List of publications of AIIMS, New Delhi for the month of March, 2019 [Source: www.pubmed.com].

1: Agarwal A, Goswami A, Vijayaraghavan GP, Srivastava A, Kandwal P, Nagaraja UB, Goel VK, Agarwal AK, Jayaswal A. Quantitative Characteristics of Consecutive Lengthening Episodes in Early-onset Scoliosis (EOS) Patients With Dual Growth Rods. Spine (Phila Pa 1976). 2019 Mar 15;44(6):397-403. doi: 10.1097/BRS.0000000000002835. PubMed PMID: 30095792.

STUDY DESIGN: A prospective single-center study.
OBJECTIVE: The aim of this study was to record the characteristic forces and lengths observed during distraction episodes in early-onset scoliosis (EOS), and analyze their interdependencies on the key variability among the patients.
SUMMARY OF BACKGROUND DATA: The goal of the growing-rod technique is to achieve deformity correction alongside maintaining growth of the spine. The deformity correction is achieved during the initial surgery, but follow-up distraction episodes are necessary to maintain the growth. The key variables, under the control of a surgeon, that affect the growth are the applied distraction forces and the distraction lengths. Since the advent of dual growth rod technique, there have been many studies exploring the relationship between these and the actual growth. However, there is sparse evidence on the actual magnitude of distraction forces, and none on its association with patient's parameters such as sex, age, and deformity.
METHODS: In a consecutive series of 47 patients implanted with dual growth rods, the distraction forces (in N) and the lengths (in mm) achieved during each distraction episode and compared against the episode-specific demographics. The values obtained from each side, that is, concave and convex sides, were averaged to calculate the mean. Statistical analysis was performed using t-distribution because for each normalized time points (distraction episode).
RESULTS: In cumulative, the distraction force increased by an amount of 268%, with 120% increase in the early stages (distractions episodes 1-6) and 68% increase in the later stages (distractions episodes 6-11), whereas the cumulative decrease in the length over 11 distractions episodes was 47%, with 34% and 20% in the early and later stages, respectively. The study does not identify any significant trend with respect to sex, age, and deformity.
CONCLUSION: The distraction force and the length increased and decreased respectively with every consecutive distraction episode, with no correlation to sex, age, extent of deformity, or the extent of correction.
LEVEL OF EVIDENCE: 5.

DOI: 10.1097/BRS.0000000000002835
PMID: 30095792

2: Agarwal P, Roy S, Azad SV, Kumar V. Juxtapapillary Focal Choroidal Excavation. Indian J Ophthalmol. 2019 Mar;67(3):400-401. doi: 10.4103/ijo.IJO_1299_18. PubMed PMID: 30777965; PubMed Central PMCID: PMC6407401.

3: Agarwal R, Maharana PK, Titiyal JS, Sharma N. Bilateral herpes simplex keratitis: lactation a trigger for recurrence! BMJ Case Rep. 2019 Mar 9;12(3). pii: e223713. doi: 10.1136/bcr-2017-223713. PubMed PMID: 30852508.

A young lactating woman presenting to us with simultaneous bilateral corneal lesions was clinically diagnosed to have herpes simplex keratitis, which was confirmed by herpes simplex virus (HSV) PCR. The patient was administered topical and systemic acyclovir therapy and therapeutic penetrating keratoplasty was done in right eye. She was advised to continue breast feeding under strict hygienic conditions. Diagnosis and management of HSV keratitis in a lactating patient can be particularly challenging for both clinician and patient and adoption of a multidisciplinary approach is necessary to ensure safety of mother and child. At 3 months follow-up, the baby was clinically healthy, there were no side effects of acyclovir therapy in the mother or the baby and the patient showed no evidence of recurrence in either eye.

DOI: 10.1136/bcr-2017-223713
PMID: 30852508 [Indexed for MEDLINE]

4: Agarwal S, Bychkov A, Jung CK, Hirokawa M, Lai CR, Hong S, Kwon HJ, Rangdaeng S, Liu Z, Su P, Kakudo K, Jain D. The prevalence and surgical outcomes of HÃ¼rthle cell lesions in FNAs of the thyroid: A multi-institutional study in 6 Asian countries. Cancer Cytopathol. 2019 Mar;127(3):181-191. doi: 10.1002/cncy.22101. Epub 2019 Jan 22. PubMed PMID: 30668897.

BACKGROUND: Hürthle cell-rich nodules (HCNs) encompass non-neoplastic to malignant lesions. There is paucity of literature on the frequency distribution of HCNs among Bethesda categories, histologic follow-up, risk of malignancy (ROM), and risk of neoplasia (RON). The objective of this retrospective, multi-institutional study was to determine the prevalence of the cytologic diagnostic category and surgical outcomes of patients with HCN.
METHODS: Nine tertiary health centers representing 6 Asian countries participated. Cases were retrieved from respective databases. The Bethesda System for Reporting Thyroid Cytopathology was used. Cytology results were correlated with surgical diagnoses.
RESULTS: Of 42,190 thyroid aspirates retrieved, 760 (1.8%) had a Hürthle cell predominance. Most (61%) were categorized as atypia of undetermined significance/follicular lesion of undetermined significance, Hürthle cell type" (AUS-H); 35% were categorized as follicular neoplasm, Hürthle cell type (FN-H); and 4% were categorized as suspicious for malignancy (SFM). Histologic follow-up was available for 288 aspirates (38%). Most were benign on resection (66%), and the most common histologic diagnosis was Hürthle cell adenoma (28.5%). The ROM for AUS-H, FN-H, and SFM, as calculated on resected nodules, was 32%, 31%, and 71%, respectively; and the RON was 47%, 81%, and 77%, respectively. The 5 institutions that had an AUS-H:HCN ratio below 0.5 diagnosed HCN less frequently as AUS-H than as FN-H.
CONCLUSIONS: This is the largest, contemporary, multi-institutional series of HCNs with surgical follow-up. Although there was wide interinstitutional variation in prevalence and surgical outcomes, there was no significant difference in the ROM among institutions. The categories AUS-H and FN-H had a similar ROM for resected nodules.

