cases of cutaneous metastases from NEC of the cervix are reported till date. Being a rare malignancy, evidence in the literature is in form of case reports and small case series. Thus, the optimal treatment strategy varies for these patients. Multimodality management with teamwork is necessary to manage individual patients.

DOI: 10.1016/j.currproblcancer.2018.04.004
PMID: 29937242

25: Dhiman R, Gorimanipalli B, Swamy DR, Sharma S, Garg A, Saxena R. Congenital Third Nerve Palsy Associated With Midbrain Hypoplasia Due to Bilateral Segmental Internal Carotid Artery Agenesis. J Neuroophthalmol. 2018 May 4. doi: 10.1097/WNO.0000000000000666. [Epub ahead of print] PubMed PMID: 29738350.

A 15-year-old girl, diagnosed with a partial right third nerve palsy, was found to have bilateral internal carotid artery agenesis. Neuroimaging with

3D-constructive interference in steady state scanning identified the possible etiology of the third nerve palsy as midbrain hypoplasia.

DOI: 10.1097/WNO.0000000000000666
PMID: 29738350

26: Dwivedi DK, Kumar R, Dwivedi AK, Bora GS, Thulkar S, Sharma S, Gupta SD, Jagannathan NR. Prebiopsy multiparametric MRI-based risk score for predicting prostate cancer in biopsy-naive men with prostate-specific antigen between 4-10â€‰ng/mL. J Magn Reson Imaging. 2018 May;47(5):1227-1236. doi: 10.1002/jmri.25850. Epub 2017 Sep 4. PubMed PMID: 28872226.

BACKGROUND: Risk calculators have traditionally utilized serum prostate-specific antigen (PSA) values in addition to clinical variables to predict the likelihood of prostate cancer (PCa).
PURPOSE: To develop a prebiopsy multiparametric MRI (mpMRI)-based risk score (RS) and a statistical equation for predicting the risk of PCa in biopsy-naive men with serum PSA between 4-10 ng/mL that may help reduce unnecessary biopsies.
STUDY TYPE: Prospective cross-sectional study.
SUBJECTS: In all, 137 consecutive men with PSA between 4-10 ng/mL underwent prebiopsy mpMRI (diffusion-weighted [DW]-MRI and MR spectroscopic imaging [MRSI]) during 2009-2015 were recruited for this study.
FIELD STRENGTH/SEQUENCE: 1.5T (Avanto, Siemens Health Care, Erlangen, Germany); T1 -weighted, T2 -weighted, DW-MRI, and MRSI sequences were used.
ASSESSMENT: All eligible patients underwent mpMRI-directed, cognitive-fusion transrectal ultrasound (TRUS)-guided biopsies.
STATISTICAL TESTS: An equation model and an RS were developed using receiver operating characteristic (ROC) curve analysis and a multivariable logistic regression approach. A 10-fold crossvalidation and simulation analyses were performed to assess diagnostic performance of various combinations of mpMRI parameters.
RESULTS: Of 137 patients, 32 were diagnosed with PCa on biopsy. Multivariable analysis, adjusted with positive pathology, showed apparent diffusion coefficient (ADC), metabolite ratio, and PSA as significant predictors of PCa ($P < 0.05$). A statistical equation was derived using these predictors. A simple 6-point mpMRI-based RS was derived for calculating the risk of PCa and it showed that it is highly predictive for PCa (odds ratio = 3.74, 95% confidence interval [CI]: 2.24-6.27, area under the curve [AUC] = 0.87). Both models (equation and RS) yielded high predictive performance (AUC ≥0.85) on validation analysis.
DATA CONCLUSION: A statistical equation and a simple 6-point mpMRI-based RS can be used as a point-of-care tool to potentially help limit the number of negative biopsies in men with PSA between 4 and 10 ng/mL.
LEVEL OF EVIDENCE: 1 Technical Efficacy: Stage 2 J. Magn. Reson. Imaging 2018;47:1227-1236.

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PMID: 28872226

27: Ekstrand ML, Heylen E, Mazur A, Steward WT, Carpenter C, Yadav K, Sinha S, Nyamathi A. The Role of HIV Stigma in ART Adherence and Quality of Life Among Rural Women Living with HIV in India. AIDS Behav. 2018 May 22. doi: 10.1007/s10461-018-2157-7. [Epub ahead of print] PubMed PMID: 29789984.

HIV stigma continues to be a barrier to physical and mental health among people living with HIV globally, especially in vulnerable populations. We examined how

stigma is associated with health outcomes and quality of life among rural women living with HIV in South India (N=600). Interviewer-administered measures assessed multiple dimensions of stigma, as well as loneliness, social support, ART adherence, time since diagnosis, and quality of life. Internalized stigma and a lack of social support were associated with a lower quality of life, while the association between internalized stigma and adherence was mediated by the use of stigma-avoidant coping strategies, suggesting that keeping one's diagnosis a secret may make it more difficult to take one's medications. These findings suggest that these women constitute a vulnerable population who need additional services to optimize their health and who might benefit from peer support interventions and stigma-reduction programs for family and community members.

DOI: 10.1007/s10461-018-2157-7
PMID: 29789984

28: G V, Agarwal SK, Agarwal S, Mahajan S, Bhowmik D, Bagchi S. Infection is the chief cause of mortality and non death censored graft loss in the first year after renal transplantation in a resource limited population: a single center study. Nephrology (Carlton). 2018 May 14. doi: 10.1111/nep.13401. [Epub ahead of print] PubMed PMID: 29761588.

BACKGROUND: Few studies have assessed the impact of infections after renal transplantation (RTX) in low and middle income countries. This single center study aimed to delineate the profile and impact of infections requiring hospitalisation (IRH) occurring in the first year after RTX in India.
METHOD: Patients who underwent RTX between July 2012 and June 2015 were followed up for 12 months after transplantation.
RESULTS: 60.2% of the 387 patients studied had atleast one IRH and total 492 infections were diagnosed. The most common were urinary tract (30.3%), gastrointestinal (17.1%) and pulmonary (11.2%) infections. Viral etiology (33.3%) was most frequent, followed by bacterial (23.6%), parasitic (5.1%), tuberculosis (4.5%), and fungal infections (3.9%). 86.4% deaths were due to infections. One year patient and graft survival were inferior among recipients with IRH compared to those with no IRH: 91.8% vs. 98.1 % (log rank= 0.010) and 90.1% vs. 97.4% (log rank= 0.006) respectively. Average monthly income/family member < 5000 Rupees (75 USD), NODAT, and acute rejection were independent risk factors for IRH.
CONCLUSION: The profile of IRH is unique involving opportunistic, community acquired and endemic infections seen in this country. It is the predominant cause of mortality and graft loss in the first year after RTX. Poor economic status is an important determinant of IRH in our population. This article is protected by copyright. All rights reserved.

DOI: 10.1111/nep.13401
PMID: 29761588

29: Galhotra P, Prabhakar P, Meghwani H, Mohammed SA, Banerjee SK, Seth S, Hote MP, Reeta KH, Ray R, Maulik SK. Beneficial effects of fenofibrate in pulmonary hypertension in rats. Mol Cell Biochem. 2018 May 14. doi: 10.1007/s11010-018-3355-3. [Epub ahead of print] PubMed PMID: 29761247.

Pulmonary hypertension (PH) is a morbid complication of cardiopulmonary as well as several systemic diseases in humans. It is rapidly progressive and fatal if left untreated. In the present study, we investigated the effect of PPARα agonist fenofibrate (FF) on monocrotaline (MCT)-induced PH in rats. FF, because of its pleiotropic property, could be helpful in reducing inflammation, oxidative stress, and reactive oxygen species. On day 1, MCT (50 mg/kg, s.c.) was given to

all the rats in MCT, sildenafil, and FF group except normal control rats. After 3 days of giving MCT, sildenafil (175 µg/kg, orally) and FF (120 mg/kg, orally) were given for 25 days. Echocardiography, hemodynamic parameters, fulton's index, histopathology, oxidative stress parameters, inflammatory markers, Bcl2/Bax gene expression ratio in the right ventricle, and protein expression for NOX-1 in lungs were studied in all the groups. FF has shown to prevent decrease in ratio of pulmonary artery acceleration time to ejection time, increase in ratio of right ventricular outflow tract dimension to aortic outflow dimension, rise in right ventricular systolic pressure, right ventricular hypertrophy, increase in the percentage medial wall thickness (%MWT), increase in oxidative stress and inflammation, increase in NADPH oxidase-1 (NOX-1) expression, and decrease in mRNA expression of Bcl2/Bax ratio caused by MCT. To conclude, FF prevented MCT-induced PH in rats by various mechanisms. It might be helpful in preventing PH in patients who are likely to develop PH.

DOI: 10.1007/s11010-018-3355-3
PMID: 29761247

30: Garg B, Gupta M, Singh M, Kalyanasundaram D. Outcome and safety analysis of 3D-printed patient-specific pedicle screw jigs for complex spinal deformities: a comparative study. Spine J. 2018 May 3. pii: S1529-9430(18)30200-6. doi: 10.1016/j.spinee.2018.05.001. [Epub ahead of print] PubMed PMID: 29730456.

BACKGROUND CONTEXT: Spinal deformities are very challenging to treat and have a great risk of neurologic complications because of hardware placement during corrective surgery. Various techniques have been introduced to ensure safe and accurate placement of pedicle screws. Patient-specific screw guides with predrawn and prevalidated trajectory seem to be an attractive option.
PURPOSE: We have focused on developing three-dimensional (3D) printing technique for complex spinal deformities in India. This study also aimed to compare the placement of pedicle screw with 3D printing and freehand technique.
STUDY DESIGN/SETTINGS: This is a retrospective comparative clinical study in an academic institutional setting.
PATIENT SAMPLE: A total of 20 patients were enrolled during the study: 10 were operated on with the help of 3D printing (Group 1) and 10 were operated on with freehand technique (Group 2). Group 1 included six patients with congenital scoliosis, three patients with adolescent idiopathic scoliosis (AIS), and one patient with post-tubercular kyphosis, and Group 2 included five patients with congenital scoliosis, four patients with AIS, and one patient with post-tubercular kyphosis.
OUTCOME MEASURES: Primary outcomes were measured in terms of screw violation, and secondary outcomes were measured in terms of surgical time, blood loss, radiation exposure (number of shoots required), and complications.
MATERIALS AND METHODS: MIMICS Base v18.0 software was used for 3D reconstruction from computed tomography scan images of all the patients. 3-Matic software was used to create a drill guide. A 3D printer from Stratasys Mojo with ABS P430 model material cartilage (a thermoplastic material) was used for the printing of the vertebra model and jigs. A two-sample test of proportion was used to compare correctly and wrongly placed pedicle screws with 3D printing and freehand technique. t Test with equal variance was used for operating surgical time and blood loss.
RESULTS: No superior or inferior screw violation was observed in any of our patients in either group. We found a significant difference (p=.03) between the two groups regarding perfect screw placement in favor of 3D printing. There were 13 Grade 2 medial perforations in the freehand group and 3 in the 3D printing group. There was no Grade 3 medial perforation in either group. Six Grade 2 lateral perforations in the freehand group and seven in the 3D printing group

were observed. Three Grade 3 lateral perforations in the freehand group and two in 3D printing group were observed. Analysis showed a statistically significant (p=.005) medial violation in the freehand group. Surgical time was significantly less (p=.03) in the 3D printing group compared with the freehand group. Mean blood loss was higher in the freehand group but was not statistically significant (p=.3) in the 3D printing group. Fluoroscopic shots required were less in number in the 3D printing group compared with the freehand group. There was no neurologic deficit in any of the patients in the two groups.
CONCLUSIONS: In our study, focusing on spinal deformities with statistically significant higher rates of accurate screw positioning and higher numbers of inserted screws with 3D printing was possible because of enhanced safety, particularly at apical levels. As such, spinal deformities are difficult to treat worldwide. In India, these deformities are often neglected and present at a very late and a much more deformed state when their treatment becomes even more challenging. Developing these patient-specific drill templates will enable an average spine surgeon to treat these patients with much ease and safety.

DOI: 10.1016/j.spinee.2018.05.001
PMID: 29730456

31: Garg M, Kumar A, Sawarkar DP, Singh PK, Agarwal D, Kale SS, Mahapatra AK. Traumatic Lateral Spondyloptosis: Case Series. World Neurosurg. 2018 May;113:e166-e171. doi: 10.1016/j.wneu.2018.01.206. Epub 2018 Feb 7. PubMed PMID: 29427815.

OBJECTIVE: To apprise readers about this rare but severest form of traumatic spine injury and its surgical management.
BACKGROUND: Complete fracture dislocation and subluxation (>100%) of 1 vertebral body in the coronal or sagittal plane with respect to the adjacent vertebra is defined as spondyloptosis. In coronal spondyloptosis the subluxated vertebral bodies lie beside each other, and the condition is lateraloptosis. Patients with lateraloptosis present unique surgical challenges because reduction and achieving realignment of spinal column require meticulous planning and execution.
METHODS: A retrospective analysis of patients admitted with lateraloptosis over a 4-year period (2013-2016) was done. Lateraloptosis was defined on computed tomography as complete subluxation of the spinal column with more than 50% of adjacent vertebral bodies lying directly lateral to each other.
RESULTS: Five men, ranging from 18 to 50 years (mean, 35.2 years) old were included in the study. Three patients had thoracic spine lateraloptosis, and in 2 the injury was at the thoracolumbar junction. All patients underwent single-stage posterior surgical reduction and fixation. Intraoperatively, cord transection was seen in 3 patients, and dural tear with cerebrospinal fluid leak was seen in 1 patient. The mean follow-up period was 14 months (range, 1-36 months), during which 1 patient died of complications arising from bedsores. All patients remained at American Spinal Injury Association grade A neurologically.
CONCLUSION: Lateraloptosis is difficult to treat, and the aim of surgery is to stabilize the spine. Rehabilitation remains the most crucial factor, but the scarcity of proper rehabilitation centers results in high mortality and morbidity.

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PMID: 29427815 [Indexed for MEDLINE]

32: Garg M, Shambanduram S, Singh PK, Sebastian LJD, Sawarkar DP, Kumar A,

Gaikwad S, Chandra PS, Kale SS. Management of Pediatric Posterior Circulation Aneurysms-12-Year Single-Institution Experience. World Neurosurg. 2018 Aug;116:e624-e633. doi: 10.1016/j.wneu.2018.05.056. Epub 2018 May 17. PubMed PMID: 29778599.

BACKGROUND: Pediatric posterior circulation aneurysms are rare, complex, poorly understood lesions on which only limited literature is currently available. We report our 12-year experience of managing this condition to enhance knowledge of this rare entity.
METHODS: Patients <18 years old with posterior circulation aneurysms managed at our institution from January 2005 to April 2017 were included. Demographic, clinical, radiologic and management details were retrieved from hospital records and characteristics of the aneurysms and treatment were analyzed.
RESULTS: During this period, 20 pediatric patients (male-to-female ratio 15:6; mean age, 13.1 years) with posterior circulation aneurysms were treated. Most of the patients (75%) presented with subarachnoid hemorrhage. The most common location was the vertebrobasilar junction and vertebral artery (31.81%) followed by the basilar artery and the posterior cerebral artery (27.72% each). Dissecting (81.8%) and large (63.63%) aneurysms were the most common types noted. Of the15 patients with 22 aneurysms treated, 13 underwent endovascular management (parent vessel sacrifice in 8 aneurysms and parent vessel preservation in 5 aneurysms), 1 patient underwent surgery, and 1 patient received medical management for central nervous system tuberculosis. During follow-up, 1 patient had recurrence of aneurysm, and 1 patient died after discharge from the hospital. Overall good outcome was recorded in 90% of patients (Glasgow Outcome Scale score 4-5).
CONCLUSIONS: Vertebrobasilar junction and vertebral artery was the most common location for posterior circulation aneurysms and most were dissecting aneurysms. Endovascular treatment was the mainstay of management. Overall good outcome was observed at long-term follow-up.

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PMID: 29778599 [Indexed for MEDLINE]

33: Garg PK, Jakhetiya A, Pandey R, Chishi N, Pandey D. Adjuvant radiotherapy versus observation following lumpectomy in ductal carcinoma in-situ: A meta-analysis of randomized controlled trials. Breast J. 2018 May;24(3):233-239. doi: 10.1111/tbj.12889. Epub 2017 Aug 22. PubMed PMID: 28833776.

The role of adjuvant radiotherapy (RT) following lumpectomy for ductal carcinoma in-situ (DCIS) was addressed in four major randomized controlled trials (RCTs) which were conducted two to three decades ago. Initial results of these trials suggested the protective role of RT in reducing the ipsilateral breast recurrences. Long-term results of all these four trials, based on more than 10-years follow-up data, have recently been published. A meta-analysis of four published RCTs which have addressed the role of adjuvant RT following lumpectomy for DCIS was conducted. Review manager (Cochrane Collaboration's software) version RevMan 5.2 was used for analysis. Evaluated events were ipsilateral breast recurrences (both DCIS and invasive), regional recurrences, contralateral breast events, distant recurrences, and overall mortality. The events were entered as dichotomous variable. The present meta-analysis included four RCTs and a total of 3680 patients - 1710 received adjuvant RT following lumpectomy while 1970 patients did not receive any adjuvant treatment. Patients who received RT had almost half of risk of ipsilateral breast recurrence (RR = 0.53, 95% CI = 0.45-0.62) and regional recurrence (RR = 0.54, 95% CI = 0.32-0.91) compared to those who did not receive adjuvant treatment - there was absolute risk reduction in 15% (95% CI = 12%-17%) for ipsilateral breast recurrences in

adjuvant RT treated patients. There was no significant difference in distant recurrence (RR = 1.06, 95% CI = 0.74-1.53), contralateral breast events (RR = 1.22, 95% CI = 0.98-1.52) and overall mortality (RR = 0.93, 95% CI = 0.79-1.09). Though addition of postoperative RT to lumpectomy does not reduce overall mortality, the present meta-analysis confirms that it decreases the ipsilateral breast and regional recurrence by almost half.