DOI: 10.1002/cncy.22101
PMID: 30668897

5: Aggarwal R, Banerjee A, Soni KD, Kumar A, Trikha A. Clinical characteristics and management of patients with fat embolism syndrome in level I Apex Trauma Centre. Chin J Traumatol. 2019 Jun;22(3):172-176. doi: 10.1016/j.cjtee.2019.01.007. Epub 2019 Mar 14. PubMed PMID: 31047796; PubMed Central PMCID: PMC6543189.

PURPOSE: Fat embolism syndrome (FES) is systemic manifestation of fat emboli in the circulation seen mostly after long bone fractures. FES is considered a lethal complication of trauma. There are various case reports and series describing FES. Here we describe the clinical characteristics, management in ICU and outcome of these patients in level I trauma center in a span of 6 months.
METHODS: In this prospective study, analysis of all the patients with FES admitted in our polytrauma intensive care unit (ICU) of level I trauma center over a period of 6 months (from August 2017 to January 2018) was done. Demographic data, clinical features, management in ICU and outcome were analyzed.
RESULTS: We admitted 10 cases of FES. The mean age of patients was 31.2 years. The mean duration from time of injury to onset of symptoms was 56 h. All patients presented with hypoxemia and petechiae but central nervous system symptoms were present in 70% of patients. The mean duration of mechanical ventilation was 11.7 days and the mean length of ICU stay was 14.7 days. There was excellent recovery among patients with no neurological deficit.
CONCLUSION: FES is considered a lethal complication of trauma but timely management can result in favorable outcome. FES can occur even after fixation of

the fracture. Hypoxia is the most common and earliest feature of FES followed by CNS manifestations. Any patient presenting with such symptoms should raise the suspicion of FES and mandate early ICU referral.

DOI: 10.1016/j.cjtee.2019.01.007
PMCID: PMC6543189
PMID: 31047796

6: Aggarwal S, John S, Sapra L, Sharma SC, Das SN. Targeted disruption of PI3K/Akt/mTOR signaling pathway, via PI3K inhibitors, promotes growth inhibitory effects in oral cancer cells. Cancer Chemother Pharmacol. 2019 Mar;83(3):451-461. doi: 10.1007/s00280-018-3746-x. Epub 2018 Dec 5. PubMed PMID: 30519710.

PURPOSE: The phosphoinositide-3-kinase (PI3K) pathway is the frequently altered in human cancer. This has led to the development and study of novel PI3K inhibitors for targeted therapy and also to overcome resistance to radiotherapy.
METHOD: The anti-tumour effects of PI3K inhibitors (PI-828, PI-103 and PX-866) in terms of cell proliferation, colony formation, induction of apoptosis, cell cycle arrest, invasion, autophagy, and pNF-κB/p65 translocation in SCC-4, SCC-9 and SCC-25 cells were studied by performing MTT, clonogenic, DAPI staining, propidium iodide staining, annexin-V binding, matrigel invasion, acridine orange staining and immuno-fluorescence assay. Western blot assay was performed to assess the alteration in the expression of various proteins.
RESULT: PI-828 and PI-103 treatment exhibited dose-dependent inhibition of growth and proliferation of OSCC cells with a concomitant induction of apoptosis, altered cell cycle regulation and decreased invasiveness ($p < 0.01$). PX-866 induced apoptosis, cell cycle arrest, autophagy and a significant decrease in the invasiveness of oral cancer cells as compared to untreated cells ($p < 0.01$). These compounds significantly reduced expression of COX-2, cyclin-D1 and VEGF in the treated cells besides cytoplasmic accumulation of pNF-κB/p65 protein. In addition to PI3Kα, inactivation of downstream components, i.e. Akt and mTOR was seen.
CONCLUSION: PI3K inhibitors such as PI-103, PI-828 and PX-866 may be developed as potential therapeutic agents for effective treatment of oral squamous cell carcinoma (OSCC) patients, associated with activated PI3K/Akt pathway.

DOI: 10.1007/s00280-018-3746-x
PMID: 30519710

7: Ahmad F, Kannan M, Obser T, Budde U, Schneppenheim S, Saxena R, Schneppenheim R. Characterization of VWF gene conversions causing von Willebrand disease. Br J Haematol. 2019 Mar;184(5):817-825. doi: 10.1111/bjh.15709. Epub 2018 Nov 29. PubMed PMID: 30488424.

We previously reported that von Willebrand Factor gene (VWF) conversions are a relatively frequent cause of von Willebrand disease (VWD), however, their molecular pathomechanisms resulting in variant phenotypes is largely unknown. Here, we characterized VWF conversions harbouring missense and synonymous mutations, through generating a series of mutant constructs followed by transient expression in 293 cells, and qualitative and quantitative analysis of recombinant VWF (rVWF). The characterization of mutant rVWF showed the critical roles of synonymous variants in the pathogenicity of VWF conversions. The gene conversion variants p.Val1229Gly, p.Asn1231Thr, p.Asn1231Ser and p.Ala1464Pro in the absence of synonymous p.Ser1263= and p.Gln1449= showed minimal effect on rVWF synthesis and activity. Interestingly, a construct including the synonymous variants displayed significantly low rVWF expression and activity. The variant p.Pro1266Leu showed gain of rVWF function toward glycoprotein Ibα; surprisingly, this function was significantly abolished in the presence of gene conversion variants p.Val1229Gly-p.Asn1231Thr. Taken together, our expression studies suggest that synonymous variants in the combination of other gene conversion variants suppress the protein expression, possibly due to defective primary mRNA

structure or processing. The variants p.Val1229Gly-p.Asn1231Thr affected the VWF gain of function caused by variant p.Pro1266Leu, probably due to conformational changes in VWF.

DOI: 10.1111/bjh.15709
PMID: 30488424

8: Albert V, Arulselvi S, Agrawal D, Pati HP, Pandey RM. Early posttraumatic changes in coagulation and fibrinolysis systems in isolated severe traumatic brain injury patients and its influence on immediate outcome. Hematol Oncol Stem Cell Ther. 2019 Mar;12(1):32-43. doi: 10.1016/j.hemonc.2018.09.005. Epub 2018 Sep 27. PubMed PMID: 30291825.

OBJECTIVE/BACKGROUND: Early coagulopathy in isolated severe traumatic brain injury occurs despite the lack of severe bleeding, shock, and fluid administration. We aimed to correlate coagulation activation/inhibition, thrombin generation and fibrinolysis with the development of acute trauma induced coagulopathy (TIC) and its effects on early mortality in isolated severe traumatic brain injury (iSTBI) patients.
METHODS: A prospective screening of iSTBI patients was done for two years. History of anticoagulants, liver disease, hypotension, extracranial injuries, transfusion, brain death were excluded. TIC was defined as international normalized ratio (INR) ≥ 1.27 and/or prothrombin time (PT) ≥ 16.7 seconds and/or activated partial thromboplastin Time (aPTT) ≥ 28.8 seconds on admission following iSTBI. Analysis of tissue factor (TF), tissue factor pathway inhibitor (TFPI), protein C (PC), protein S (PS), thrombin/antithrombin complex (TAT), soluble fibrin monomer (sFM), tissue plasminogen activator (tPA) and plasminogen activator inhibitor-1 (PAI-1) was done. Cases were categorized as presence or absence of TIC and 20 healthy controls participants were included.
RESULTS: A total of 120 cases met the inclusion criteria, aged 35.7 ± 12.12 years, 96% males. TIC was identified in 50 (41.6%). TIC occurred independently of age, sex, Glasgow coma scale (GCS) but was associated with acidosis (60%; p = .01). Following iSTBI significant decline was seen in coagulation activation. Thrombin generation and fibrinolysis were markedly increased. TF, TFPI, PC and PS were low in TIC compared with control. Significant depletion of PS was seen in TIC versus No-TIC. TBI patients with depleted PS had an odds ratio (OR) of 7.10 (1.61-31.2) for TIC. Receiver operating characteristic curve (ROC) analysis depicted area under the curve (AUC) of 0.73 (95% confidence interval [CI] 0.63-0.84) with a cut-off of ≥74 of PS (specificity 63.9%, sensitivity 72.7%). In-hospital mortality was higher in TIC group (44%) compared with no-TIC (20%) with OR of 4.73 (95% CI 1.68-13.3) and hazard ratio [HR] of 2.8 (95 % CI 1.2-6.4).
CONCLUSION: Incidence of TIC in iSTBI is 41.6%, with 4.7 times odds for mortality. Traumatic brain injury causes enhanced coagulation activation, inadequate inhibition, exacerbation of thrombin generation, and subsequent increased fibrinolysis. ROC curve analysis revealed a cut-off of PS ≤ 74 with specificity 63.8%, sensitivity 72.7% for development of TIC.

DOI: 10.1016/j.hemonc.2018.09.005
PMID: 30291825 [Indexed for MEDLINE]

9: Ali Beg MM, Fahdil SR, Yadav P, Shukla KK, Mohan A, Saxena A. Association of EGFR 1 Gene Alteration and their Association with Lung Adenocarcinoma Patients. Asian Pac J Cancer Prev. 2019 Mar 26;20(3):825-830. PubMed PMID: 30912007.

Background: The epidermal growth factor receptor 1 (EGFR1) plays a significant role in cell proliferation and development. Its regulation in humans is very critical and incompletely understood in Non small cell lung cancer (NSCLC).