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PMID: 28833776

34: Goyal A, Boro H, Khadgawat R. Brown Tumor as an Index Presentation of Severe Vitamin D Deficiency in a Teenage Girl. Cureus. 2018 May 31;10(5):e2722. doi: 10.7759/cureus.2722. PubMed PMID: 30079288; PubMed Central PMCID: PMC6067807.

Brown tumor is a non-neoplastic fibro-cystic expansile bone lesion caused by parathyroid hormone excess. It has been commonly described in patients with primary hyperparathyroidism and secondary hyperparathyroidism due to chronic kidney disease. However, it is very rare to encounter a brown tumor in the setting of nutritional vitamin D deficiency. We describe the case of a 16-year-old girl who presented with brown tumor-like lytic lesion of femur caused by severe longstanding vitamin D deficiency. Treatment with elemental calcium and cholecalciferol resulted in correction of hyperparathyroid state, with the resultant disappearance of the bony lesion and remarkable symptomatic improvement. Unnecessary orthopaedic intervention may be avoided using a high index of suspicion and performing targeted investigations in such cases.

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PMCID: PMC6067807
PMID: 30079288

Conflict of interest statement: The authors have declared that no competing interests exist.

35: Goyal A, Gupta Y, Kalaivani M, Sankar MJ, Kachhawa G, Bhatla N, Gupta N, Tandon N. Long term (>1â€¯year) postpartum glucose tolerance status among Indian women with history of Gestational Diabetes Mellitus (GDM) diagnosed by IADPSG criteria. Diabetes Res Clin Pract. 2018 Aug;142:154-161. doi: 10.1016/j.diabres.2018.05.027. Epub 2018 May 24. PubMed PMID: 29802954.

AIM: To determine prevalence of long term dysglycemia and its risk factors among women with history of GDM diagnosed using IADPSG criteria at a tertiary care hospital in North India.
METHODS: Women with GDM diagnosed between 2012 and 2016 were invited. Socio-demographic, anthropometric, medical data were collected and 75 gm OGTT with serum insulin estimation, HbA1c and fasting lipid profile were done at the hospital visit.
RESULTS: Women (N = 267) were tested at 32.5 (±4.6) years of age and at a median (q25-q75) of 20 (12-44) months following the index delivery. Dysglycemia was found in 57.7% by ADA criteria [Diabetes in 10.5% and prediabetes in 47.2%]. Risk factors for cardiovascular disease were significantly more prevalent among these women. On multivariable analysis, HOMA-IR correlated positively, while insulinogenic index correlated negatively with postpartum dysglycemia.
CONCLUSION: This is possibly the first long term (>1 year) glucose tolerance outcome study in South Asian women with history of GDM diagnosed by IADPSG criteria, which demonstrates significantly elevated risk of postpartum dysglycemia. While the IADPSG criteria identify women with a lower future

conversion to diabetes compared with previous criteria, prediabetes conversion remains high, thereby offering an opportunity to intervene early and prevent progression to future diabetes.

DOI: 10.1016/j.diabres.2018.05.027
PMID: 29802954 [Indexed for MEDLINE]

36: Gupta A, Sachdeva A, Mahajan N, Gupta A, Sareen N, Pandey RM, Ramakrishnan L, Sati HC, Sharma B, Sharma N, Kapil U. Prevalence of Pediatric Metabolic Syndrome and Associated Risk Factors among School-Age Children of 10-16 Years Living in District Shimla, Himachal Pradesh, India. Indian J Endocrinol Metab. 2018 May-Jun;22(3):373-378. doi: 10.4103/ijem.IJEM_251_17. PubMed PMID: 30090730; PubMed Central PMCID: PMC6063189.

Introduction: Recently, an increasing trend in the prevalence of pediatric metabolic syndrome (PMS) among school-age children has been documented in different parts of India. There is lack of data on the prevalence of PMS and its associated risk factors among school-age children living in district Shimla, Himachal Pradesh. Hence, to fill in the gap in the existing knowledge, the present study was conducted.
Methodology: A cross-sectional study was conducted during 2015-2016. Thirty clusters (schools) were identified from a list of all schools using population proportionate to size sampling methodology. From each school, 70 children in the age group of 10-16 years were selected. Data was collected on the sociodemographic characteristics, anthropometry, waist circumference, blood pressure, and physical activity. Fasting venous blood samples were collected for estimation of blood glucose, triglycerides, and high-density lipoprotein levels.
Results: The prevalence of PMS using International Diabetes Federation classification was 3.3% and using modified-adult treatment panel classification criteria was 3.5%. Risk factors identified to be associated with PMS among school-age children were (i) male gender, (ii) high family monthly income, (iii) sedentary lifestyle, (iv) consumption of evening snack, (v) television/computer viewing, and (vi) motorized transportation for commuting to school.
Conclusion: The PMS prevalence was 3.3% in school-age children residing in District Shimla. There is a need to formulate interventions to prevent and correct metabolic syndrome among them for reducing early onset of cardiovascular disease during adulthood.

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PMID: 30090730

Conflict of interest statement: There are no conflicts of interest.

37: Gupta A, Shukla G. Polysomnographic determinants of requirement for advanced positive pressure therapeutic options for obstructive sleep apnea. Sleep Breath. 2018 May;22(2):401-409. doi: 10.1007/s11325-017-1556-8. Epub 2017 Aug 18. PubMed PMID: 28822020.

BACKGROUND: A small percentage of adult patients with severe obstructive sleep apnea (OSA) has been recognized to be extraordinarily difficult to treat with conventional continuous or Bi-level positive airway pressure (together referred to as PAP) therapy.
AIM AND OBJECTIVES: The aim of this study was to determine polysomnographic (PSG) characteristics, which may help predict the requirement for advanced therapeutic

options for OSA.
METHODS: Consecutive patients who underwent PAP titration at our sleep laboratory over a 2-year period were included. Patients with technically inadequate studies, those with incomplete titration due to intolerance, mask-related problems, or lack of sleep and those with significant co-morbidity and with other primary sleep disorders, were excluded. The PSGs (diagnostic + titration parts) were categorized into three types: type A (respiratory events evenly distributed over all sleep stages), type B (REM dominant respiratory events), and type C (non-REM dominant respiratory events, mainly during cyclic alternating pattern [CAP] sleep). Group A was further subdivided into A1 (those whose hypnogram normalized after adequate titration) and A2 (those whose hypnogram converted to a type C pattern on titration). These were categorized again into treatment group I (adequately PAP titrated) and group II (poor response to conventional PAP) for studying factors determining poor response to PAP.
RESULTS: Among 249 patients evaluated in the sleep laboratory over the study period, 123 (103 males, mean age 49.9 ± 10.8 years, mean BMI 29.3 ± 4) fulfilled inclusion criteria. These could be grouped as type A (n = 85), B (n = 33), and C (n = 5). On titration, 57 patients of type A and 21 of type B could be successfully titrated, while 24 in type A and 11 in type B, converted into type C. Therefore, in group II (n = 43), 38 patients fell in type C, overtly and after titration. Twelve of these had been successfully treated using adaptive servo ventilation (ASV) while another 28 could be treated using the Bi-level PAP-ST mode. The only PSG feature predicting poor response to conventional PAP was the presence of post-arousal central apnea (p = 0.001). The main difference between the A1 + B groups and A2 + C groups was the significantly higher non-REM apnea hypopnea index in the latter. Among these, on 1-year follow-up, eight patients were using Bi-level PAP-ST mode, while four patients were using ASV and were asymptomatic.
CONCLUSION: Non-REM sleep instability and the presence of post-arousal central apneas may be important determinants of poor response to conventional PAP and requirement for advanced therapeutic options among patients with severe OSA.

DOI: 10.1007/s11325-017-1556-8
PMID: 28822020

38: Gupta P, Parshad R, Balakrishna P, Saraya A, Makharia GK, Sachdeva S, Sharma R. Angle of His Accentuation Is a Viable Alternative to Dor Fundoplication as an Adjunct to Laparoscopic Heller Cardiomyotomy: Results of a Randomized Clinical Study. Dig Dis Sci. 2018 Sep;63(9):2395-2404. doi: 10.1007/s10620-018-5130-4. Epub 2018 May 24. PubMed PMID: 29796913.

BACKGROUND: There is no consensus regarding the type of anti-reflux procedure to be used as an adjunct to laparoscopic Heller cardiomyotomy (LHCM). The aim of this study was to compare Angle of His accentuation (AOH) with Dor Fundoplication (Dor) as an adjunct to LHCM.
METHODS: A total of 110 patients with achalasia cardia presenting for LHCM from March 2010 to July 2015 were randomized to Dor and AOH. Symptom severity, achalasia-specific quality of life (ASQOL), new onset heartburn, and patient satisfaction were assessed using standardized scores preoperatively, at 3, 6 months, and then yearly. The primary outcome was relief of esophageal symptoms while secondary outcomes were new onset heartburn and ASQOL.
RESULTS: Both groups were comparable with respect to the baseline demographic characteristics. There was no conversion to open and no mortality in either group. Median operative time was 128 min in AOH and 144 min in Dor group ($p < 0.01$). Mean follow-up was 36 months and was available in 98% patients. There was significant improvement in esophageal symptoms in both groups with no statistically significant difference between the two groups ($p > 0.05$). There was no difference in cumulative symptom scores between the two groups over the period

of follow-up. New onset heartburn was seen in 11% in AOH and 9% in Dor group. Mean ASQOL score improved in both groups with no difference between the two groups (p=0.83). Patient satisfaction was similar in both groups.
CONCLUSION: AOH is similar to Dor as an adjunct to LHCM in safety and efficacy and can be performed in shorter time.
CLINICAL REGISTRATION NUMBER: CTRI: REF/2014/06/007146.

DOI: 10.1007/s10620-018-5130-4
PMID: 29796913 [Indexed for MEDLINE]

39: Gupta R, Talwar P, Talwar P, Khurana S, Kushwaha S, Jalan N, Thakur R. Diagnostic accuracy of nucleic acid amplification based assays for tuberculous meningitis: A meta-analysis. J Infect. 2018 Oct;77(4):302-313. doi: 10.1016/j.jinf.2018.04.017. Epub 2018 May 25. PubMed PMID: 29758242.

BACKGROUND: Numerous in-house and commercial nucleic acid amplification tests (NAAT) have been evaluated using variable reference standards for diagnosis of TBM but their diagnostic potential is still not very clear.
METHODS: We conducted a meta-analysis to assess the diagnostic accuracy of different NAAT based assays for diagnosing TBM against 43 data sets of confirmed TBM (n=1066) and 61 data sets of suspected TBM (n=3721) as two reference standards. The summary estimate of the sensitivity and the specificity were obtained using the bivariate model. QUADAS-2 tool was used to perform the Quality assessment for bias and applicability. Publication bias was assessed with Deeks' funnel plot.
RESULTS: Studies with confirmed TBM had better summary estimates as compared to studies with clinically suspected TBM irrespective of NAAT and index tests used. Among in-house assays, MPB as the gene target had best summary estimates in both confirmed [sensitivity:90%(83-95), specificity:97-%(87-99), DOR:247 (50-1221), AUC:99%(97-100), PLR:38.8-(6.6-133), NLR:0.11(0.05-0.18), I2=15%] and clinically suspected [sensitivity:69%(47-85), specificity:96%(90-98), DOR:62(16.8-232), AUC:94%(92-97), PLR:16.9(6.5-36.8), NLR:0.33(0.16-0.56), I2:15.3%] groups. GeneXpert revealed good diagnostic accuracy only in confirmed TBM group [sensitivity=57%(38-74), specificity=98%(89-100), DOR=62(7-589), AUC=87%(79-96), PLR=33.2(3.8-128), NLR=0.45(0.26-0.68), I2=0%].
CONCLUSIONS: This meta-analysis identified potential role of MPB gene among in-house assays and GeneXpert as commercial assay for diagnosing TBM.

DOI: 10.1016/j.jinf.2018.04.017
PMID: 29758242

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41: Hadda V, Chawla G, Tiwari P, Madan K, Khan MA, Mohan A, Khilnani GC, Guleria R. Noninvasive Ventilation for Acute Respiratory Failure due to Noncystic Fibrosis Bronchiectasis. Indian J Crit Care Med. 2018 May;22(5):326-331. doi: 10.4103/ijccm.IJCCM_474_17. PubMed PMID: 29910541; PubMed Central PMCID: PMC5971640.

Purpose of the Study: Data regarding the use of noninvasive ventilation (NIV) for treatment of acute respiratory failure (ARF) among patients with noncystic fibrosis (CF) bronchiectasis are limited. We intend to describe our experience

with NIV use in this setting.
Methodology: This was a retrospective study which included 99 patients with bronchiectasis and ARF who required either NIV or invasive mechanical ventilation (IMV).
Results: NIV was started as the primary modality of ventilatory support in 81 (66.3%) patients. Fifty-three (65.4%) patients were managed successfully with NIV. Twenty-eight (34.56%) patients failed NIV and required endotracheal intubation. Reasons for NIV failure were worsening or nonimprovement of ventilatory or oxygenation parameters (n = 15), hypotension (n = 6), worsening of sensorium (n = 3), and intolerance (n = 4). None of the patients failed NIV due to excessive respiratory secretions. The rate of correction of arterial blood gases was comparable between NIV and IMV groups. The total duration of stay (median [interquartile range] days) in hospital was comparable between patients treated with NIV and IMV (8 [7-10] vs. 11 [5-11]; P = 0.99), respectively. The mortality rate between NIV and IMV groups were statistically comparable (8.64% vs. 16.6%; P = 0.08). High APACHE score at admission was associated with NIV failure (odd's ratio [95% confidence interval]: 1.21 (1.07-1.38)].
Conclusions: NIV is feasible for management of ARF with non-CF bronchiectasis. High APACHE may predict NIV failure among these patients.

DOI: 10.4103/ijccm.IJCCM_474_17
PMCID: PMC5971640
PMID: 29910541

Conflict of interest statement: There are no conflicts of interest.

42: Jain S, Midha S, Mahapatra SJ, Gupta S, Sharma MK, Nayak B, Jacob TG, Shalimar, Garg PK. Interleukin-6 significantly improves predictive value of systemic inflammatory response syndrome for predicting severe acute pancreatitis. Pancreatology. 2018 May 14. pii: S1424-3903(18)30086-3. doi: 10.1016/j.pan.2018.05.002. [Epub ahead of print] PubMed PMID: 29779831.

BACKGROUND: Predicting severe acute pancreatitis (AP) is important for triage, prognosis, and designing therapeutic trials. Persistent systemic inflammatory response syndrome (SIRS) predicts severe AP but its diagnostic accuracy is suboptimal. Our objective was to study if cytokine levels could improve the predictive value of clinical variables for the development of severe AP.
METHODS: Consecutive patients with AP were included in a prospective cohort study at a tertiary care center. Serum levels of IL-6, TNF-α, IL-10, MCP-1, GM-CSF and IL-1β were measured at day 3 of onset of AP. Variables such as age, co-morbidity, etiology, SIRS, and cytokines were modeled to predict severe AP by multivariable regression analysis. Genotyping was done to correlate IL-6, TNF-α and MCP-1 gene polymorphisms with cytokine levels.
RESULTS: Of 236 patients with AP, 115 patients admitted within 7 days of onset formed the study group. 37 of the 115 (32%) patients developed organ failure. Independent predictors of organ failure were persistent SIRS (OR 34; 95% CI: 7.2-159) and day 3 serum IL-6 of >160 pg/ml (OR 16.1; 95% CI:1.8-142). IL-6 gene (-174 G/C) GG genotype was associated with significantly higher levels of IL-6 compared to CC/CG genotype. Serum IL-6 >160 pg/ml increased the positive predictive value of persistent SIRS from 56% to 85% and specificity from 64% to 95% for predicting OF without compromising its sensitivity and negative predictive value.
CONCLUSION: Serum IL-6 of >160 ng/ml added significantly to the predictive value of SIRS for severe AP.

DOI: 10.1016/j.pan.2018.05.002
PMID: 29779831

43: Jaiswal RK, Kumar P, Kumar M, Yadava PK. hTERT promotes tumor progression by enhancing TSPAN13 expression in osteosarcoma cells. Mol Carcinog. 2018 Aug;57(8):1038-1054. doi: 10.1002/mc.22824. Epub 2018 May 18. PubMed PMID: 29722072.

Telomerase complex maintains the length of the telome, cbre, and protects erosion of the physical ends of the eukaryotic chromosome in all actively dividing cells including cancer cells. Telomerase activation extends the lifespan of cells in culture by maintaining the length of the telomere. Compared to terminally differentiated somatic cells, telomerase activity remains high in over 90% of cancer cells. It has now become clear that the role of telomerase is much more complex than just telomere lengthening. The remaining 10% of cancers deploy ALT (alternative lengthening of telomeres) pathway to maintain telomere length. Telomerase inhibitors offer a good therapeutic option. Also, telomerase-associated molecules can be targeted provided their roles are clearly established. In any case, it is necessary to understand the major role of telomerase in cancer cells. Many studies have already been done to explore gene profiling of a telomerase positive cell by knocking down expression of hTERT (telomerase reverse transcriptase). To complement these studies, we performed global gene profiling of a telomerase negative cell by ectopically expressing hTERT and studied changes in the global gene expression patterns. Analysis of microarray data for telomerase negative cells ectopically expressing telomerase showed 76 differentially regulated genes, out of which 39 genes were upregulated, and 37 were downregulated. Three upregulated genes such as TSPAN13, HMGCS2, DLX5, and three downregulated genes like DHRS2, CRYAB, and PDLIM1 were validated by real-time PCR. Knocking down of TSAPN13 in hTERT overexpressing U2OS cells enhanced the apoptosis of the cells. TSPAN13 knockdown in these cells suppressed mesenchymal properties and enhanced epithelial character.