Methods: 100 newly diagnosed NSCLC (lung adenocarcinoma) patients and 100 healthy controls were included and allele specific (AS) polymerase chain reaction (PCR) was used to genotype and expression was analyzed by quantitative real time PCR. Overall survival of patients was analyzed by Kaplan-Meier method and for prognostic significance ROC curve was plotted. Results: A statistically significant difference (p<0.0001) in CC, AA and CA genotypes distribution among patients and healthy controls was observed. Compared to the CC genotype as reference, OR was 30.40 (95%CI 1.75- 524.9, p=0.0002) and 3.97 (95%CI 1.49-10.52, p=0.003) for the homozygous AA and heterozygous CA genotypes respectively. Kaplan-Meier survival analysis was also performed to analyze the relationship of EGFR1 (-191C/A) genotypes with progression free median survival of NSCLC patients and the difference was found to be significantly (p=0.0002) associated with different genotypes. In the ROC curve with respect to TNM stage at optimal cut-off value of 9.88 fold increase in EGFR1 mRNA expression, sensitivity and specificity were 92.9%, 83.3% respectively (AUC=0.95, p<0.0001). ROC curve w.r.t. distant metastases at optimal cut-off value of 13.5 fold change EGFR1 mRNA expression, sensitivity and specificity were 68.2%, 71.4% respectively (AUC=0.81, p<0.0001). In ROC curve w.r.t to presence/ absence of pleural effusion at optimal cut-off value of 14.8 fold change EGFR1 mRNA expression sensitivity and specificity were 66.7%, 68.2% respectively (AUC=0.71, p=0.009). Conclusions: Study concluded EGFR1 promoter polymorphism could be a risk factor associated with disease and may be used as prognostic marker for patients' survival and predictor for disease worseness.

DOI: 10.31557/APJCP.2019.20.3.825
PMID: 30912007

10: Ambekar A, Mishra A, Parmar A, Kumar R, Kumar M, Rao R, Agrawal A. Are non-injecting opioid users at risk of transition to injecting drug use? A multi-site study from India. Asian J Psychiatr. 2019 Apr;42:79-84. doi: 10.1016/j.ajp.2019.03.017. Epub 2019 Mar 26. PubMed PMID: 30978557.

BACKGROUND: Most people who inject drugs (PWID) start their drug use careers by using non-injecting opioid drugs. A variety of interconnected factors may influence the risk of transition from non-injecting to injecting drug use (IDU). However, such factors have not been studied well in India. As almost all non-injecting opioid users (NIOU) are at potential risk of switching to IDU in future, it is important to understand the phenomenon of transition.
METHOD: In this multi-site, cross-sectional observational study, we compared injecting and non-injecting opioid users on the pattern of progression of drug use and their knowledge, attitude and belief about IDU/HIV. Data were collected from people who use drugs coming in contact with Non-Governmental Organizations providing drug treatment or HIV prevention services, in ten cities of six states located in North/North-West India. Following informed consent, a total of 1987 male participants (n = 1234 PWID and n = 753 NIOU) were interviewed using a semi-structured questionnaire. Factors associated with risk of transition were analyzed using logistic regression analysis.
RESULT: The age of onset of heroin and other opiates as well as other substances was not different between two groups. Among PWID, a majority (n = 713; 57.77%) reported using opioids through non-injecting route before switching to injecting route. The mean duration between first use of non-injecting opioid and first use of injecting opioid was 1.80 ± 3.32 years (range 0-26 years). Awareness and exposure to the act of injecting were amongst factors associated with perceived risk of transition to injecting (p < 0.01). On a univariate logistic regression analysis, less education was associated with increased likelihood while being employed was associated with less likelihood of being offered injection (p < 0.001).
CONCLUSION: Though, NIOU are almost indistinguishable from PWID in many respects, there may be certain factors putting them at risk of transition to injecting route. As the majority of PWID start their injecting career by non-injecting route, interventions targeted atrisk NIOU (as suggested by our study) could

interrupt the HIV transmission.

DOI: 10.1016/j.ajp.2019.03.017
PMID: 30978557

11: Ambrosy AP, Stevens SR, Al-Khalidi HR, Rouleau JL, Bouabdallaoui N, Carson PE, Adlbrecht C, Cleland JGF, Dabrowski R, Golba KS, Pina IL, Sueta CA, Roy A, Sopko G, Bonow RO, Velazquez EJ; STICH Trial Investigators. Burden of medical co-morbidities and benefit from surgical revascularization in patients with ischaemic cardiomyopathy. Eur J Heart Fail. 2019 Mar;21(3):373-381. doi: 10.1002/ejhf.1404. Epub 2019 Jan 30. PubMed PMID: 30698316.

AIMS: The landmark STICH trial found that surgical revascularization compared to medical therapy alone improved survival in patients with heart failure (HF) of ischaemic aetiology and an ejection fraction (EF) ≤35%. However, the interaction between the burden of medical co-morbidities and the benefit from surgical revascularization has not been previously described in patients with ischaemic cardiomyopathy.
METHODS AND RESULTS: The STICH trial (ClinicalTrials.gov Identifier: NCT00023595) enrolled patients ≥18 years of age with coronary artery disease amenable to coronary artery bypass grafting (CABG) and an EF ≤35%. Eligible participants were randomly assigned 1:1 to receive medical therapy (MED) (n=602) or MED/CABG (n=610). A modified Charlson co-morbidity index (CCI) based on the availability of data and study definitions was calculated by summing the weighted points for all co-morbid conditions. Patients were divided into mild/moderate (CCI 1-4) and severe (CCI ≥5) co-morbidity. Cox proportional hazards models were used to evaluate the association between CCI and outcomes and the interaction between severity of co-morbidity and treatment effect. The study population included 349 patients (29%) with a mild/moderate CCI score and 863 patients (71%) with a severe CCI score. Patients with a severe CCI score had greater functional limitations based on 6-min walk test and impairments in health-related quality of life as assessed by the Kansas City Cardiomyopathy Questionnaire. A total of 161 patients (Kaplan-Meier rate=50%) with a mild/moderate CCI score and 579 patients (Kaplan-Meier rate=69%) with a severe CCI score died over a median follow-up of 9.8 years. After adjusting for baseline confounders, patients with a severe CCI score were at higher risk for all-cause mortality (hazard ratio 1.44, 95% confidence interval 1.19-1.74; P<0.001). There was no interaction between CCI score and treatment effect on survival (P=0.756).
CONCLUSIONS: More than 70% of patients had a severe burden of medical co-morbidities at baseline, which was independently associated with increased risk of death. There was not a differential benefit of surgical revascularization with respect to survival based on severity of co-morbidity.

DOI: 10.1002/ejhf.1404
PMID: 30698316

12: Angmo D, Selvan H, Behera AK, Suman PK. Response to comment on 'Unilateral corneal edema in young: A diagnostic dilemma'. Indian J Ophthalmol. 2019 Mar;67(3):442-443. doi: 10.4103/ijo.IJO_2079_18. PubMed PMID: 30777985; PubMed Central PMCID: PMC6407402.

13: Aparna P, Salve HR, Anand K, Ramakrishnan L, Gupta SK, Nongkynrih B. Knowledge and behaviors related to dietary salt and sources of dietary sodium in north India. J Family Med Prim Care. 2019 Mar;8(3):846-852. doi: 10.4103/jfmpc.jfmpc_49_19. PubMed PMID: 31041212; PubMed Central PMCID: PMC6482771.

Sodium, an element needed for the normal human physiology is known to be associated with high blood pressure and other consequences if consumed in excess. The assessment of knowledge and behavior related to sodium that is consumed in the form of salt plays an important role in the control of cardiovascular diseases. To control the intake of sodium, dietary sources of sodium need to be identified. To address this, a community-based cross-sectional study was conducted among women aged 20 to 59 years in north India, where knowledge, attitude, and behavior questionnaire given by the World Health Organization and 24-h dietary recall were used. The mean age of the participants was 34.5 years, and the majority of them were homemakers. Approximately, 80% of the participants believed that high salt diet causes serious health problems, and only 5% of the participants were aware of the existence of a recommendation for daily salt intake. Less than 20% of the participants took measures to control their salt intake. Vegetable-based dishes were found to be the major contributors to the daily salt intake followed by pulse-based and cereal-based dishes. This is because of the high quantity in which they are consumed. Food cooked at home contributed to 90% of the daily salt intake. To control the salt intake, we should cut- down the discretionary salt use. Dietary advice should be customized to the individual, and the family physician plays an important role in this. Behavioral change is the need of the hour to control the epidemic of non-communicable diseases.

DOI: 10.4103/jfmpc.jfmpc_49_19
PMCID: PMC6482771
PMID: 31041212

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

14: Arora P, Jadaun SS, Das P, Shalimar, Datta SK. Unusually Low Serum Alkaline Phosphatase Activity in a Patient with Acute on Chronic Liver Failure and Hemolysis. EJIFCC. 2019 Mar 1;30(1):99-105. eCollection 2019 Mar. PubMed PMID: 30881280; PubMed Central PMCID: PMC6416816.

A 28-year-old male with acute on chronic liver failure (ACLF) and hepatic encephalopathy had deranged liver function with curiously low level (0-15 IU/L) of serum alkaline phosphatase (ALP). Peripheral smear examination suggested hemolytic anemia. The finding of persistent low ALP, after ruling out pre-analytical causes, in ACLF has been reported in Wilson's disease (WD) with/ without autoimmune hemolytic anemia (AIHA). Definitive evidences of WD were not seen in our case. Positive DCT and histological features suggest a diagnosis of autoimmune hepatitis with secondary hemochromatosis and cholangitis. Low ALP might not always be a determinant of bile duct pathology in patients of ACLF with AIHA.

PMCID: PMC6416816
PMID: 30881280

15: Bade G, Chandran DS, Kumar Jaryal A, Talwar A, Deepak KK. Contribution of systemic vascular reactivity to variability in pulse volume amplitude response during reactive hyperemia. Eur J Appl Physiol. 2019 Mar;119(3):753-760. doi: 10.1007/s00421-018-04066-6. Epub 2019 Jan 14. PubMed PMID: 30637458.

PURPOSE: The aim of the present study was to investigate why the magnitude of reactive hyperemia (RH) observed by pulse volume amplitude (PVA) after arm occlusion differs greatly among study subjects.
METHODS: Healthy subjects (n = 12) in the age range of 22-30 years participated in this study. Vascular reactivity was assessed by measuring the changes in finger PVA simultaneously in the test (occluded arm) and control arm (contralateral non-occluded arm) using two separate Photoplethysmographic sensors. Short-term HRV was computed from simultaneously acquired lead II ECG signal to monitor the changes in cardiac sympathetic nervous activity.
RESULTS: The observed coefficient of variation for inter-subject variability in PVA response in test arm during second minute of RH was 115.3%. In the control arm, significantly reduced PVA was observed during the period of occlusion as

well as RH. This observation was corroborated by simultaneously acquired short-term HRV which showed a significant rise in total power (p value < 0.005) and low-frequency (LF) power (p value < 0.05) during release of occlusion when compared to the baseline. A significant positive correlation (Spearman r = 0.33; p = 0.02) was observed between % change in PVA in the control arm and in the test arm for first 3 min of RH.
CONCLUSIONS: Sympathetic activation possibly plays an important role in mediating the inter-subject variability of vascular responses during reactive hyperemia which warrants simultaneous recording of both the test and the control arm responses during RH to accurately assess endothelial function.