DOI: 10.1002/mc.22824
PMID: 29722072

44: Kakkar A, Sharma MC, Nambirajan A, Gulati S, Bhatia R, Suri V, Sarkar C. Pompe disease: An Indian series diagnosed on muscle biopsy by ultrastructural characterization. Ultrastruct Pathol. 2018 May-Jun;42(3):211-219. doi: 10.1080/01913123.2018.1447624. Epub 2018 Mar 22. PubMed PMID: 29565761.

Pompe disease (PD) is a lysosomal storage disorder characterized by glycogen accumulation in muscle, with infantile-onset (IOPD) and late-onset (LOPD) types. Nineteen cases of PD were diagnosed over a 14-year period on muscle biopsy by ultrastructural examination. Pools of glycogen (intralysosomal and cytoplasmic) and excessive phagocytosis were seen in myofibers on electron microscopy. Glycogen was noted in endothelial cells in IOPD. Although PD accounts for a small fraction of muscle diseases, timely accurate diagnosis is imperative as it is treatable. Ultrastructural examination is necessary to confirm the diagnosis in cases with non-diagnostic light microscopic features, especially in adult LOPD patients.

DOI: 10.1080/01913123.2018.1447624
PMID: 29565761 [Indexed for MEDLINE]

45: Kalra P, Dhiman A, Cho WC, Bruno JG, Sharma TK. Simple Methods and Rational Design for Enhancing Aptamer Sensitivity and Specificity. Front Mol Biosci. 2018

May 14;5:41. doi: 10.3389/fmolb.2018.00041. eCollection 2018. PubMed PMID: 29868605; PubMed Central PMCID: PMC5966647.

Aptamers are structured nucleic acid molecules that can bind to their targets with high affinity and specificity. However, conventional SELEX (Systematic Evolution of Ligands by EXponential enrichment) methods may not necessarily produce aptamers of desired affinity and specificity. Thus, to address these questions, this perspective is intended to suggest some approaches and tips along with novel selection methods to enhance evolution of aptamers. This perspective covers latest novel innovations as well as a broad range of well-established approaches to improve the individual binding parameters (aptamer affinity, avidity, specificity and/or selectivity) of aptamers during and/or post-SELEX. The advantages and limitations of individual aptamer selection methods and post-SELEX optimizations, along with rational approaches to overcome these limitations are elucidated in each case. Further the impact of chosen selection milieus, linker-systems, aptamer cocktails and detection modules utilized in conjunction with target-specific aptamers, on the overall assay performance are discussed in detail, each with its own advantages and limitations. The simple variations suggested are easily available for facile implementation during and/or post-SELEX to develop ultrasensitive and specific assays. Finally, success studies of established aptamer-based assays are discussed, highlighting how they utilized some of the suggested methodologies to develop commercially successful point-of-care diagnostic assays.

DOI: 10.3389/fmolb.2018.00041
PMCID: PMC5966647
PMID: 29868605

46: Kapil U, Pandey RM, Sharma B, Ramakrishnan L, Sharma N, Singh G, Sareen N. Prevalence of Vitamin D Deficiency in Children (6-18Â years) Residing in Kullu and Kangra Districts of Himachal Pradesh, India. Indian J Pediatr. 2018 May;85(5):344-350. doi: 10.1007/s12098-017-2577-9. Epub 2018 Jan 2. PubMed PMID: 29292488.

OBJECTIVE: To assess the prevalence of Vitamin D deficiency (VDD) and associated risk factors amongst children in the age group of 6-18 y residing at an altitude of 1000 mts and above.
METHODS: A community based cross-sectional study was conducted in the year 2015-2016. Two districts (namely: Kangra and Kullu) of Himachal Pradesh state, India was selected for the present study. In each district thirty clusters/schools were identified using Population Proportionate to Size (PPS) sampling methodology. In the identified school, all the children in schools were enlisted. Twenty children per school were selected by using random number tables. A total of 1222 children (Kangra: 610; Kullu: 612) in the age group of 6-18 y were enrolled. The data on socio economic status, physical activity and sunlight exposure was collected. The blood samples were collected and serum 25-hydroxyvitamin D, intact parathyroid hormone, serum calcium, phosphorous, albumin and alkaline phosphate were assessed using standard procedures.
RESULTS: Eighty one percent (Kangra) and 80.0% (Kullu) of school age children were found Vitamin D deficient as per serum 25(OH) D levels (less than 20 ng/ml).
CONCLUSIONS: A high prevalence of VDD was found in children residing in 2 districts located at high altitude regions of Himachal Pradesh, India.

DOI: 10.1007/s12098-017-2577-9
PMID: 29292488

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52: Kaushal S, Mathur SR, Kumar S. Coexisting squamous cell carcinoma and high-grade neuroendocrine carcinoma, small cell type: a rare collision in cervix. BMJ Case Rep. 2018 May 18;2018. pii: bcr-2017-223127. doi: 10.1136/bcr-2017-223127. PubMed PMID: 29778998.

Collision tumours of the uterine cervix are extremely uncommon with exact incidence not known. Unlike squamous cell carcinoma (SCC) and adenocarcinoma that are known to coexist, small cell neuroendocrine carcinoma (SCNEC) is rarely documented with other histological types in the cervix. We report such rare case of a collision tumour in cervix displaying dual histological component of SCNEC and SCC in a 36-year-old woman. The case is being presented because of its rarity and represents a unique and hitherto seldom-reported combination of two malignant tumours with distinct and often contrasting epidemiology, histology and prognosis coexisting in the same patient.

DOI: 10.1136/bcr-2017-223127
PMID: 29778998 [Indexed for MEDLINE]

Conflict of interest statement: Competing interests: None declared.

53: Kedia S, Ahuja V. Is the emergence of inflammatory bowel disease a prime example of "the third epidemiological transition"? Indian J Gastroenterol. 2018 May;37(3):183-185. doi: 10.1007/s12664-018-0852-y. Epub 2018 Jun 12. PubMed PMID: 29948992.

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Fanconi-Bickel syndrome, caused by mutations in SLC2A2 encoding the glucose transporter 2 (GLUT2), is characterized by generalized proximal renal tubular dysfunction manifesting in late infancy. We describe phenotypic heterogeneity of

Fanconi-Bickel syndrome in three siblings, including early and atypical presentation with transient neonatal diabetes mellitus in one. The second-born of a non-consanguineous couple, evaluated for polyuria and growth retardation, had rickets, hepatomegaly and proximal tubular dysfunction from 4 to 6 months of age. A male sibling, who expired at 4 months, also had hepatomegaly and growth retardation. The third sibling had polyuria, glucosuria and mild proteinuria on day 3 of life. Hyperglycemia was detected 2 weeks later, which required therapy with insulin for 3 months. Mild metabolic acidosis was present at 2 weeks; hypercalciuria, phosphaturia and aminoaciduria were seen at 6 months. Sanger sequencing showed a homozygous missense mutation in SLC2A2 (exon 7, c.952G>A), causing glycine to arginine substitution; both parents were heterozygous carriers. Patients with SLC2A2 mutations may present either with isolated neonatal diabetes or with hepatomegaly and the renal Fanconi syndrome. Fanconi-Bickel syndrome shows phenotypic heterogeneity and may manifest early with subtle or atypical features, mandating a high index of suspicion.

DOI: 10.1007/s13730-017-0278-x
PMCID: PMC5886911
PMID: 29116606

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In acute lymphoblastic leukemia (ALL), limited data are available on mTOR gene expression in clinical samples and its role in predicting response to induction chemotherapy. mRNA expression of mTOR gene was determined quantitatively by real-time PCR in 50 ALL patients (30 B-ALL and 20 T-ALL) and correlated with clinical outcome after induction chemotherapy. Expression level of mTOR was upregulated in more than 50% of cases of ALL. In T-ALL, high expression of mTOR was commonly seen, more in adults than children (82 vs. 55% cases), while in B-ALL it was same (~ 63% cases) in both adults and children. Mean fold change of mTOR expression was significantly higher in non-responders compared to responders of both adult B-ALL (7.4 vs. 2.7, p = 0.05) and T-ALL (13.9 vs. 2.4, p = 0.001). Similar results were seen in pediatric non-responders when compared to responders of both B-ALL (14.5 vs. 2.5, p = 0.006) and T-ALL (24.2 vs. 1.7, p = 0.002). Interestingly, we have observed that mTOR expression was two times higher in non-responders of children compared to adults in both B-ALL (14.5 vs. 7.4, p = 0.05) and T-ALL (24.2 vs. 13.9, p = 0.01). Multivariate analysis with other known prognostic factors revealed that mTOR expression independently predicts clinical response to induction chemotherapy in ALL. This study demonstrates that high mTOR expression is associated with poor clinical outcome in ALL and can serve as a potential target for novel therapeutic strategies.

DOI: 10.1007/s10238-017-0478-x
PMID: 29076004 [Indexed for MEDLINE]

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Epithelioid glioblastoma (e-gbm) is a recently described variant of glioblastoma (GBM) which is associated with short survival and now added as a provisional entity to WHO 2016 classification of CNStumors. About half of these tumors show

characteristic BRAF-V600E mutation. However, unlike conventional GBMs, e-gbm lack specific diagnostic and prognostic markers. Hence, we aimed to molecularly characterize these tumors. An extensive review of literature was performed.In a multi-institutional effort, all the cases of glioblastoma of year 2017 were reviewed. Cases with predominant epithelioid morphology were analysed. Seven cases of e-gbm (adults:4 and pediatric: 3) were identified. Duration of symptoms varied from 2 weeks to one month. Radiologically, all cases were supratentorial, contrast enhancing with solid and cystic appearance. Majority of the cases were immunopositive for GFAP (71%), EMA (71%), S100 (71%) and vimentin (85%). All the cases showed ATRX, INI-1 and H3K27me3 expression. BRAFV600Emutation was seen in 28% of cases. TERT mutation was seen in 40% cases, while one case showed EGFR amplification. H3F3A mutations and PTEN deletions were seen in none. Although e-gbms are rare, epithelioid morphology of a CNS tumor in a young adult or children with areas of necrosis needs thorough histomorphological and genetic workup.

DOI: 10.1016/j.prp.2018.03.019
PMID: 29615337 [Indexed for MEDLINE]

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58: Khanna P, Saini K, Sinha R, Nisa N, Kumar S, Maitra S. Correlation between duration of preoperative fasting and emergence delirium in pediatric patients undergoing ophthalmic examination under anesthesia: A prospective observational study. Paediatr Anaesth. 2018 Jun;28(6):547-551. doi: 10.1111/pan.13381. Epub 2018 May 12. PubMed PMID: 29752842.

BACKGROUND: Preoperative fasting in children can cause anxiety, which may ultimately lead to postoperative emergence delirium. However, no data are available whether duration of preoperative fasting correlates with postoperative emergence delirium.
AIMS: The aim of this study was to identify if there is any correlation between the duration of preoperative fasting and emergence delirium in children undergoing ophthalmic examination under anesthesia.
METHODS: In this prospective observational study, 100 children between the age group 2-6 years of American Society of Anesthesiologists physical status I or II, scheduled for examination of the eye under general anesthesia with sevoflurane were recruited. Data regarding preoperative fasting was recorded and presence of emergence delirium was assessed by the Pediatric Anesthesia Emergence Delirium (PAED) scale at 5 minute interval till 30 minutes from the time of leaving the operation theater. No premedication was used in any patients but parental presence was allowed in all of them.
RESULTS: Mean (standard deviation) duration of fasting to clear liquid was 6.3 (1.7) hrs. Twenty-four children (24%) had at least 1 recorded PAED score >10 at any time point in the postoperative period. PAED scores at 15 and 25 minutes were significantly correlated with duration of fasting (r2 [95% CI] = .24 [0.04, 0.41], P = .02, Pearsons's correlation and r2 [95% CI] = .23 [0.04, 0.41], P = .02, Pearsons's correlation, respectively). No correlation has been found between duration of fasting and blood glucose level (r2 [95% CI] = -.05 [-0.24, 0.15], P = .65, Pearsons's correlation) between fasting blood glucose and PAED score at any time point.
CONCLUSION: Increased preoperative fasting duration may be a risk factor for postoperative emergence delirium in children undergoing ophthalmic examination under general anesthesia.

DOI: 10.1111/pan.13381
PMID: 29752842

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BACKGROUND: Histological assessment of dysplasia in Barrett's esophagus (BE) has high inter-observer variability. Hence, use of ancillary markers for early detection of dysplasia in BE is an important clinical question.
METHODS: In this retrospective study consecutive cases of BE (n = 59), over a period of 4 years were included. Hematoxylin and eosin stained sections were reviewed independently by 3 senior qualified pathologists, who graded the dysplasia according to the Vienna Classification system and inter-observer agreement was analysed using the Kappa statistics. Subsequently Alpha-Methyl Acyl-CoA Racemase (AMACR), p53, CyclinD1, β-catenin, H2AX and M30 immunohistochemical (IHC) stains were examined on the following disease categories: BE with no dysplasia [NFD] (45), BE with indefinite for dysplasia (IFD) (4), low grade dysplasia (LGD) (3), high grade dysplasia (HGD) (2) and in adenocarcinomas (5). H score was calculated by adding up products of different grades of stain distribution and stain intensities (range of scores 0-300).
RESULTS: Among the 3 pathologists, overall agreement was poor (k 0.06; 95% CI -0.089 to 0.145), with highest disagreement noted for differentiating the LGD and IFDs (k = 0.21). After revising the histological criteria, the kappa improved to 0.53. Among the IHC stains performed, p53, β-catenin, H2AX and M30 stains were significantly useful to differentiate between IFD and LGD (P values: 0.04, 0.004, 0.05 & 0.04, respectively). AMACR and β-catenin stains though were up-regulated in HGD/adenocarcinomas than in other categories, their expression were not statistically different between the IFD and LGDs.
CONCLUSIONS: A detail histological scoring system may bring uniformity in histological interpretation of dysplasia in BE. Using a combined panel of IHC stains seems helpful in detection of dysplasia in BE, especially to differentiate the IFD and LGD changes in BE.

DOI: 10.1016/j.prp.2018.05.006
PMID: 29764708 [Indexed for MEDLINE]

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HH, Megarbane A, Kozel BA, van Haelst MM, Stevenson RE, Summar M, Adeyemo AA, Morris CA, Moretti-Ferreira D, Linguraru MG, Muenke M. Williams-Beuren syndrome in diverse populations. Am J Med Genet A. 2018 May;176(5):1128-1136. doi: 10.1002/ajmg.a.38672. PubMed PMID: 29681090; PubMed Central PMCID: PMC6007881.

Williams-Beuren syndrome (WBS) is a common microdeletion syndrome characterized by a 1.5Mb deletion in 7q11.23. The phenotype of WBS has been well described in populations of European descent with not as much attention given to other ethnicities. In this study, individuals with WBS from diverse populations were assessed clinically and by facial analysis technology. Clinical data and images from 137 individuals with WBS were found in 19 countries with an average age of 11 years and female gender of 45%. The most common clinical phenotype elements were periorbital fullness and intellectual disability which were present in greater than 90% of our cohort. Additionally, 75% or greater of all individuals with WBS had malar flattening, long philtrum, wide mouth, and small jaw. Using facial analysis technology, we compared 286 Asian, African, Caucasian, and Latin American individuals with WBS with 286 gender and age matched controls and found that the accuracy to discriminate between WBS and controls was 0.90 when the entire cohort was evaluated concurrently. The test accuracy of the facial recognition technology increased significantly when the cohort was analyzed by specific ethnic population (P-value < 0.001 for all comparisons), with accuracies for Caucasian, African, Asian, and Latin American groups of 0.92, 0.96, 0.92, and 0.93, respectively. In summary, we present consistent clinical findings from global populations with WBS and demonstrate how facial analysis technology can support clinicians in making accurate WBS diagnoses.

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PMCID: PMC6007881 [Available on 2019-05-01]
PMID: 29681090

62: Kumar A, Paswan SS, Prashad R, Kumari R, Kumar B. Intrapericardial gossypiboma: Rare cause of intrathoracic mass. Int J Surg Case Rep. 2018;47:75-79. doi: 10.1016/j.ijscr.2018.04.024. Epub 2018 May 3. PubMed PMID: 29751199; PubMed Central PMCID: PMC5994740.

INTRODUCTION: Gossypiboma is a retained surgical sponge inside our body after surgical intervention. It is most commonly found in abdominal cavity. Its occurrence in thoracic cavity as intrapericardial gossypiboma is extremely rare.
PRESENTATION OF CASE: We present a 25 year old male with complaint of chest pain for 1 year. He had a history of total correction of Tetralogy of fallot 14 years back, at another hospital. On clinical examination and investigations including contrast enhanced computed tomography (CECT) of thorax; diagnosis of right anterior mediastinal mass of germ cell tumor was made and planned for thoracotomy. On exploration, the gauze piece of 31 cm was removed from the pericardial mass and a final diagnosis of gossypiboma was made.
DISCUSSION: Although gossypibomas are commonly reported in abdominal and pelvic surgery but a prolonged operative time, untrained staff, poor communication in sponge count may favour the occurrence in thoracic cavity. A patient with intrathoracic gossypiboma usually presents with chest pain, dyspnoea, thoracic mass or fever. CECT and Magnetic resonance Imaging (MRI) are useful imaging modality in such cases. Surgical exploration with histopathological examination confirms the diagnosis of gossypiboma.
CONCLUSION: In a postoperative patient who presents with chest pain and intrathoracic mass, gossypiboma should be a differential diagnosis even it is rare to occur in thorax.