DOI: 10.1007/s00421-018-04066-6
PMID: 30637458 [Indexed for MEDLINE]

16: Bagchi S, Lingaiah R, Mani K, Barwad A, Singh G, Balooni V, Bhowmik D, Agarwal SK. Significance of serum galactose deficient IgA1 as a potential biomarker for IgA nephropathy: A case control study. PLoS One. 2019 Mar 27;14(3):e0214256. doi: 10.1371/journal.pone.0214256. eCollection 2019. PubMed PMID: 30917188; PubMed Central PMCID: PMC6436754.

BACKGROUND: IgA nephropathy(IgAN) is a common glomerular disease with a higher risk of progression to end stage renal disease (ESRD) in certain ethnic populations. Since galactose deficient IgA1(Gd-IgA1) is a critical molecule in its pathogenesis, it has generated interest as a biomarker for this disease.
METHODS: We measured serum Gd-IgA1 levels using a non- lectin based enzyme linked immunoassay(ELISA) in 136 immunosuppression naïve patients with primary IgAN and 110 controls(60-non IgA glomerular diseases, 50-healthy volunteers).
RESULTS: Median serum Gd-IgA1 levels were significantly higher in IgAN patients [13135.6(2723.3,59603.8)ng/ml] compared to those with non IgA glomerular disease [4954.8(892.9,18256.2) ng/ml] and healthy controls [6299.5(1993.2,19256) ng/ml] and this was observed even after log transformation and adjustment for age and gender(p<0.0001). Considering a cut-off value of serum Gd-IGA1≥7982.1ng/ml, the sensitivity for diagnosing IgAN compared to healthy controls was 74.3% and specificity was 72.0% with a positive predictive value of 87.8% and negative predictive value of 50.7%. The serum Gd-IgA1 level did not co-relate with baseline estimated glomerular filtration rate, urine protein creatinine ratio and the M, E, S, T and C scores on renal biopsy. The renal survival (absence of >30% decrease in eGFR, ESRD or death) was lower in patients with higher serum Gd-IgA1 levels(≥7982ng/ml) than those who had lower levels but it was not statistically significant(p = 0.486).
CONCLUSION: Serum Gd-IgA1 level is higher in IgAN patients compared to non-IgA glomerular diseases and healthy controls and has a good positive predictive value for diagnosis. However, it does not correlate with clinical and histological characteristics of disease severity and does not predict disease progression.

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PMCID: PMC6436754
PMID: 30917188

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

17: Bain SC, Mosenzon O, Arechavaleta R, BogdaÅ„ski P, Comlekci A, Consoli A, Deerochanawong C, Dungan K, Faingold MC, Farkouh ME, Franco DR, Gram J, Guja C, Joshi P, Malek R, Merino-Torres JF, Nauck MA, Pedersen SD, Sheu WH, Silver RJ, Tack CJ, Tandon N, Jeppesen OK, Strange M, Thomsen M, Husain M. Cardiovascular safety of oral semaglutide in patients with type 2 diabetes: Rationale, design and patient baseline characteristics for the PIONEER 6 trial. Diabetes Obes Metab. 2019 Mar;21(3):499-508. doi: 10.1111/dom.13553. Epub 2018 Nov 11. PubMed PMID: 30284349; PubMed Central PMCID: PMC6587508.

AIMS: To assess the cardiovascular (CV) safety of oral semaglutide, the first tablet formulation of a glucagon-like peptide-1 receptor agonist.
MATERIALS AND METHODS: PIONEER 6 is a multinational, randomized, placebo-controlled, double-blind trial in patients with type 2 diabetes at high risk of CV events (defined as being aged ≥50 years and having established CV disease [CVD] or moderate [stage 3] chronic kidney disease [CKD], or being aged ≥60 years with ≥1 other CV risk factor). Patients were randomized to once-daily oral semaglutide (up to 14 mg) or placebo added to standard of care. The primary composite endpoint is time to first occurrence of CV death or non-fatal myocardial infarction or non-fatal stroke. The primary hypothesis was to exclude an excess in CV risk with oral semaglutide by assessing non-inferiority versus placebo for the primary endpoint (non-inferiority margin of 1.8 for the upper boundary of the 95% confidence interval of the hazard ratio). PIONEER 6 is event-driven, with follow-up continuing until accrual of at least 122 primary outcome events. There is no pre-defined minimal duration.
RESULTS: Overall, 3183 patients have been enrolled (mean age 66.1 years, 31.6% females) in 214 sites across 21 countries. At baseline, the mean duration of diabetes was 14.9 years, mean glycated haemoglobin concentration was 66 mmol/mol (8.2%), and 84.6% of patients had established CVD/moderate CKD.
CONCLUSIONS: PIONEER 6 will provide evidence regarding the CV safety of oral semaglutide in patients with type 2 diabetes and high CV risk.

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PMCID: PMC6587508
PMID: 30284349

18: Bandesh K, Prasad G, Giri AK, Kauser Y, Upadhyay M; INDICO, Basu A, Tandon N, Bharadwaj D. Genome-wide association study of blood lipids in Indians confirms universality of established variants. J Hum Genet. 2019 Jun;64(6):573-587. doi: 10.1038/s10038-019-0591-7. Epub 2019 Mar 25. PubMed PMID: 30911093.

Lipids foster energy production and their altered levels have been coupled with metabolic ailments. Indians feature high prevalence of metabolic diseases, yet uncharacterized for genes regulating lipid homeostasis. We performed first GWAS for quantitative lipids (total cholesterol, LDL, HDL, and triglycerides) exclusively in 5271 Indians. Further to corroborate our genetic findings, we investigated DNA methylation marks in peripheral blood in Indians at the identified loci (N = 233) and retrieved gene regulatory features from public domains. Recurrent GWAS loci-CELSR2, CETP, LPL, ZNF259, and BUD13 cropped up as lead signals in Indians, reflecting their universal applicability. Besides established variants, we found certain unreported variants at sub-genome-wide level-QKI, REEP3, TMCC2, FAM129C, FAM241B, and LOC100506207. These variants though failed to attain GWAS significance in Indians, but largely turned out to be active CpG sites in human subcutaneous adipose tissue and showed robust association to two or more lipid traits. Of which, QKI variants showed significant association to all four lipid traits and their designated region was observed to be a key gene regulatory segment denoting active transcription particularly in human subcutaneous adipose tissue. Both established and novel loci were observed to be significantly associated with altered DNA methylation in Indians for specific CpGs that resided in key regulatory elements. Further, gene-based association analysis pinpointed novel GWAS loci-LINC01340 and IQCJ-SCHIP1 for TC; IFT27, IFT88, and LINC02141 for HDL; and TEX26 for TG. Present study ascertains universality of selected known genes and also identifies certain novel loci for lipids in Indians by integrating data from various levels of gene regulation.

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PMID: 30911093

19: Bandesh K, Jha P, Giri AK, Marwaha RK; INDICO, Scaria V, Tandon N, Bharadwaj D. Normative range of blood biochemical parameters in urban Indian school-going

adolescents. PLoS One. 2019 Mar 7;14(3):e0213255. doi: 10.1371/journal.pone.0213255. eCollection 2019. PubMed PMID: 30845211; PubMed Central PMCID: PMC6405124.

Adolescence is the most critical phase of human growth that radically alters physiology of the body and wherein any inconsistency can lead to serious health consequences in adulthood. The timing and pace at which various developmental events occur during adolescence is highly diverse and thus results in a drastic change in blood biochemistry. Monitoring the physiological levels of various biochemical measures in ample number of individuals during adolescence can call up for an early intervention in managing metabolic diseases in adulthood. Today, only a couple of studies in different populations have investigated blood biochemistry in a small number of adolescents however, there is no comprehensive biochemical data available worldwide. In view, we performed a cross-sectional study in a sizeable group of 7,618 Indian adolescents (3,333 boys and 4,285 girls) aged between 11-17 years to inspect the distribution of values of common biochemical parameters that generally prevails during adolescence and we observed that various parameters considerably follow the reported values from different populations being 3.56-6.49mmol/L (fasting glucose), 10.60-199.48pmol/L (insulin), 0.21-3.22nmol/L (C-peptide), 3.85-6.25% (HbA1c), 2.49-5.54mmol/L (total cholesterol), 1.16-3.69mmol/L (LDL), 0.78-1.85mmol/L (HDL), 0.33-2.24mmol/L (triglycerides), 3.56-11.45mmol/L (urea), 130.01-440.15μmol/L (uric acid) and 22.99-74.28μmol/L (creatinine). Barring LDL and triglycerides, all parameters differed significantly between boys and girls ($p < 0.001$). Highest difference was seen for uric acid ($p = 1.3 \times 10^{-187}$) followed by C-peptide ($p = 6.6 \times 10^{-89}$). Across all ages during adolescence, glycemic and nitrogen metabolites parameters varied markedly with gender. Amongst lipid parameters, only HDL levels were found to be significantly associated with gender following puberty ($p < 0.001$). All parameters except urea, differed considerably in obese and lean adolescents ($p < 0.0001$). The present study asserts that age, sex and BMI are the essential contributors to variability in blood biochemistry during adolescence. Our composite data on common blood biochemical measures will benefit future endeavors to define reference intervals in adolescents especially when the global availability is scarce.

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

20: Banerjee J, Satapathy S, Upadhyay AD, Dwivedi SN, Chatterjee P, Kumar L, Rath GK, Dey AB. A short geriatric assessment tool for the older person with cancer in India-Development and psychometric validation. J Geriatr Oncol. 2019 Mar;10(2):222-228. doi: 10.1016/j.jgo.2018.09.001. Epub 2018 Sep 15. PubMed PMID: 30224183.