DOI: 10.1016/j.ijscr.2018.04.024
PMCID: PMC5994740
PMID: 29751199

63: Kumar N, Burman S, Yadav A, Tomar GS. Stuck guidewire due to soft tissue imposition: a rare complication of central line catheter placement. BMJ Case Rep. 2018 May 23;2018. pii: bcr-2018-224219. doi: 10.1136/bcr-2018-224219. PubMed PMID: 29794012.

Central venous catheter (CVC) placement is a commonly done procedure but is associated with a few complications, and guidewire-related complications are one of them. In our case after induction of general anaesthesia, we planned to insert a CVC in the right internal jugular vein under ultrasound guidance. After the insertion of the introducer needle, when we tried to insert the guidewire, it got stuck and was neither moving forward nor in a backward direction. Too much force was not applied to remove the guidewire as it might have caused shearing of the guidewire and further complicated the picture. This problem was solved by simultaneous withdrawal of guidewire along with the needle, and on examination we found soft tissue debris lodged within the lumen which was preventing the guidewire movement in both directions. So, it is suggested that guidewire should be removed along with needle as a single unit if it is required.

DOI: 10.1136/bcr-2018-224219
PMID: 29794012

Conflict of interest statement: Competing interests: None declared.

64: Kumar P, Ghosh A, Sinha N, Tonk RS. Secondary Hypertriglyceridemia Causing Recurrent Acute Pancreatitis with Normal Pancreatic Enzymes. Indian J Crit Care Med. 2018 May;22(5):381-383. doi: 10.4103/ijccm.IJCCM_353_17. PubMed PMID: 29910554; PubMed Central PMCID: PMC5971653.

65: Kumar R, Gautam M, Prasoon P, Gupta S, Ray SB. Comparison of the peripheral antinociceptive effect of somatostatin with bupivacaine and morphine in the rodent postoperative pain model. Eur J Anaesthesiol. 2018 May 18. doi: 10.1097/EJA.0000000000000825. [Epub ahead of print] PubMed PMID: 29762151.

BACKGROUND AND OBJECTIVES: Infiltration of surgical wound with local anaesthetics attenuate postoperative pain. However, side effects can also occur. Somatostatin (SST) and its analogues like octreotide reportedly reduce peripheral sensitisation. The current study evaluates peripherally mediated antinociceptive effect of SST in a rat model of postoperative pain. This was compared with bupivacaine and morphine under identical experimental conditions.
DESIGN: Randomised vehicle-controlled blind study.
SETTING: Pain research laboratory, All India Institute of Medical Sciences, New Delhi from February 2014 to July 2017.
EXPERIMENTAL SUBJECT: Rodent hind paw incision model.
INTERVENTIONS: Sprague-Dawley rats were subjected to incision and one of the following drugs administered into the open wound once by a micropipette: SST (10, 30 or 100μg), bupivacaine (3, 10, 30, 50 or 100μg) or morphine (100μg). Antinociceptive effect of SST was further evaluated for its reversibility, site of action, effect on spinal c-fos expression and blood glucose level. The site of

action of morphine was also investigated.
MAIN OUTCOME MEASURE: Nociception was estimated by nonevoked (guarding behaviour) and evoked (mechanical allodynia and thermal hyperalgesia) pain behaviours between 2h and days 4 to 7.
RESULTS: Nociception was maximum 2h after incision. SST (10 to 100μg) significantly attenuated guarding behaviour between 2h and day 2. A delayed inhibitory effect was observed on allodynia. Bupivacaine (10 to 100μg doses) similarly decreased guarding score up to day 2 though evoked pain behaviours were relatively unaffected. In contrast, morphine produced a potent but transient inhibitory effect on guarding score at 2h, which was mediated by both peripheral and central opioid receptors. The antinociceptive effect of SST was peripherally mediated by type 2 receptors and was associated with decreased c-fos staining. Blood glucose level was unaltered.
CONCLUSION: Guarding behaviour, which likely represents pain-at-rest following surgery, was attenuated by both bupivacaine and SST to comparable extents. This novel peripherally mediated antinociceptive effect of SST needs further evaluation.

DOI: 10.1097/EJA.0000000000000825
PMID: 29762151

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Evidence on influenza vaccine effectiveness from low and middle countries (LMICs) is limited due to limited institutional capacities; lack of adequate resources; and lack of interest by ministries of health for influenza vaccine introduction. There are concerns that the highest ethical standards will be compromised during trials in LMICs leading to mistrust of clinical trials. These factors pose regulatory and operational challenges to researchers in these countries. We conducted a community-based vaccine trial to assess the efficacy of live attenuated influenza vaccine and inactivated influenza vaccine in rural north India. Key regulatory challenges included obtaining regulatory approvals, reporting of adverse events, and compensating subjects for trial-related injuries; all of which were required to be completed in a timely fashion. Key operational challenges included obtaining audio-visual consent; maintaining a low attrition rate; and administering vaccines during a narrow time period before the influenza season, and under extreme heat. We overcame these challenges through advanced planning, and sustaining community engagement. We adapted the trial procedures to cope with field conditions by conducting mock vaccine camps; and planned for early morning vaccination to mitigate threats to the cold chain. These lessons may help investigators to confront similar challenges in other LMICs.

DOI: 10.1080/21645515.2018.1460182
PMCID: PMC6150048
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69: Kumar S, Singh S, Parmar A, Verma R, Kumar N. Effect of high-frequency repetitive transcranial magnetic stimulation (rTMS) in patients with comorbid panic disorder and major depression. Australas Psychiatry. 2018 Aug;26(4):398-400. doi: 10.1177/1039856218771517. Epub 2018 May 8. PubMed PMID: 29737182.

OBJECTIVE: To explore the role of dorsolateral prefrontal cortex (DLPFC) stimulation in the treatment of panic disorder with comorbid depression.
METHODS: The present study reports findings from retrospective analysis of 13 treatment-resistant patients diagnosed with comorbid panic disorder and depression, given 20 sessions of high-frequency transcranial magnetic stimulation (rTMS) over left-DLPFC over a period of 1 month.
RESULTS: There was a significant reduction in both the panic and depressive symptom severity, assessed by applying Panic Disorder Severity Scale (PDSS) and Hamilton Depression Rating Scale (HDRS) at baseline and after 20 sessions of rTMS. There was a 38% and 40% reduction of PDSS and HDRS scores, respectively, in the sample. The changes in PDSS and HDRS scores were not significantly correlated ($\rho = -0.103$, $p = 0.737$).
CONCLUSIONS: High-frequency rTMS delivered at left-DLPFC may have a potential role in treatment of comorbid panic disorder and depression. Future studies done on a larger sample in a controlled environment are required to establish its role.

DOI: 10.1177/1039856218771517
PMID: 29737182

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OBJECTIVES: Childhood immunisation is one of the important public health interventions, and poor migrants are vulnerable to forego these services. The objective of the study is to understand the access of childhood immunisation services to the socio-economically disadvantaged migrants and the determinants of full immunisation uptake up to the age of 1 year.
METHODS: In a cross-sectional survey, 458 migrant households with a child aged up to 2 years were identified. Data on sociodemographics, migration history, receipt of various vaccines and maternal healthcare services were collected through interviewer-administered pretested questionnaires. Multiple logistic regression analysis was performed to identify the determinants of full immunisation status.
RESULTS: Childhood immunisation coverage rates were low as only 31% of recent-migrant children and 53% of settled-migrant children were fully immunised against seven vaccine-preventable diseases (VPDs) by 12 months of age. Lack of awareness of the immunisation schedule and location of health facilities, mobility, illness of the child, fear of vaccines and side-effects were the main reasons for incomplete or no immunisation. Mother's educational attainment, TV viewership, hospital birth and receipt of information on childhood immunisation from the health workers during postnatal visits increased chances of getting the child fully immunised against seven VPDs by 1 year of age.
CONCLUSION: The migrants, particularly the recent migrants, are at the risk of foregoing immunisation services because of livelihood insecurity, mobility and

non-familiarity of services in the new urban environment. There is a need to deliver services with a focus on recent migrants. Investing in education and socio-economic development and providing secured livelihoods and equitable services are important to improve and sustain access to healthcare services in the long run.

DOI: 10.1016/j.puhe.2018.03.006
PMID: 29602525 [Indexed for MEDLINE]

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BACKGROUND: In low and middle-income countries, reliable data on the epidemiology of childhood acute kidney injury (AKI) is lacking. The Global Snapshot, conducted by the ISN "0by25" AKI initiative, was a world-wide cross-sectional, observational study to evaluate AKI in hospitalized patients. Here we report the pediatric results of this study.
PATIENTS AND METHODS: We prospectively collected data on children who met the Kidney Disease Improving Global Outcomes AKI criteria during a 10-week window in late 2014. AKI risk factors, etiological factors, management and outcomes were recorded using standardized forms and protocols. Countries were classified according to their 2014 gross national income (GNI) per person into high-income countries (HIC), upper-middle income countries (UMIC) and low and low-middle income countries (LLMIC). Need for renal replacement therapy, mortality, and renal recovery were assessed 7 days after AKI diagnosis or at hospital discharge, whichever came first.
RESULTS: 92 centers from 41 countries collected data on 354 pediatric AKI patients; 53% of the children developed AKI while hospitalized and 47% in the community. The most common etiological factors for AKI differed across GNI categories as well as between patients with community-acquired vs. hospital-acquired AKI. Children from HIC were younger, and larger proportion of AKI in this group were due to post-surgical complications vs. other etiologies when compared to other income categories. In patients with hypotension as the cause of AKI, the adjusted risk of death was almost 10-fold higher compared to patients without hypotension as an etiological factor for AKI development. Mortality was similar within AKI stages in HIC and UMIC. In LLMIC, patients with the highest AKI level of severity had higher mortality than patients in higher income categories. Patients from LLMIC and UMIC had a 57-fold and 11 fold higher adjusted risk of death, respectively, compared to patients from HIC.
CONCLUSION: In resource-limited countries, pediatric AKI-associated mortality is disproportionately higher when compared to high-resource areas, especially among patients with more severe AKI.

DOI: 10.1371/journal.pone.0196586
PMCID: PMC5929512
PMID: 29715307 [Indexed for MEDLINE]

72: Mahajan S, Gupta K, Sinha S, Malhotra A, Mahajan S. Effect of kidney transplantation on sleep-disordered breathing in patients with End Stage Renal Disease: a polysomnographic study. Sleep Med. 2018 May;45:140-145. doi: 10.1016/j.sleep.2017.11.1151. Epub 2018 Feb 15. PubMed PMID: 29680422; PubMed Central PMCID: PMC6186151.

BACKGROUND: Sleep-disordered breathing (SDB) is common in patients with end-stage renal disease (ESRD). SDB is associated with comorbidities such as hypertension, diabetes mellitus, and obesity, interplaying with metabolic derangements in the form of uremia, acidosis, and hypervolemia. Renal transplant has been observed to correct most of these metabolic derangements and to control progression of comorbidities. While SDB is highly prevalent among patients in the pretransplant stage, it remains to be seen whether the beneficial aspects of transplant are extended to improvement in SDB in patients with ESRD.
METHODS: Eighteen patients undergoing thrice-weekly hemodialysis (HD) for ESRD at the transplant clinic of All India Institute of Medical Sciences (AIIMS), New Delhi, underwent detailed clinical, laboratory, and polysomnographic evaluation. The average number of apneas and hypopneas per hour of sleep, ie, Apnea-Hypopnea Index (AHI), was used to define the severity of sleep apnea. All patients underwent polysomnography (PSG) within 24 h of the last HD and after three months of living-donor transplant.
RESULTS: Of 18 patients, there were 14 males and four females. The median age was 28 years (range 19-50 years). They had already spent a median period of six months (range 3-31 months) on HD before inclusion. The prevalence of SDB (AHI ≥ 5/h) was 44.4% (8/18) before transplant, which decreased to 5.6% (1/18) after transplant (p = 0.016). The oxygen desaturation index had a median value of 5.8 events/h (range 0.1-35.4) in the pretransplant stage, which decreased to 0 events/h (range 0-6.6) in the post-transplant stage (p = 0.035).
CONCLUSION: There was a significant improvement in the prevalence and severity of SDB after transplant. Whether improvement in SDB is sustained on a long-term follow-up remains to be seen.

DOI: 10.1016/j.sleep.2017.11.1151
PMCID: PMC6186151 [Available on 2018-11-01]
PMID: 29680422

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BACKGROUND: Epidural steroids injections (ESI) are frequently used to treat lumbar radicular pain. Although different volume have been used for interlaminar ESI in adults, there is no controlled trial comparing the effect of different volumes on pain relief for the same dose of steroid .
OBJECTIVE: To compare the effect of increase in volume of epidural drug on pain relief in lumbar ESI.
STUDY DESIGN: Randomized double blind trial SETTING: Pain OR of a tertiary care centre METHODS: Sixty patients were randomly allocated to 1 of 3 groups: Group A (4 mL), Group B (6 mL), and Group C (8 mL). Pain was evaluated using visual analog scale (VAS) and improvement in disability using modified Oswestry Disability Questionnaire scores (MODQS) at 2, 4, 8, 12, and 24 weeks. Patients having less than 50% pain relief from baseline received an additional epidural injection of the same volume with a maximum of 3 injections at least 15 days apart. The primary objective of the study was incidence of patients attaining more than 50% pain relief at 6 months. Secondary outcome included MODQS and pattern of spread of iodinated contrast on fluoroscopy.
RESULTS: At the end of 6 months, there was no significant difference in the effective pain relief between the 3 groups (Group A-16/22 (72.7%), Group B-15/20 (75%), Group C-13/18 (72.2%); P = 0.98, chi- square test). All groups demonstrated a significant reduction in mean VAS scores. There was no significant

intergroup difference in VAS sores and MODQS at all the time intervals. The pattern of contrast spread did not differ between the 3 groups.
LIMITATION: Not a placebo controlled trial.
CONCLUSIONS: An increase in volume of the injectate from 4 mL to 8 mL did not increase the efficacy of interlaminar ESI.
KEY WORDS: Epidural steroid, volume, low back pain, interlaminar.

PMID: 29871368

74: Malgulwar PB, Nambirajan A, Pathak P, Faruq M, Rajeshwari M, Singh M, Suri V, Sarkar C, Sharma MC. C11orf95-RELA fusions and upregulated NF-KB signalling characterise a subset of aggressive supratentorial ependymomas that express L1CAM and nestin. J Neurooncol. 2018 May;138(1):29-39. doi: 10.1007/s11060-018-2767-y. Epub 2018 Jan 22. PubMed PMID: 29354850.

Ependymomas (EPN) show site specific genetic alterations and a recent DNA methylation profiling study identified nine molecular subgroups. C11orf95-RELA and YAP1 fusions characterise the RELA and YAP1 molecular subgroups, respectively, of supratentorial (ST)-EPNs. Current guidelines recommend molecular subgrouping over histological grade for accurate prognostication. Clinicopathological features of ST-EPNs in correlation with C11orf95-RELA and YAP1 fusions have been assessed in only few studies. We aimed to study these fusions in EPNs, and identify diagnostic and prognostic markers. qRT-PCR and Sanger Sequencing for the detection of C11orf95-RELA, YAP1-MAMLD1 and YAP1-FAM118B fusion transcripts, gene expression analysis for NFKB1, and immunohistochemistry for p53, MIB-1, nestin, VEGF, and L1CAM were performed. 88 EPNs (10-Grade I and 78-Grade II/III) from all sites were included. RELA fusions were unique to Grade II/III ST-EPNs, detected in 81.4% (22/27) and 18.5% (5/27) of pediatric and adult ST-EPNs respectively. ST-EPNs harbouring RELA fusions showed frequent grade III histology (81.5%), clear cell morphology (70.3%), upregulated NFKB1 expression, MIB-1 labelling indices (LI) ≥10% (77.8%), and immunopositivity for nestin (95.7%), VEGF (72%), L1CAM (79%), and p53 (64%). Presence of RELA fusions, L1CAM immunopositivity and MIB-1 LI ≥10% associated with poor outcome. L1CAM showed 81% concordance with RELA fusions. YAP1-MAMLD1 fusion was identified in a single RELA fusion negative adult anaplastic ST-EPN. RELA fusions are frequent in ST-EPNs and associate with poor outcome. L1CAM is a surrogate immunohistochemical marker. RELA fusion positive ST-EPNs strongly express nestin indicating increased stemness. Further evaluation of the interactions between NFKB and stem cell pathways is warranted.

DOI: 10.1007/s11060-018-2767-y
PMID: 29354850

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We wish to present a case of 47-year-old patient with Juvenile Rheumatoid Arthritis and ankylosis of both hips and both knees treated by bilateral hip and knee arthroplasty in a single anaesthesia i.e. Quadruple joint replacement in single sitting. He was back on his feet from his bed-ridden state within the fortnight following surgery. He has been followed up for four years and has been performing his activities of daily living independently. We discuss the preoperative planning, surgical details and post-operative rehabilitation and unique challenges pertaining to this case.

PMCID: PMC5990718
PMID: 29911143

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Large bone defects in femur or tibia are common at the setting of revision knee arthroplasty. Filling up the defect remains a challenging problem to the orthopaedic surgeons. A variety of options are available to fill up these defects depending upon the type of defect. We report a case of large contained defect in proximal tibia managed with distal tibial metaphyseal allograft cone. We also discuss the operative details and the advantages of using the allograft.

DOI: 10.1016/j.jor.2018.05.026
PMCID: PMC5990296 [Available on 2019-06-01]
PMID: 29881205

77: Mallick S, Benson R, Melgandi W, Giridhar P, Rath GK. Grade II Pleomorphic Xanthoastrocytoma; a meta-analysis of data from previously reported 167 cases. J Clin Neurosci. 2018 Aug;54:57-62. doi: 10.1016/j.jocn.2018.05.003. Epub 2018 May 24. Review. PubMed PMID: 29803334.

Pleomorphic Xanthoastrocytoma [PXA] is a rare low grade glial tumor commonly affecting young adults. We did this systematic review and meta-analysis to identify prognostic factors and optimal treatment in these patients. A thorough search of the PubMed, Google scholar was made to find all possible publications related to grade II PXA. A total of 167 patients from 89 articles were included in the analysis. Median age of the entire cohort was 20 years. Headache was the most common presentation in 49.1% of the patients followed by seizure in 27.9%. Temporal lobe was the most common location of the tumor. 63% patents underwent a gross total resection [GTR] and 26.7% underwent a sub total excision [STR]. Adjuvant radiation was given to 17.6% of patients. Median follow-up for the entire cohort was 33 months. Estimated median overall survival [OS] for the entire cohort was 209.0 months [96% CI: 149.7-268.3]. Estimated median progression free survival [PFS] was 48 months [95% CI: 31.9-64.0]. In univariate and multivariate analysis younger patients and patients who underwent a GTR had a significantly better survival outcome. Use of adjuvant therapy was not found to be a significant factor affecting PFS or OS. Radiotherapy was used in salvage treatment in 76.1% of the patients. Younger patients and patients who undergo a GTR, have better survival outcomes. There is inadequate evidence to recommend routine adjuvant radiation or chemotherapy in all patients with grade II PXA.

DOI: 10.1016/j.jocn.2018.05.003
PMID: 29803334 [Indexed for MEDLINE]

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The anterior cruciate ligament is one of the six ligaments in the human knee joint that provides stability during articulations. It is relatively prone to

acute and chronic injuries as compared to other ligaments. Repair and self-healing of an injured anterior cruciate ligament are time-consuming processes. For personnel resuming an active sports life, surgical repair or replacement is essential. Untreated anterior cruciate ligament tear results frequently in osteoarthritis. Therefore, understanding of the biomechanics of injury and properties of the native ligament is crucial. An abridged summary of the prominent literature with a focus on key topics on kinematics and kinetics of the knee joint and various loads acting on the anterior cruciate ligament as a function of flexion angle is presented here with an emphasis on the gaps. Briefly, we also review mechanical characterization composition and anatomy of the anterior cruciate ligament as well as graft materials used for replacement/reconstruction surgeries. The key conclusions of this review are as follows: (a) the highest shear forces on the anterior cruciate ligament occur during hyperextension/low flexion angles of the knee joint; (b) the characterization of the anterior cruciate ligament at variable strain rates is critical to model a viscoelastic behavior; however, studies on human anterior cruciate ligament on variable strain rates are yet to be reported; (c) a significant disparity on maximum stress/strain pattern of the anterior cruciate ligament was observed in the earlier works; (d) nearly all synthetic grafts have been recalled from the market; and (e) bridge-enhanced repair developed by Murray is a promising technique for anterior cruciate ligament reconstruction, currently in clinical trials. It is important to note that full extension of the knee is not feasible in the case of most animals and hence the loading pattern of human ACL is different from animal models. Many of the published reviews on the ACL focus largely on animal ACL than human ACL. Further, this review article summarizes the issues with autografts and synthetic grafts used so far. Autografts (patellar tendon and hamstring tendon) remains the gold standard as nearly all synthetic grafts introduced for clinical use have been withdrawn from the market. The mechanical strength during the ligamentization of autografts is also highlighted in this work.

DOI: 10.1155/2018/4657824
PMCID: PMC5971278
PMID: 29861784

79: Mathur P, Hasan F, Singh PK, Malhotra R, Walia K, Chowdhary A. Five-year profile of candidaemia at an Indian trauma centre: High rates of Candida auris blood stream infections. Mycoses. 2018 May 8. doi: 10.1111/myc.12790. [Epub ahead of print] PubMed PMID: 29738604.

Candidaemia is a potentially fatal infection with varied distribution of Candida species and their antifungal susceptibility profiles. The recent emergence of Candida auris in invasive candidiasis is a cause for concern. This study describes the profile of candidaemia at an Indian tertiary care hospital and reports the emergence of C. auris. All patients diagnosed with candidaemia between 2012 and 2017 were studied. The isolates were identified using conventional methods, VITEK 2 and MALDI-TOF MS. The isolates not identified by MALDI-TOF were sequenced. Antifungal susceptibility testing was done by the CLSI broth microdilution method and VITEK 2. A total of 114 isolates of Candida species were analysed. Candida tropicalis (39.4%) was the most common species, followed by C. auris (17.5%), C. albicans (14%) and C. parapsilosis (11.4%). Notably, Diutina mesorugosa isolates (n = 10) were not identified by MALDI-TOF and were confirmed by sequencing. Furthermore, 45% (n = 9) C. auris strains exhibited low MICs of FLU (0.05-4 µg/mL) and the remaining 55% (n = 11) isolates had high MICs ≥ 64 µg/mL. Also, D. mesorugosa exhibited high MICs of FLU (32 µg/mL) in 2 isolates. A high rate of errors in antifungal susceptibility was noted with the VITEK 2 as compared to the CLSI method. Candida auris was the second most prevalent species causing candidaemia warranting infection control

practices to be strengthened to prevent its spread.

DOI: 10.1111/myc.12790
PMID: 29738604

80: Menon V, Shanmuganathan B, Thamizh JS, Arun AB, Kuppili PP, Sarkar S. Personality traits such as neuroticism and disability predict psychological distress in medically unexplained symptoms: A three-year experience from a single centre. Personal Ment Health. 2018 May;12(2):145-154. doi: 10.1002/pmh.1405. Epub 2017 Nov 17. PubMed PMID: 29148230.

BACKGROUND: People with medically unexplained symptoms (MUS) may have psychological co-morbidities.
AIMS: Our objectives were to assess the rates and identify correlates of psychological distress in MUS.
METHODS: A total of 171 subjects with MUS seeking treatment at a tertiary care facility were assessed over a 3-year period. Psychological distress was assessed using the Tamil version of General Health Questionnaire-12. Apart from socio-demographic factors, personality, coping, perceived social support and subjective disability were assessed using standard instruments.
RESULTS: Ninety subjects (52.6%) endorsed symptoms of psychological distress. MUS subjects with psychological distress reported higher levels of neuroticism ($p < 0.001$), lower extraversion ($p < 0.001$), lower perceived social support ($p = 0.002$), higher disability ($p < 0.001$), lower problem focused engagement ($p = 0.378$) and higher emotion focused engagement ($p = 0.009$). In multivariate analysis, high neuroticism scores (odds ratio 1.579, 95% CI 1.108 to 2.251) and high disability (odds ratio 1.302, 95% CI 1.147 to 1.478) emerged as independent predictors of psychological distress in MUS.
CONCLUSION: More than half of subjects with MUS have associated psychological distress. High levels of neuroticism and disability are potential markers of psychological distress in MUS. Copyright © 2017 John Wiley & Sons, Ltd.

DOI: 10.1002/pmh.1405
PMID: 29148230

81: Nair S, Vanathi M, Mahapatra M, Seth T, Kaur J, Velpandian T, Ravi A, Titiyal JS, Tandon R. Tear inflammatory mediators and protein in eyes of post allogenic hematopoeitic stem cell transplant patients. Ocul Surf. 2018 Jul;16(3):352-367. doi: 10.1016/j.jtos.2018.04.007. Epub 2018 May 1. PubMed PMID: 29723628.

AIM: To analyze tear cytokines levels and their correlation to ocular surface parameters in allogenic hematopoietic stem cell transplants (allo-HSCT) patients.
METHODS: Prospective longitudinal study of allo-HSCT patients and controls for ocular surface evaluation (OSDI, TBUT, Schirmer's test, staining scores), tear biochemical analysis for protein, cytokines [IL-10, IL-12, IL-2, IL-4, IL-6, IL-17, interferon (IFN)-gamma, tumor necrosis factor (TNF)-alpha, VEGF], MMPs [MMP 2, 9, 7, 13, 10 and chemokine (IL-8)], & VEGF on three consecutive follow up visits (at three monthly interval) was done.
RESULTS: Of 24 post allo-HSCT patients (19 males, 5 females) & 12 controls (mean age 34.3 + 5.8 years) enrolled, 20 patients [mean age 33.4 + 7.77 years; mean time of recruitment of 5.2 + 2.12 months following alloHSCT] who completed three consecutive follow up visits were included for analysis. Ocular GVHD (oGVHD) was seen in 8 patients (33.3%). Tears biochemical analysis showed elevated levels of interferon γ, IL 6, IL 8, IL 10, IL 12AP70, IL 17A, MMP 9 and VEGF in oGVHD eyes

as compared to non-oGVHD & control eyes. Non-oGVHD eyes showed elevated tear MMP 7 and MMP 9 as compared to healthy controls. Tear protein levels were significantly decreased in oGVHD eyes and were equivocal in nonGVHD and control eyes. TBUT and ocular staining scores to correlate best with tear interleukins and MMPs.
CONCLUSION: Evaluation of levels of tear VEGF, total protein & MMP 9 can be of significance in identifying oGVHD in post alloHSCT patients.

DOI: 10.1016/j.jtos.2018.04.007
PMID: 29723628

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83: Narain P, Pandey A, Gupta S, Gomes J, Bhatia R, Vivekanandan P. Targeted next-generation sequencing reveals novel and rare variants in Indian patients with amyotrophic lateral sclerosis. Neurobiol Aging. 2018 Nov;71:265.e9-265.e14. doi: 10.1016/j.neurobiolaging.2018.05.012. Epub 2018 May 17. PubMed PMID: 29895397.

Studies on genetic aberrations among Indian amyotrophic lateral sclerosis (ALS) patients are limited to C9orf72 and ATXN2 repeat expansions and mutations in the SOD1 gene. In this study, we used targeted next-generation sequencing to analyze 25 ALS-associated genes in a cohort of 154 Indian ALS patients. We identified known pathogenic mutations in SOD1 (G148D; H44R), TARDBP (M337V; N267S), DAO (R199Q), and ANG (K41I). In addition, we also identified 7 potentially pathogenic missense variants that have not been previously reported in ALS patients; this includes 3 novel variants (OPTN: K489E, DAO: E121K, and SETX: L2163V) that are not reported in large population databases and 4 rare variants (CHMP2B: E45K, SQSTM1: G262R and P438L, ERBB4: R103H) with a minor allele frequency of <0.01 in large population databases. All known pathogenic, novel, and rare variants were detected in only 1 ALS patient each with the exception of the OPTN (K489E) variant that was detected in 2 patients in our cohort. In sum, we identified known and potentially pathogenic novel and rare mutations in 14 (9.1%) ALS patients in our cohort. This study represents the first comprehensive genetic analysis in the ethnically diverse population and thus provides a new insight into the genetics of Indian ALS patients.

DOI: 10.1016/j.neurobiolaging.2018.05.012
PMID: 29895397

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Clustered miRNAs can affect functioning of downstream pathways due to possible coordinated function. We observed 78-88% of the miR-379/miR-656 cluster (C14MC) miRNAs were downregulated in three sub-types of diffuse gliomas, which was also

corroborated with analysis from The Cancer Genome Atlas (TCGA) datasets. The miRNA expression levels decreased with increasing tumor grade, indicating this downregulation as an early event in gliomagenesis. Higher expression of the C14MC miRNAs significantly improved glioblastioma prognosis (Pearson's r = 0.62; p < 3.08e-22). ENCODE meta-data analysis, followed by reporter assays validated existence of two novel internal regulators within C14MC. CRISPR activation of the most efficient internal regulator specifically induced members of the downstream miRNA sub-cluster and apoptosis in glioblastoma cells. Luciferase assays validated novel targets for miR-134 and miR-485-5p, two miRNAs from C14MC with the most number of target genes relevant for glioma. Overexpression of miR-134 and miR-485-5p in human glioblastoma cells suppressed invasion and proliferation, respectively. Furthermore, apoptosis was induced by both miRs, individually and in combination. The results emphasize the tumor suppressive role of C14MC in diffuse gliomas, and identifies two specific miRNAs with potential therapeutic value and towards better disease management and therapy.

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Chronic polyneuropathy is a disabling condition of the peripheral nerves, characterized by symmetrical sensory motor symptoms and signs. There is paucity of studies on the etiological spectrum of polyneuropathy and its impact on quality of life (QoL). The present cross-sectional study in a referral based tertiary care center in North India found diabetic neuropathy as the commonest cause (25.5%) amongst 212 patients with chronic polyneuropathy. Idiopathic axonal polyneuropathy was present in 14.2% patients. Leprosy presenting as confluent mononeuritis multiplex constituted 11.3% of the patients. Additionally, it revealed a significantly worse QoL in these patients in all domains measured by short form (SF-36). This is the first study conducted in India to determine the QoL in chronic neuropathy patients. The current study demonstrates the clinical feasibility and applicability of the SF-36 generic health status in patients with polyneuropathies.

DOI: 10.1111/jns.12269
PMID: 29687564

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29758362.

Secondary osteoporosis is the major concern associated with long term intake of antiepileptic drugs (AEDs). Women are the vulnerable targets owing to post-menopausal bone loss. In the present work, we evaluated the effect of 10 weeks of treatment with AED therapy (carbamazepine, CBZ, 75 mg/kg; sodium valproate, SVP, 300 mg/kg; levetiracetam, LTM, 150 mg/kg) on bone mineral density and microarchitecture at femoral epiphysis, lumbar vertebrae and proximal tibia of normal and ovariectomised Wistar rats. In addition, we measured serum levels of vitamin D, receptor activator of nuclear factor kappa β-ligand (RANKL), procollagen type 1 amino-terminal propeptide (P1NP) and wnt inhibitors (sclerostin and DKK-1) following AED therapy. Micro-computed tomography analysis of bones revealed significant reduction in BMD at femur epiphysis and lumbar vertebrae with all the three AEDs evaluated. At proximal tibia, only CBZ showed a significant decline. The reduction in BMD was more pronounced in ovariectomised rats. AEDs also resulted in alteration of micro-CT parameters. These changes were accompanied by an increased serum RANKL with all AEDs while vitamin D levels were reduced only with CBZ treatment and P1NP levels were reduced with SVP and CBZ. Serum sclerostin levels were elevated following all AEDs in normal and ovariectomised rats except with CBZ in normal rats. However, increase in DKK-1 levels was observed with only LTM. Ovariectomy itself resulted in increased RANKL, sclerostin and DKK-1 and reduced vitamin D and P1NP levels. Significant differences were discernible between normal and ovariectomised rats treated with AEDs in all the parameters. However, while sclerostin increased further upon AEDs treatment, P1NP decreased with SVP and CBZ and serum DKK-1 levels showed a declining trend with all the three AEDs studied. We confirm adverse effects on bone following AEDs in female rats. Further, our results demonstrate for the first time that these effects are more pronounced in ovariectomised rats as compared to normal rats and that this could be related to estrogen deficiency which in turn enhances bone resorption via increased RANKL and reduces bone formation via increased sclerostin and reduced P1NP. Finally, our study demonstrated for the first time that AED treatment displayed changes in the serum levels of wnt inhibitors and hence modulation of wnt inhibitors might be partly involved in their adverse effects on bone.

DOI: 10.1016/j.bone.2018.05.011
PMID: 29758362

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Background: Minimally invasive surgery (MIS) has a significant and evolving role in the treatment of displaced intra articular calcaneal fractures (DIACFs), but there is limited literature on this subject. The objective was hence to assess the clinicoradiological outcomes of DIACFs fixed with an innovative open-envelope MIS technique.
Materials and Methods: 42 closed Sanders Type 2 and 3; DIACFs were included in this study. The Open-envelope approach was developed, which is essentially a limited open, dual incision, modified posterior longitudinal approach allowing excellent visualisation and direct fragment manipulation. The main outcome measures were American Orthopaedic Foot and Ankle Score (AOFAS) hindfoot score and preoperative and postoperative radiological angles.
Results: The Bohler angle improved from a preoperative mean of 14.3° (range 0°-28°) to a postoperative mean of 32.46° (range 22°-42°). The Gissane angle

improved from a preoperative mean of 135.83° to a postoperative mean of 128.33°. The postoperative improvement in Bohler and Gissane angles was highly significant (P < 0.001). The AOFAS scores at 6 months were excellent in nine patients, good in 15 patients, and fair in six patients. Three patients had residual valgus deformity of the heel.
Conclusions: Open-envelope technique minimized soft tissue complications and achieved acceptable radiological reductions with good clinical outcomes.

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PMCID: PMC5961259
PMID: 29887624

Conflict of interest statement: There are no conflicts of interest.

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BACKGROUND: Dhat syndrome is regarded by many as a culture bound syndrome of the Indian sub-continent. However the nosological status, conceptual understanding of the condition as well as the diagnostic guidelines are all mired in controversy.
AIMS: The current study aims to study the psychopathology of Dhat syndrome in men by using a qualitative approach and to arrive at an operational definition for diagnosing Dhat syndrome.
METHOD: The qualitative approach consisted of five Focus Group Discussions (FGD) and five Key Individual Interviews (KII) with participants, consisting of patients as well as doctors - both allopathic as well as traditional.
RESULTS: Detailed analysis revealed valuable data regarding the symptoms, causes, treatment measures, socio-cultural context, psychiatric co-morbidity, nature of the disorder and various other phenomenological dimensions. Ideas for future nosological positioning were also specifically looked for. Operational definition and diagnostic guidelines were also arrived at based on the analysis as well as on previous literature.
CONCLUSION: Although lot of agreement existed among various stakeholders about symptoms and presentation, they varied significantly in their opinion on nature of the condition and treatment. Suggestions for ICD 11 have been made.

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BACKGROUND: Oral squamous cell carcinoma (OSCC) is a cancer of the oral cavity that is a major health problem in India. There is an urgent need to identify biomarkers that have prognostic significance. We studied HIF-1α levels as well as single-nucleotide polymorphism of HIF-1α gene in cancer and healthy controls.

METHODS: Fifty newly diagnosed OSCC patients and 50 age and sex-matched healthy control were included in the study. Serum concentrations of HIF-1α were measured by sandwich ELISA; whereas HIF-1α gene polymorphism study was performed using restriction enzyme digestion by HpH I.
RESULTS: The major genotype observed was CC genotype in both control (84%) and patients (86%) followed by CT genotype (control 16%, cases 14%). CT genotype led to more aggressive tumors. On subgroup analysis based on prognosis, the median overall survival of patients who were treatment responders was 488 days (16.2 months) and that of the patients with progressive disease was 365 days (12.1 months). The patients who expired during the study observation period had median survival of 330 days (11 months).
CONCLUSION: Our study showed that CT genotype for C1772T polymorphism of HIF-1α predisposes to aggressive tumor phenotype in patients with OSCC. Moreover, patients with CT genotype had poor survival rate as compared to CC genotype. A cut-off value of 460 pg/mL of HIF-1α can help to segregate patients with OSCC from healthy controls.

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Carcinoma showing thymus-like differentiation of the thyroid (CASTLE) is a rare tumor involving the thyroid and perithyroidal soft tissues. It shares morphological, immunohistochemical and molecular similarities with thymic carcinomas. Due to its relatively better prognosis, it needs differentiation from other primary and metastatic tumors of this region. A 40-year-old lady presented with a gradually progressive anterior neck swelling for one year. Imaging showed bulky right and left lobes of thyroid along with a solid soft tissue mass in the pretracheal region. Fine needle aspiration smears showed features of poorly differentiated carcinoma. Total thyroidectomy with excision of the mass revealed histopathological features characteristic of CASTLE, with evidence of thyroiditis in adjoining thyroid. Epidermal growth factor receptor (EGFR) assay revealed presence of EGFR T790M somatic mutation in exon 20. The same was not detectable on direct sequencing. We present a rare case of CASTLE, occurring in association with Hashimoto thyroiditis, with emphasis on cytological features and report for the first time the presence of a low level somatic mutation in EGFR (EGFR T790M mutation).

DOI: 10.1002/dc.23859
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The loss of vision after damage to the retina, optic nerve, or brain has often grave consequences in everyday life such as problems with recognizing faces, reading, or mobility. Because vision loss is considered to be irreversible and often progressive, patients experience continuous mental stress due to worries, anxiety, or fear with secondary consequences such as depression and social isolation. While prolonged mental stress is clearly a consequence of vision loss, it may also aggravate the situation. In fact, continuous stress and elevated cortisol levels negatively impact the eye and brain due to autonomous nervous system (sympathetic) imbalance and vascular dysregulation; hence stress may also be one of the major causes of visual system diseases such as glaucoma and optic neuropathy. Although stress is a known risk factor, its causal role in the development or progression of certain visual system disorders is not widely appreciated. This review of the literature discusses the relationship of stress and ophthalmological diseases. We conclude that stress is both consequence and cause of vision loss. This creates a vicious cycle of a downward spiral, in which initial vision loss creates stress which further accelerates vision loss, creating even more stress and so forth. This new psychosomatic perspective has several implications for clinical practice. Firstly, stress reduction and relaxation techniques (e.g., meditation, autogenic training, stress management training, and psychotherapy to learn to cope) should be recommended not only as complementary to traditional treatments of vision loss but possibly as preventive means to reduce progression of vision loss. Secondly, doctors should try their best to inculcate positivity and optimism in their patients while giving them the information the patients are entitled to, especially regarding the important value of stress reduction. In this way, the vicious cycle could be interrupted. More clinical studies are now needed to confirm the causal role of stress in different low vision diseases to evaluate the efficacy of different anti-stress therapies for preventing progression and improving vision recovery and restoration in randomized trials as a foundation of psychosomatic ophthalmology.

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PMCID: PMC5972137 [Available on 2019-06-01]
PMID: 29896314

Conflict of interest statement: Compliance with ethical standardsB. Sabel is co-owner of a private medical practice (www.savir-center.com) where the two patients described in this paper were treated.For this type of study, formal consent is not required. We thank our patients for their consent to publish their case histories.

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OBJECTIVE: Available findings from cross-sectional studies have demonstrated cognitive impairments in bipolar I disorder (BD-I) during various phases of illness. However, very little is known about the longitudinal course of these cognitive impairments. The purpose of the study was to explore the longitudinal pattern of changes in cognitive functioning of BD-I patients.
METHODS: A total of 129 BD-I subjects (manic, depressed and euthymic groups) and 49 healthy controls were recruited using predefined selection criteria. All four study groups were assessed on various clinical and cognitive parameters (for attention, memory, executive functions and working memory) at study intake and at 3-monthly intervals over the next year.
RESULTS: All three patient groups performed poorly compared to controls on all cognitive measures at study intake and on some cognitive measures at the 3-, 6-,

9- and 12-month assessments. No significant time effects were observed for any cognitive test. A significant group by time interaction effect was found for executive functions (β = -44.74; P = .018) and working memory (β = 0.77; P ≤ .019) in the depressed group at 12 months; for visual memory (β = 1.21; P = .039) and working memory (β = 1.17; P ≤ .029) in the manic group at 12 months; and for working memory (β = -0.52; P ≤ .036) in the euthymic group at 12 months.
CONCLUSION: The patient groups showed significant impairments in all or some test domains relative to controls at all time-points. The cognitive functions largely remained stable in all patient groups, with slight improvement over time in a few tests. Further investigation is warranted in larger samples in longitudinal studies.

DOI: 10.1111/bdi.12584
PMID: 29314557

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Purpose: The p38 mitogen-activated protein kinase (MAPKs) play a crucial role in the production of pro-inflammatory cytokines and over-expression of it increase cytokines which promote cancer. Among four isoforms, p38α has been well studied in head and neck squamous cell carcinoma (HNSCC) and other cancers as a therapeutic target.p38δ has recently emerged as a potential disease-specific drug target. Elevated serum p38α level in HNSCC was reported earlier from our lab. This study aims to estimate the levels of p38 MAPK-isoforms in the serum of HNSCC and design peptide inhibitor targeting the same.
Materials and Methods: Levels of p38 MAPK isoforms in the serum of HNSCC and healthy controls were quantified by surface plasmon resonance technology. The peptide inhibitor for p38 MAPK was designed by molecular modeling using Grid-based Ligand Docking with Energetics tools and compared with known specific inhibitors.
Results: We have observed highly elevated levels of all four isoforms of p38 MAPK in serum of HNSCC patients compared to the control group. Further, serum p38α, p38β, and p38δ levels were down regulated after therapy in follow up patients, while p38γ showed no response to the therapy. Present study screened designed peptide WFYH as a specific inhibitor against p38δ. The specific inhibitor of p38δ was found to have no effect on p38α due to great structural difference at ATP binding pocket.
Conclusion: In this study, first time estimated the levels of p38 MAPK isoforms in the serum of HNSCC. It can be concluded that p38 MAPK isoforms can be a diagnostic and prognostic marker for HNSCC and p38δ as a therapeutic target.

DOI: 10.4143/crt.2018.105
PMID: 29747487

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We employed Fourier Transform Infrared Microspectroscopy to examine, in situ, the

effects of waterborne Cu, Cd and Zn, alone and in binary mixtures, during acute exposure on the integrity of major lipid and protein constituents of the gill of a model teleost species, rainbow trout (Oncorhynchus mykiss). Our findings demonstrated that acute exposure to metals, both individually and in binary mixture, resulted in the degradations of various components of proteins and lipids in the gill tissue. Generally, when comparing the effects of individual metals, Cu was found to induce the maximum adverse effects followed by Cd and Zn, respectively. Among the binary metal-mixture combinations, Cu and Cd produced additive effects on the degradation of major proteins and lipid moieties, whereas the co-exposure of Zn with Cd or Cu elicited ameliorative effects, indicating antagonistic (less than additive) interactions between Zn and Cd or Cu in the rainbow trout gill. Overall, the present study demonstrates that FTIRM can be a useful tool to gain novel mechanistic insights into the biochemical changes induced by metals in the fish gill, which could influence the overall toxicity of metals to fish.

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PMID: 29803893 [Indexed for MEDLINE]

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BACKGROUND AND AIMS: Brain-Derived Neurotrophic Factor (BDNF), a neuropeptide important for neural growth and differentiation has been explored in patients with opioid dependence. We aimed to compare the serum BDNF levels in patients with opioid dependence with age and gender matched controls, and to assess change in BDNF levels during initial withdrawal period.
METHODS: Thirty cases with a diagnosis of opioid dependence were compared to forty healthy controls. BDNF levels were measured at inclusion for all participants. Additionally, BDNF levels were measured in patients with opioid dependence after 10 days of inpatient detoxification.
RESULTS: There were no group differences in BDNF levels between cases and controls for day 1 BDNF levels. Also, there was no significant difference observed in the BDNF levels in patients at day 1 and 10 of inpatient detoxification. BDNF levels did not correlate with severity of nicotine dependence, age of the cases or duration of opioid dependence.
CONCLUSION: The results from the study provide further insights into the relationship of BDNF levels and opioid dependence.

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PMID: 29859931

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INTRODUCTION AND AIM: Multiple prognostic scores are available for acute liver failure (ALF). Our objective was to compare the dynamicity of model for end stage liver disease (MELD), MELD-sodium, acute liver failure early dynamic model (ALFED), chronic liver failure (CLIF)-consortium ACLF score and King's College Hospital Criteria (KCH) for predicting outcome in ALF.
MATERIALS AND METHODS: All consecutive patients with ALF at a tertiary care centre in India were included. MELD, MELD-Na, ALFED, CLIF-C ACLF scores and KCH criteria were calculated at admission and day 3 of admission. Area under receiver operator characteristic curves (AUROC) were compared with DeLong method. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratio (LR) and diagnostic accuracy (DA) were reported.
RESULTS: Of the 115 patients included in the study, 73 (63.5%) died. The discrimination of mortality with baseline values of prognostic scores (MELD, MELD-Na, ALFED, CLIF-C ACLF and KCH) was modest (AUROC: 0.65-0.77). The AUROC increased on day 3 for all scores, except KCH criteria. On day 3 of admission, ALFED score had the highest AUROC 0.95, followed by CLIF-C ACLF 0.88, MELD 0.81, MELD-Na 0.77 and KCH 0.52. The AUROC for ALFED was significantly higher than MELD, MELD-Na and KCH (P < 0.001 for all) and CLIF-C ACLF (P = 0.05). ALFED score ≥ 4 on day 3 had the best sensitivity (87.1%), specificity (89.5%), PPV (93.8%), NPV (79.1%), LR positive (8.3) and DA (87.9%) for predicting mortality.
CONCLUSIONS: Dynamic assessment of prognostic scores better predicts outcome. ALFED model performs better than MELD, MELD, MELD-Na, CLIF-C ACLF scores and KCH criteria for predicting outcome in viral hepatitis- related ALF.

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PMID: 29735790

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BACKGROUND: Acute on chronic liver failure (ACLF) is associated with high short term mortality. We aimed to evaluate the prevalence, predictors and impact of bacterial infection in ACLF.
METHODS: Consecutive hospitalized patients with cirrhosis and acute decompensation (AD), from January 2011-March 2017, were included. Predictors of survival and infection were assessed.
RESULTS: 572 patients with cirrhosis and AD were classified into 3 groups - no infection (group 1, n = 190, 33.2%), infection at admission/within 48 h (group 2, n = 298, 52.1%) and infection after 48 h (group 3, n = 84, 14.7%). Higher frequency of organ failures - kidney, brain, circulation and respiratory failure - were seen in groups 2 and 3 as compared with group 1 (P < 0.001 for all). Most common site of infection was lungs, followed by spontaneous bacterial peritonitis and urinary tract infection. The frequency of infection increased with higher ACLF grades. Among ACLF patients, on Cox-proportional multivariate analysis, presence of infection was associated with significantly higher mortality [group 2 (HR 2.93; 95%CI, 1.97-4.38, P < 0.001) and group 3 (HR 1.84; 95%CI, 1.16-2.91, P = 0.009)], as compared with group 1. On multivariate logistic regression analysis, advanced hepatic encephalopathy and elevated total leucocyte count were

independently associated with development of infection.
CONCLUSIONS: Infections are common in ACLF, and associated with poor outcome.

DOI: 10.1016/j.dld.2018.05.013
PMID: 29910108

104: Sharma A, Khan R, Gupta N, Sharma A, Zaheer MS, Abbas M, Khan SA. Acute phase reactant, Pentraxin 3, as a novel marker for the diagnosis of rheumatoid arthritis. Clin Chim Acta. 2018 May;480:65-70. doi: 10.1016/j.cca.2018.01.035. Epub 2018 Feb 20. PubMed PMID: 29408170.

INTRODUCTION: Pentraxins are a group of highly conserved acute-phase reactant proteins and play crucial role as modulators of inflammatory processes. Pentraxin 3 (PTX3) is primarily produced and released by vascular cell wall, hence, we attempt to establish the role of PTX3 as a biomarker for Rheumatoid Arthritis (RA) compared to CRP.
METHODS: Thirty patients having active RA as cases and 30 osteoarthritis (OA) patients as controls were recruited. Paired serum and synovial fluid samples were analysed for concentrations of both PTX3 and CRP by using high sensitivity ELISA kit and ROC curve was plotted.
RESULTS: Concentrations of PTX3 and CRP were significantly higher in RA patient serum ($p < 0.0001$) as well as in synovial fluid ($p < 0.0001$) and correlated with disease severity. Upon correlation analysis, positive correlation was found between serum and synovial fluid concentrations of PTX3 and CRP. The diagnostic potential of PTX3 was observed in synovial fluid while combination of PTX3 and CRP showed better sensitivity in serum.
CONCLUSION: PTX3 found to be sensitive non-invasive indicator of clinical arthritic activity in RA patients when compared to traditional markers like CRP. Combination of PTX3 and CRP could serve as better differential diagnostic markers for RA after validation in larger patient cohort.

DOI: 10.1016/j.cca.2018.01.035
PMID: 29408170 [Indexed for MEDLINE]

105: Sharma R, Phalak M, Katiyar V, Borkar S, Kale SS, Mahapatra AK. Microvascular decompression versus stereotactic radiosurgery as primary treatment modality for trigeminal neuralgia: A systematic review and meta-analysis of prospective comparative trials. Neurol India. 2018 May-Jun;66(3):688-694. doi: 10.4103/0028-3886.232342. Review. PubMed PMID: 29766927.

Objective: The current opinion among neurosurgeons regarding the selection between microvascular decompression (MVD) and gamma knife radiosurgery for trigeminal neuralgia is not based on clear evidence. In this meta-analysis, we have attempted to synthesize the findings of the prospective trials comparing the efficacy and complications of the two procedures as primary treatment modality for medically refractory trigeminal neuralgia.
Materials and Methods: The authors performed a systematic review of PubMed for manuscripts comparing the efficacy or complications of MVD and stereotactic radiosurgery for medically refractory trigeminal neuralgia. The data of the identified studies was pooled and a meta-analysis was done.
Results: Five prospective studies fulfilling the eligibility criteria were identified. The mean age of the patients subjected to gamma knife therapy (GKT) was more than those who underwent MVD. The initial success rate in the pooled

data with MVD was 96% (95% confidence interval [C.I.] 93.3%-98.6%) as compared to GKT which was 71.8% (95% C.I. 64.9%-78.7%) with the ratio of 1.309 (95% C.I. 1.217-1.409; P= <0.001). This superiority was sustained till the last follow up available in all the studies. Out of the complications common to both procedures, MVD had a lower rate of facial numbness, with a risk ratio of 0.481 (95% C.I. 0.297-0.778); and dysesthetic pain, with a risk ratio of 0.470 (95% C.I. 0.172-1.286).
Conclusions: MVD seems to be more efficacious than GKT as a first line treatment for trigeminal neuralgia immediately as well as on a long term basis. However, the dilemma regarding the choice of treatment to be adopted still remains for special subgroups of patients, like the elderly patients and those in whom no vascular compression has been found during surgery. Further studies are needed for elucidating the unequivocal treatment plan under these circumstances.

DOI: 10.4103/0028-3886.232342
PMID: 29766927

Conflict of interest statement: There are no conflicts of interest

106: Sharma R, Katiyar V, Sharma P, Vora Z, Gurjar H. Posterior fossa crowdedness in idiopathic trigeminal neuralgia: Is it the real perpetrator? J Clin Neurosci. 2018 Aug;54:165-166. doi: 10.1016/j.jocn.2018.04.068. Epub 2018 May 21. PubMed PMID: 29793777.

107: Sharma VK, Gupta V, Ramam M. Authors' reply. Indian J Dermatol Venereol Leprol. 2018 May-Jun;84(3):314-315. doi: 10.4103/ijdvl.IJDVL_103_18. PubMed PMID: 29600797.

108: Shrivastava N, Nayak B, Singh P. Renal cell carcinoma with sarcomatoid transformation, presenting as skin rashes. BMJ Case Rep. 2018 May 30;2018. pii: bcr-2017-223338. doi: 10.1136/bcr-2017-223338. PubMed PMID: 29848522.

A 68-year-old man presented to our outpatient department, with chief complaints of rashes all over the body. On physical examination, purpuric rashes were present over all four limbs and a lump was palpable in right flank. Contrast-enhanced CT scan showed enhancing large right renal mass. He underwent right radical nephrectomy, and histopathological analysis showed features of renal cell carcinoma. Skin lesions disappeared after surgery.

DOI: 10.1136/bcr-2017-223338
PMID: 29848522

Conflict of interest statement: Competing interests: None declared.

109: Shukla G, Gupta A. High time we focus on sleep in amyotrophic lateral sclerosis! Neurol India. 2018 May-Jun;66(3):664-665. doi: 10.4103/0028-3886.232309. PubMed PMID: 29766917.

110: Sikri K, Duggal P, Kumar C, Batra SD, Vashist A, Bhaskar A, Tripathi K, Sethi T, Singh A, Tyagi JS. Multifaceted remodeling by vitamin C boosts sensitivity of Mycobacterium tuberculosis subpopulations to combination treatment by anti-tubercular drugs. Redox Biol. 2018 May;15:452-466. doi: 10.1016/j.redox.2017.12.020. Epub 2018 Jan 3. PubMed PMID: 29413958; PubMed Central PMCID: PMC5975079.

Bacterial dormancy is a major impediment to the eradication of tuberculosis (TB), because currently used drugs primarily target actively replicating bacteria. Therefore, decoding of the critical survival pathways in dormant tubercle bacilli is a research priority to formulate new approaches for killing these bacteria. Employing a network-based gene expression analysis approach, we demonstrate that redox active vitamin C (vit C) triggers a multifaceted and robust adaptation response in Mycobacterium tuberculosis (Mtb) involving ~ 67% of the genome. Vit C-adapted bacteria display well-described features of dormancy, including growth stasis and progression to a viable but non-culturable (VBNC) state, loss of acid-fastness and reduction in length, dissipation of reductive stress through triglyceride (TAG) accumulation, protective response to oxidative stress, and tolerance to first line TB drugs. VBNC bacteria are reactivatable upon removal of vit C and they recover drug susceptibility properties. Vit C synergizes with pyrazinamide, a unique TB drug with sterilizing activity, to kill dormant and replicating bacteria, negating any tolerance to rifampicin and isoniazid in combination treatment in both in-vitro and intracellular infection models. Finally, the vit C multi-stress redox models described here also offer a unique opportunity for concurrent screening of compounds/combinations active against heterogeneous subpopulations of Mtb. These findings suggest a novel strategy of vit C adjunctive therapy by modulating bacterial physiology for enhanced efficacy of combination chemotherapy with existing drugs, and also possible synergies to guide new therapeutic combinations towards accelerating TB treatment.

DOI: 10.1016/j.redox.2017.12.020
PMCID: PMC5975079
PMID: 29413958 [Indexed for MEDLINE]

111: Singh AD, Suri TM, Jagdish RK, Kumar U. Unravelling the NERDS syndrome. BMJ Case Rep. 2018 May 12;2018. pii: bcr-2017-223506. doi: 10.1136/bcr-2017-223506. PubMed PMID: 29754136.

A 22-year-old man presented with symmetric polyarthritis, pruritus and deviation of angle of mouth to the right side since the last 7 years. His symptoms were persistent despite receiving ayurvedic medications and symptomatic therapy. Examination revealed dry skin, cutaneous nodules, xanthelasma, periarticular non-tender swellings, pitting oedema of hands and feet and lower motor neuron type right facial palsy. Haematological investigations revealed eosinophilia and skin biopsy had cutaneous eosinophilic infiltration. The constellation of above findings comprises the nodules, eosinophilia, rheumatism, dermatitis and swelling syndrome. It a rare syndrome with few reported cases in literature. The patient was started on oral corticosteroids which was subsequently tapered and methotrexate therapy. His polyarthritis and skin rashes resolved with therapy. He has been followed-up for 2 years and is presently asymptomatic for the last 1 year.

DOI: 10.1136/bcr-2017-223506
PMID: 29754136

Conflict of interest statement: Competing interests: None declared.

112: Singh AK, Kant S, Abdulkader RS, Lohiya A, Silan V, Nongkynrih B, Misra P, Rai SK. Prevalence and correlates of sexual health disorders among adult men in a rural area of North India: An observational study. J Family Med Prim Care. 2018 May-Jun;7(3):515-521. doi: 10.4103/jfmpc.jfmpc_348_17. PubMed PMID: 30112300; PubMed Central PMCID: PMC6069647.

Background and Objectives: Sexual health disorders are an important but less researched public health issue in India. We aimed to estimate the prevalence of sexual health disorders and their associated factors among adult men in a rural community of Haryana, India.
Materials and Methods: A community-based cross-sectional study was conducted among adult men aged 18-60 years using a multistage stratified random sampling. Information pertaining to sociodemographic characteristics, lifestyle and sexual practices, and self-reported sexual problems were collected. Sexual health disorders were defined based on International Statistical Classification of Diseases-10 classification of mental and behavioral disorders. Step-wise logistic regression was carried out to identify factors independently associated with sexual disorders.
Results: At least one sexual health disorder was reported by 81% of the men. The most commonly reported disorder was self-perceived defect in semen (64.4%), followed by loss of libido (21%), masturbation guilt (20.8%), erectile dysfunction (5%), and premature ejaculation (4.6%). Factors significantly associated with sexual health disorders among all men were being never married (odds ratio = 2.04; 95% confidence interval: 1.51, 2.77), smoking (1.57; 1.16, 2.14), cannabis use (4.20; 1.68, 10.48), diabetes (2.40; 1.22, 4.73), and hypertension (3.17; 1.12, 8.92).
Interpretation and Conclusions: A high burden of sexual health disorders was identified among the rural men. Wider recognition of this issue is needed among the health-care providers and policymakers.

DOI: 10.4103/jfmpc.jfmpc_348_17
PMCID: PMC6069647
PMID: 30112300

Conflict of interest statement: There are no conflicts of interest.

113: Singh DV, Reddy RR, Mathur G, Sharma YR. Intravitreal gas injection with prone positioning for giant retinal pigment epithelial tear. Oman J Ophthalmol. 2018 May-Aug;11(2):164-165. doi: 10.4103/ojo.OJO_161_2016. PubMed PMID: 29930453; PubMed Central PMCID: PMC5991055.

We report a 78 year old male with acute RPE tear with sudden vision loss, who underwent intravitreal C3F8 injection for reattaching the RPE. The impact of gas on detached RPE was studied by serial OCTs and Fundus pictures.

DOI: 10.4103/ojo.OJO_161_2016
PMCID: PMC5991055
PMID: 29930453

Conflict of interest statement: There are no conflicts of interest.

114: Singh MK, Pushker N, Meel R, Chodsol K, Sen S, Bakhshi S, Singh L, Kashyap S. Does NEMO/IKKÎ³ protein have a role in determining prognostic significance in uveal melanoma? Clin Transl Oncol. 2018 May 23. doi: 10.1007/s12094-018-1895-3. [Epub ahead of print] PubMed PMID: 29796997.

PURPOSE: Uveal melanoma, although a rare form of cancer, is the most common

primary malignancy of the eye in adults. Nuclear factor-κB (NF-κB) is a transcription factor that transactivates genes involved in the regulation of cell growth, apoptosis, angiogenesis, and metastasis, but the molecular mechanisms that negatively regulate NF-κB activation are not fully understood. NF-κB can also be activated by DNA damage pathway through NEMO protein. Therefore, the objective of this study is to elucidate the role of NEMO/IKKγ protein in uveal melanoma patients.
METHODS: Seventy-five formalin-fixed paraffin-embedded prospective tissues of uveal melanoma were included in the present study. These cases were reviewed and investigated for the expression of NEMO/IKKγ protein by immunohistochemistry and validated by western blotting along with the qRT-PCR for mRNA expression. Expression levels were correlated with the clinicopathological parameters and patients' outcome.
RESULTS: Immunohistochemistry showed cytoplasmic expression of NEMO/IKKγ expression in only 22 out of 75 (29.33%) cases. This result was confirmed by western blotting, and correlated well with the immunohistochemical expression of NEMO/IKKγ protein (48 kDa). In addition, downregulation of this gene was found in 87.93% of the cases when compared with the normal tissues. On statistical analysis, loss of NEMO/IKKγ protein was correlated with neovascularization, high mitotic count, and presence of vascular loop ($p < 0.05$). There was less overall survival rate with low expression of NEMO/IKKγ protein in patients with uveal melanoma.
CONCLUSION: This was the first study suggesting the relevant role of NEMO/IKKγ protein, and highlights the prognostic significance with outcome in uveal melanoma patients. This protein might be used as a screening biomarker in these patients after large-scale validation and translational studies.

DOI: 10.1007/s12094-018-1895-3
PMID: 29796997

115: Singh S, Bhari N, Agrawal S, Verma KK. Rapid response of Kasabach-Meritt phenomenon to a combination of oral prednisolone and sirolimus. Indian J Dermatol Venereol Leprol. 2018 May 23. doi: 10.4103/ijdvl.IJDVL_453_17. [Epub ahead of print] PubMed PMID: 29798936.

116: Singh S, Chouhan RS, Bindra A, Radhakrishna N. Comparison of effect of dexmedetomidine and lidocaine on intracranial and systemic hemodynamic response to chest physiotherapy and tracheal suctioning in patients with severe traumatic brain injury. J Anesth. 2018 Aug;32(4):518-523. doi: 10.1007/s00540-018-2505-9. Epub 2018 May 3. PubMed PMID: 29725828.

PURPOSE: Chest physiotherapy and tracheal suction cause sympathetic stimulation and increase heart rate (HR), mean arterial pressure (MAP) and intracranial pressure (ICP) which may have deleterious effect in the head injured. We planned to compare the effect of intravenous dexmedetomidine and lidocaine on intracerebral and systemic hemodynamic response to chest physiotherapy (CP) and tracheal suctioning (TS) in patients with severe traumatic brain injury (sTBI).
METHODS: Prospective, randomized study in patients with sTBI, 18-60 years of age, undergoing mechanical ventilation and intraparenchymal ICP monitoring. Patients were randomized to receive either iv dexmedetomidine 0.5 mcg/kg (group I; $n = 30$) or iv lidocaine 2 mg/kg (group II; $n = 30$) over 10 min. After infusion of test drug, CP with vibrator and manual compression was performed for 2 min and TS was done over next 15-20 s. The hemodynamic response was recorded before, during and at interval of 1 min for 10 min after CP and TS. A 20% change in hemodynamic parameters was considered significant.
RESULTS: The baseline hemodynamic (HR, MAP), intracranial (ICP, CPP) and respiratory (SPO2, AWPpeak) parameters were normal and comparable in both the

groups. After dexmedetomidine infusion, MAP and CPP decreased significantly from baseline value. In group II, there was no significant change in HR, MAP, ICP and CPP. At end of CP and TS, HR, MAP and CPP in group I was lower as compared to group II. During the 10-min observation period following CP and TS, MAP and CPP in group I remained significantly lower as compared to baseline and group II. There was no significant change in value of other measured parameters.
CONCLUSIONS: Both dexmedetomidine and lidocaine were effective to blunt rise in HR, MAP and ICP in response to CP and TS in patients with sTBI. However, intravenous dexmedetomidine caused significant decrease in MAP and CPP as compared to the baseline and lidocaine.

DOI: 10.1007/s00540-018-2505-9
PMID: 29725828

117: Singhal D, Sahay P, Maharana PK, Amar SP, Titiyal JS, Sharma N. Clinical presentation and management of corneal fistula. Br J Ophthalmol. 2018 May 29. pii: bjophthalmol-2018-312375. doi: 10.1136/bjophthalmol-2018-312375. [Epub ahead of print] PubMed PMID: 29844083.

PURPOSE: To describe the clinical features and management of corneal fistula in patients of healed keratitis.
METHODS: Medical records of all patients of healed keratitis presenting to the cornea clinic from November 2016 to September 2017 were reviewed. Eightcases of corneal fistula (six true fistulas, two closed fistulas) were identified. Six patients were managed with autologous tenon patch graft while two patients were managed medically. Various risk factors and treatment outcomes of corneal fistulisation were evaluated.
RESULTS: The patients included two patients of failed therapeutic keratoplasty (with resolved graft infection) and six patients of healed keratitis. The age of the patients ranged between 10 and 60 years. Five of the patients were male while three were female. The size of the fistula measured between 1 and 2 mm. A surrounding cystic area of diameter ranging between 1 and 4.5 mm was seen in all the patients. In all of the patients, the treating physician missed the diagnosis. Complete healing was noted at 6-8 weeks in all the patients who underwent tenon graft. One patient refused to undergo any surgery and was lost to follow-up. In another case, surgery was deferred due to uncontrolled hypertension and he developed anterior staphyloma subsequently.
CONCLUSION: Corneal fistula can often be missed in an apparently healed perforated corneal ulcer. Tenon patch graft is an effective technique for the management of corneal fistula.

DOI: 10.1136/bjophthalmol-2018-312375
PMID: 29844083

Conflict of interest statement: Competing interests: None declared.

118: Singhal R, Chawla S, Batra H, Gupta S, Ojha A, Rathore DK, Seth T, Guchhait P. Engulfment of Hb-activated platelets differentiates monocytes into pro-inflammatory macrophages in PNH patients. Eur J Immunol. 2018 Aug;48(8):1285-1294. doi: 10.1002/eji.201747449. Epub 2018 May 17. PubMed PMID: 29677388.

The distinct response shown by different phenotypes of macrophages and monocytes under various clinical conditions has put the heterogeneity of these cells into

focus of investigation for several diseases. Recently, we have described that after engulfing hemoglobin (Hb)-activated platelets, classical monocytes differentiated into pro-inflammatory phenotypes, which were abundant in the circulation of paroxysmal nocturnal hemoglobinuria (PNH) and sickle cell disease patients. Our current study shows that upon engulfment of Hb-activated platelets, monocytes differentiate into M1-macrophages under M1-polarization stimulus (GM-CSF, IFN-γ + LPS). When grown under M2-polarization stimulus (M-CSF, IL-4 + IL13), the cells exhibited an M1-like phenotype, secreted elevated levels of pro-inflammatory cytokines including TNF-α and IL-1β, and displayed loss of the secretion of cytokine such as IL-10 and also phagocytic ability unlike the conventional M2 macrophages. Interestingly, when differentiated under the above polarization stimulus, monocytes from PNH patients expressed high levels of CD80 and phospho-STAT1, like M1 macrophages. Hemolytic mice also exhibited a gradual increase in monocyte-platelet aggregates in circulation and accumulation of CD80high macrophages in thioglycollate-induced inflamed peritoneum. The spleen of the mice was also populated by CD80high macrophages with compromised phagocytic capacity. Our findings suggest that the hemolytic environment and specifically the Hb-activated platelets, which are abundant in circulation during intravascular hemolysis, closely regulate monocyte differentiation.

DOI: 10.1002/eji.201747449
PMID: 29677388

119: Sinha A, Bagga A. Screening Urinalysis in Detection of Chronic Kidney Disease in Children. Indian J Pediatr. 2018 Aug;85(8):603-604. doi: 10.1007/s12098-018-2707-z. Epub 2018 May 23. Review. PubMed PMID: 29790006.

120: Sofi R, Qureshi T, Gupta V. Electric cataracts: a cause of bilateral blindness in Kashmir. Eye (Lond). 2018 Oct;32(10):1676-1677. doi: 10.1038/s41433-018-0128-x. Epub 2018 May 23. PubMed PMID: 29795130; PubMed Central PMCID: PMC6189119.

121: Srujana D, Kaur M, Urkude J, Rathi A, Sharma N, Titiyal JS. Long-term Functional and Anatomic Outcomes of Repeat Graft After Optically Failed Therapeutic Keratoplasty. Am J Ophthalmol. 2018 May;189:166-175. doi: 10.1016/j.ajo.2018.03.011. Epub 2018 Mar 14. PubMed PMID: 29550189.

PURPOSE: To evaluate the functional and anatomic outcomes of repeat penetrating keratoplasty (PK) in optically failed therapeutic grafts.
DESIGN: Prospective interventional case series.
METHODS: All cases admitted at the apex tertiary care center for repeat keratoplasty following optically failed therapeutic PK were enrolled over a period of 1 year. Repeat optical PK was performed in all eyes. Primary outcome measures were postoperative graft clarity and visual acuity. Secondary outcome measures were complications including graft rejection, infections, failure, and secondary glaucoma. Follow-up examinations were undertaken on day 1; on day 7; at 1, 3, 6, and 12 months; and yearly thereafter.
RESULTS: Thirty-two eyes underwent repeat PK with mean follow-up of 18.4 ± 8.9 months. Clear grafts were observed in 63.14% of cases 1 year after regraft, and graft survival further decreased to 50% at last follow-up. Visual acuity ≥ 20/200 was achieved in 43.8% of cases, and no case had a visual acuity of ≥ 20/40. Multivariate Cox regression analysis analyzed risk factors for regraft survival, and observed a hazard ratio of 3.56 with size of initial therapeutic graft ≥ 8.75 mm, and 10.99 with deep vascularization in 1 or more quadrants. Graft survival (P = .004), visual acuity (P = .039), and rejection rates (P = .036) were significantly better in cases with initial therapeutic graft size <

8.75 mm. Secondary glaucoma was present in 59.4% (19/32) after regrafts.
CONCLUSION: Regraft after therapeutic PK is associated with suboptimal visual outcomes and long-term graft survival. Large size of initial therapeutic graft and deep vascularization adversely affect graft survival.

DOI: 10.1016/j.ajo.2018.03.011
PMID: 29550189

122: Subhadarshani S, Gupta V, Taneja N, Yadav S, Gupta S. Efficacy and Safety of a Novel Method of Insulated Intralesional Radiofrequency Ablation for Deep Dermal and Subcutaneous Lesions: A 3-Year Institutional Experience. Dermatol Surg. 2018 May;44(5):714-720. doi: 10.1097/DSS.0000000000001437. PubMed PMID: 29701624.

BACKGROUND: Although insulated intralesional radiofrequency ablation (IL-RFA) is being increasingly used in other specialties, not much information on its safety and efficacy in dermatology is available.
OBJECTIVE: To describe our experience with insulated IL-RFA for various dermatological conditions.
METHODS: This is a retrospective review of the patients who underwent IL-RFA in the past 3 years. Our technique involved creating a small window in the proximal end of plastic sheath of an intravenous cannula using a surgical blade, and then touching the RF probe to the cannula through the window to deliver the electric current. Information regarding diagnosis, number of sessions, adverse effects, and follow-up was recorded. Clinical improvement was assessed on a visual analog scale by the patient and 2 independent observers.
RESULTS: Data on 19 patients with lymphangioma circumscriptum (n = 9), venous or capillary-venous malformation (n = 4), angiolymphoid hyperplasia with eosinophilia (n = 3), arteriovenous malformation, hidradenitis suppurativa, and hypertrophic scar (n = 1 each) was available. The mean number of IL-RFA sessions was 2.26 ± 1.61. The mean patient and physician global assessment scores were 7.6 ± 2.22 and 7.3 ± 2.42, respectively. Adverse effects were seen in 9 (47.4%) patients. All patients, except 1, had sustained improvement in the mean follow-up period of 11.4 ± 11.6 months.
CONCLUSION: Insulated IL-RFA seems to be safe and effective in selectively targeting deep-seated cutaneous lesions.

DOI: 10.1097/DSS.0000000000001437
PMID: 29701624 [Indexed for MEDLINE]

123: Takkar B, Khokhar S, Kumar U, Venkatesh P. Necrotising scleritis, keratitis and uveitis in primary antiphospholipid syndrome. BMJ Case Rep. 2018 May 14;2018. pii: bcr-2017-220647. doi: 10.1136/bcr-2017-220647. PubMed PMID: 29764818.

Ocular manifestations of antiphospholipid syndrome typically include thromboembolic and neuro-ophthalmic complications. In this report we present a case of inflammation of the ocular coats in a patient diagnosed with antiphospholipid syndrome 16 years prior. We discuss management of the case and the possible aetiology of the rare association.

DOI: 10.1136/bcr-2017-220647
PMID: 29764818 [Indexed for MEDLINE]

Conflict of interest statement: Competing interests: None declared.

124: Tandon PN, Bhargava B. Founders of Indian Neurosciences: Professor Krishna Prasad Bhargava(5(th) October 1925- 16(th) August 1991). Neurol India. 2018 May-Jun;66(3):610-612. doi: 10.4103/0028-3886.232314. PubMed PMID: 29766910.

125: Tandon V, Lang M, Chandra PS, Sharan A, Garg A, Tripathi M. Is Edema a Matter of Concern After Laser Ablation of Epileptogenic Focus? World Neurosurg. 2018 May;113:366-372.e3. doi: 10.1016/j.wneu.2018.01.201. Epub 2018 Feb 6. PubMed PMID: 29425986.

BACKGROUND: A stereotactically placed laser fiber can deliver thermal energy to an epileptogenic focus in the brain. This procedure is done under intraoperative (thermography) magnetic resonance imaging (MRI) guidance. Thermoablation can lead to edema in the surrounding area and can cause a secondary insult. In this report of 3 cases, we have quantified the edema produced after laser ablation by sequential MRI in the immediate postoperative period.
CASE DESCRIPTIONS: Three patients with intractable epilepsy underwent a detailed neurologic and neuroradiologic workup to localize the site of epileptogenic foci. Two of the patients had mesial temporal lobe sclerosis, and the other patient had hypothalamic hamartoma. A laser fiber was placed stereotactically in the epileptogenic zone, and MRI-guided thermoablation was done. Postoperatively, T1-weighted and fluid-attenuated inversion recovery (FLAIR)-based volumetric MRI sequences were performed on postoperative days 1, 3, and 5 to quantify the edema. I-Plan software was used for volumetric analysis. Targeted volumes were 0.22, 4.2, and 3.5 mL, and lesions were 0.3, 6.5, and 6 mL, respectively. FLAIR hyperintensity was 2.3, 11.8, and 8.4 mL on the first postoperative day and 1.5, 12.6, and 6.3 mL on postoperative day 8. All patients remained seizure-free during the postoperative period. No complications were observed.
CONCLUSIONS: Laser ablation of epileptic focus is safe. FLAIR hyperintensity in the postoperative period is 3-5 times the targeted volume. However, no significant increase occurs during the first 8 days, and thus steroids can be stopped within 5 days of surgery.

DOI: 10.1016/j.wneu.2018.01.201
PMID: 29425986 [Indexed for MEDLINE]

126: Taneja DK, Garg B. Legends of Indian Orthopedics: Prof. B Mukhopadhaya. Indian J Orthop. 2018 May-Jun;52(3):339-340. doi: 10.4103/ortho.IJOrtho_227_18. PubMed PMID: 29887639; PubMed Central PMCID: PMC5961274.

127: Tanwar P, Das P, Barwad A, Shukla N, Ramteke P. Aspirate from an abdominal lump in a known case of breast carcinoma. Cytopathology. 2018 Aug;29(4):394-395. doi: 10.1111/cyt.12546. Epub 2018 May 7. PubMed PMID: 29732667.

128: Tewari R, Kumar V, Ravani R, Dubey D, Chandra P, Kumar A. Macular hole-associated retinal detachment in Best vitelliform dystrophy: Series of two cases and literature review. Indian J Ophthalmol. 2018 May;66(5):708-711. doi: 10.4103/ijo.IJO_1046_17. Review. PubMed PMID: 29676326; PubMed Central PMCID: PMC5939174.

Two eyes of 2 patients with macular hole-associated retinal detachment in clinically diagnosed vitelliruptive stage of Best vitelliform dystrophy were

surgically managed by 25-gauge sutureless pars plana vitrectomy, internal limiting membrane (ILM) peeling with inverted ILM flap, and short-acting (SF6) gas tamponade. The patients were assessed with respect to best-corrected visual acuity, color fundus photographs, shortwave fundus autofluorescence, and swept source optical coherence tomography. Surgical intervention led to Type 1 closure of macular hole, resolution of retinal detachment, and improvement in vision in both patients.

DOI: 10.4103/ijo.IJO_1046_17
PMCID: PMC5939174
PMID: 29676326 [Indexed for MEDLINE]

129: Thelengana A, Radhakrishnan DM, Prasad M, Kumar A, Prasad K. Tenecteplase versus alteplase in acute ischemic stroke: systematic review and meta-analysis. Acta Neurol Belg. 2018 May 4. doi: 10.1007/s13760-018-0933-9. [Epub ahead of print] PubMed PMID: 29728903.

Tenecteplase is a product of genetic modification of recombinant tissue plasminogen activator with superior pharmacodynamic and pharmacokinetic properties. This meta-analysis was to determine whether intravenous thrombolysis with tenecteplase in patients with acute ischemic stroke has better efficacy and safety outcomes than with intravenous alteplase. PubMed, Cochrane Central Register of Controlled Trials, WHO International clinical trials registry platform (ICTRP), Australian New Zealand Clinical Trials Registry (ANZCTR), EU Clinical Trials Register (EU-CTR) and ClinicalTrials.gov were searched for trials comparing tenecteplase with alteplase in acute ischemic stroke. Functional outcomes (modified Rankin Scale at 90 days), early major neurological improvement, rates of any intracerebral haemorrhage, symptomatic intracerebral haemorrhage and mortality rate at 90 days were the outcomes compared. Four randomized controlled trials involving 1334 patients were included. The Tenecteplase group compared to the alteplase group had significantly better early major neurological improvement (RR=1.56, 95% CI [1.00, 2.43], p=0.05). There was no significant difference between tenecteplase and alteplase in excellent functional outcome at 90 days, good functional outcome at 90 days, any intracerebral haemorrhage, symptomatic intracerebral haemorrhage or mortality at 90 days. Our meta-analysis found tenecteplase to be significantly favouring one outcome: early major neurological improvement. Other outcomes did not differ between the tenecteplase and alteplase groups. Trials of cost-effective/benefit analysis comparing tenecteplase versus alteplase and tenecteplase versus endovascular treatment are necessary to reinforce the evidence for the potential cost advantage of tenecteplase.

DOI: 10.1007/s13760-018-0933-9
PMID: 29728903

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131: Togarsimalemath SK, Si-Mohammed A, Puraswani M, Gupta A, Vabret A, Liguori S, Mariani-Kurkdjian P, Bagga A, Dragon-Durey MA. Gastrointestinal pathogens in anti-FH antibody positive and negative Hemolytic Uremic Syndrome. Pediatr Res. 2018 Jul;84(1):118-124. doi: 10.1038/s41390-018-0009-9. Epub 2018 May 23. PubMed PMID: 29795200.

BACKGROUND: Prodromal symptoms are frequently reported in the atypical form of

Hemolytic uremic syndrome (aHUS) suggesting implication of infectious triggers. Some pathogens may also play a role in the mechanisms of production of autoantibody directed against Factor H (FH), a complement regulator, leading to aHUS.
METHODS: The presence of 15 gastrointestinal (GI) pathogens was investigated by using xTAG-based multiplex PCR techniques on stools collected at the acute phase in a cohort of Indian HUS children classified according to the presence or absence of anti-FH autoantibodies.
RESULTS: Prevalence of pathogens in patients with anti-FH antibody (62.5%) was twice that in those without (31.5%). Different pathogens were detected, the most frequent being Clostridium difficile, Giardia intestinalis, Salmonella, Shigella, Rotavirus, Norovirus and Entamoeba histolytica. No stool was positive for Shigatoxin.
CONCLUSION: This study reveals a higher prevalence of GI pathogens in anti-FH positive than in negative patients. No single pathogen was implicated exclusively in one form of HUS. These pathogens may play a role in the disease initiation by inducing complement activation or an autoimmune response.

DOI: 10.1038/s41390-018-0009-9
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Role of mitochondrial DNA variations, particularly in D loop region, remains investigational in acute myeloid leukaemia (AML). Consecutive 151 pediatric AML patients were prospectively enrolled from June 2013 to August 2016, for evaluating pattern of variations in mitochondrial D-loop region and to determine their association, if any, with expression of mitochondrial-encoded genes. For each patient, D-loop region was sequenced on baseline bone marrow, buccal swab and mother's blood sample. Real time PCR was used for relative gene expression of four mitochondrial DNA encoded genes viz.
Nicotinamide-adenine-dineucleotide-dehydrogenase subunit 3 (ND3), Cytochrome-B (Cyt-B), Cytochrome c oxidase-I (COX1) and ATP-synthetase F0 subunit-6 (ATP6). Total 1490 variations were found at 237 positions in D-Loop; 1206 (80.9%) were germline and 284 (19.1%) were somatic. Positions 73-263 were identified as a probable hotspot region. G bases appeared to be most stable nucleotide (least number of single base substitutions) whereas T appeared to be most susceptible to variations with germline T-C being the commonest. Gene expression of Cyt-B was found to be significantly higher for any variation (somatic or germline) at positions 16,192 and 16,327 while it was significantly lower for variations at positions 16,051 and 207. Any variation at positions 152, 207 and 513 significantly decreased COX1 expression while those at positions 16,051 and 152 attenuated ATP6 expression. This first study evaluated type and overall pattern of D-loop variations in AML, and also showed that some of these variations in D loop region might have an effect on the mitochondrial-encoded genes which is new and valuable information in AML genomics.

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PMID: 29883862

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pro-inflammatory cytokines. Chem Biol Interact. 2018 Jun 25;290:6-11. doi: 10.1016/j.cbi.2018.05.003. Epub 2018 May 9. PubMed PMID: 29752894.

Cisplatin has been widely used as a first-line agent against various forms of solid cancers. However, nephrotoxicity is the major limiting factor for its clinical use. Several clinical and pre-clinical studies have suggested different strategies for the reduction of cisplatin-induced nephrotoxicity. The present study was conducted to investigate the efficacy of D-Pinitol, against cisplatin-induced nephrotoxicity in Swiss albino mice. A single intraperitoneal injection of cisplatin (20 mg/kg) was used to induce nephrotoxicity in mice. Administration of cisplatin in mice is linked with elevated oxidative stress, imbalanced biochemical parameters, apoptosis and stimulation of mitogen-activated protein kinase (MAPK) pathway. D-Pinitol is a member of the flavonoid family and a chief constituent of Sutherlandia fruitesecnce. It was administered with saline water (10, 20, 40 mg/kg, p.o.) for seven consecutive days after a single dose of cisplatin. At the end of experiment, animals were sacrificed and biochemical parameters in serum and urine were recorded. Kidneys were isolated for the estimation of tumor necrosis factor-alpha, interleukin-1β, interlukin-6 levels and histopathological evaluations. It was noted that D-Pinitol significantly ameliorated biochemical levels of serum and urinary creatinine and blood urea nitrogen. Tissue homogenate levels of TNF-α, IL-6, IL-1β and the renal expression of tissue nitrites were also significantly decreased in D-Pinitol treated mice. These results were supplemented by histopathological findings. This study highlights the potential role of D-Pinitol against cisplatin-induced toxicity, exhibited through favorable alterations in biochemical and histological changes as well as reduction in oxidative stress and cytokine levels.

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In spite of significant advancement in hydrogel technology, low mechanical strength and lack of electrical conductivity have limited their next-level biomedical applications for skeletal muscles, cardiac and neural cells. Host-guest chemistry based hybrid nanocomposites systems have gained attention as they completely overcome these pitfalls and generate bioscaffolds with tunable electrical and mechanical characteristics. In recent years, carbon nanotube (CNT)-based hybrid hydrogels have emerged as innovative candidates with diverse applications in regenerative medicines, tissue engineering, drug delivery devices, implantable devices, biosensing, and biorobotics. This article is an attempt to recapitulate the advancement in synthesis and characterization of hybrid hydrogels and provide deep insights toward their functioning and success as biomedical devices. The improved comparative performance and biocompatibility of CNT-hydrogels hybrids systems developed for targeted biomedical applications are addressed here. Recent updates toward diverse applications and limitations of CNT hybrid hydrogels is the strength of the review. This will provide a holistic approach toward understanding of CNT-based hydrogels and their applications in nanotheranostics.

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PMID: 29388356

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Hydrogel-based drug delivery systems (DDSs) have versatile applications such, as tissue engineering, scaffolds, drug delivery, and regenerative medicines. The drawback of higher size and poor stability in such DDSs are being addressed by developing nano-sized hydrogel particles, known as nanogels, to achieve the desired biocompatibility and encapsulation efficiency for better efficacy than conventional bulk hydrogels. In this review, we describe advances in the development of nanogels and their promotion as nanocarriers to deliver therapeutic agents to the central nervous system (CNS). We also discuss the challenges, possible solutions, and future prospects for the use of nanogel-based DDSs for CNS therapies.

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BACKGROUND: Chronic pancreatitis (CP) is a progressive inflammatory disorder currently diagnosed by morphologic features. In contrast, an accurate diagnosis of Early CP is not possible using imaging criteria alone. If this were possible and early treatment instituted, the later, irreversible features and complications of CP could possibly be prevented.
METHOD: An international working group supported by four major pancreas societies (IAP, APA, JPS, and EPC) and a PancreasFest working group sought to develop a consensus definition and diagnostic criteria for Early CP. Ten statements (S1-10) concerning Early CP were used to gauge consensus on the Early CP concept using anonymous voting with a 9 point Likert scale. Consensus required an alpha ≥0.80.
RESULTS: No consensus statement could be developed for a definition of Early-CP or diagnostic criteria. There was consensus on 5 statements: (S2) The word "Early" in early chronic pancreatitis is used to describe disease state, not disease duration. (S4) Early CP defines a stage of CP with preserved pancreatic function and potentially reversible features. (S8) Genetic variants are important risk factors for Early CP and can add specificity to the likely etiology, but they are neither necessary nor sufficient to make a diagnosis. (S9) Environmental risk factors can provide evidence to support the diagnosis of Early CP, but are neither necessary nor sufficient to make a diagnosis. (S10) The differential

diagnosis for Early CP includes other disorders with morphological and functional features that overlap with CP.
CONCLUSIONS: Morphology based diagnosis of Early CP is not possible without additional information. New approaches to the accurate diagnosis of Early CP will require a mechanistic definition that considers risk factors, biomarkers, clinical context and new models of disease. Such a definition will require prospective validation.

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INTRODUCTION: This study sought to determine the prevalence and predictors of peripheral neuropathy in nondiabetic children with chronic kidney disease (CKD).
METHODS: Fifty-one consecutive normally nourished children, 3-18 years of age, with CKD stages IV and V of nondiabetic etiology were enrolled from May to December 2012. Nerve conduction studies were performed in 50 children. Blood samples were analyzed for the biochemical parameters, trace elements, and micronutrients.
RESULTS: The prevalence of peripheral neuropathy in our cohort was 52% (95% confidence interval 37.65, 66.34). The majority (80.8%) of the children had axonal neuropathy, and 11.5% had demyelinating neuropathy. Isolated motor neuropathy was identified in 92.3% of the children, and sensorimotor neuropathy was identified in 7.6%. The significant risk factors associated with peripheral neuropathy were older age, low serum copper, and dialysis therapy.
DISCUSSION: Electrodiagnostic studies should be performed in children with CKD to assess for peripheral neuropathy for the purpose of optimizing medical care. Muscle Nerve 57: 792-798, 2018.

DOI: 10.1002/mus.26027
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