INTRODUCTION: With rise in incidence and prevalence of cancers in the ageing population, the need for an age sensitive comprehensive assessment measure has been felt. Comprehensive Geriatric Assessment (CGA) is often difficult to implement due to time and logistic constraints. A brief assessment tool encompassing the specific domains of the CGA would be a better way to assess older adults with cancer. These tools exist but have not necessarily been culturally adapted. The main aim of the study was to develop a culturally relevant short geriatric assessment tool and explore its psychometric properties.
METHODOLOGY: An initial item pool was formed after review of the literature and study of the existing scales. This draft tool was then pre and pilot tested to finalize the items and check the feasibility of application. The final tool was validated by exploratory factor analysis on a sample of 100 older patients with cancer.
RESULTS: After pre and pilot study on fifteen and thirty older patients with cancer respectively, this tool consisting of a total of 38 items spread over eight domains was developed and validated on a sample of 100 subjects. Due to

co-linearity, three items were deleted after exploratory factor analysis, bringing the final item number to35. The Cronbach's alpha was 0.93 and the intra-class correlation co-efficient (ICC) was 0.94. Thus, the final tool had 13 questions with sub-parts (35 items in total). The time taken to administer the tool was around 25 min.
CONCLUSION: The tool developed is valid and reliable and can be used for the initial assessment and further care planning of older Indian patients with cancer.

DOI: 10.1016/j.jgo.2018.09.001
PMID: 30224183

21: Banerjee S, Biswas S, Ray A, Vaithiyam V. Expansile cough impulse: a useful clinical sign for empyema necessitans. BMJ Case Rep. 2019 Mar 31;12(3). pii: e229696. doi: 10.1136/bcr-2019-229696. PubMed PMID: 30936366.

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23: Bansal D, Seth A. Spontaneous prostatic haematoma in a case of benign prostatic hyperplasia. BMJ Case Rep. 2019 Mar 31;12(3). pii: e228787. doi: 10.1136/bcr-2018-228787. PubMed PMID: 30936357.

A 61-year-old man presented with urinary retention with obstructive uropathy (urea/creatinine: 126/9.2 mg/dL) secondary to a large prostatic haematoma while being medically managed for benign enlargement of the prostate. The patient did not have any fever or local symptoms and the prostate was enlarged and non-tender on examination. Ultrasound and MRI of the pelvis showed a 9.4×10.4×11.1 cm sized prostatic haematoma seen displacing and compressing the urinary bladder anteriorly with bilateral hydroureteronephrosis. The patient was managed with per-urethral catheterisation, haemodialysis and injectable antibiotics. Percutaneous pigtail placement into the prostatic haematoma led to gradual drainage of the haematoma with improvement in the renal parameters. Definitive surgery in the form of transurethral resection of the prostate was done at a later date. Intraoperatively multiple encapsulated cavities containing organised clots were deroofed. On follow-up, the patient did well and had good urinary flow and normal renal parameters.

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PMID: 30936357

Conflict of interest statement: Competing interests: None declared.

24: Bhakuni T, Singhal R, Annarapu GK, Sharma A, Mahapatra M, Saxena R, Guchhait P. Unique case of autoantibody mediated inactivation of ADAMTS13 in an Indian TTP patient. Blood Cells Mol Dis. 2019 Jul;77:29-33. doi: 10.1016/j.bcmd.2019.03.003. Epub 2019 Mar 23. PubMed PMID: 30953939.

A young Indian female visited hospital as a suspected case of thrombotic thrombocytopenic purpura (TTP) with relapsed thrombotic complications with low platelet counts, infarct in middle cerebral artery and thrombi in microvessels. We first confirmed the deficiency of ADAMTS13 metalloprotease in this patient showing improper cleavage of vWF multimers by her plasma unlike her parents and brother. Although patient had very less ADAMTS13 antigen in plasma, but it did not appear to be the cause of deficiency of the enzyme, because her father had

similarly low antigen level and he never had prothrombotic complications. While investigating the genetic change in ADAMTS13, we observed four homozygous-SNPs (g.420T>C, g.1342C>G, g.1716G>A and g.2280T>C) in exon 5, 12, 15 and 19 respectively in patient and her father unlike the heterozygous form of same SNPs in mother and brother. Further to investigate the cause of ADAMTS13 deficiency, we observed an elevated level of antibody against ADAMTS13 in patient unlike her father and other family members. Our study therefore provides the molecular approach of diagnosis of TTP in this patient and also highlights the use of such techniques in India. More importantly, study provides the clue of alternate treatment such as immunosuppressant therapy to this patient.

DOI: 10.1016/j.bcmd.2019.03.003
PMID: 30953939

25: Bharati J, Bhatia D, Khandelwal P, Gupta N, Sinha A, Khadgawat R, Hari P, Bagga A. C-Terminal Fibroblast Growth Factor-23 Levels in Non-Nutritional Hypophosphatemic Rickets. Indian J Pediatr. 2019 Jun;86(6):555-557. doi: 10.1007/s12098-019-02909-4. Epub 2019 Mar 5. PubMed PMID: 30835073.

Fibroblast growth factor-23 (FGF23) is central to phosphate homeostasis. The author examined if blood levels of FGF23 allow discrimination of classic hypophosphatemic rickets from other causes of non-nutritional rickets with hypophosphatemia. Forty-two children (median age: 102 mo) with non-nutritional rickets and hypophosphatemia were clinically classified as having distal renal tubular acidosis (RTA, n=12), Fanconi syndrome (n=8), classic hypophosphatemic rickets (n=11), vitamin D dependent rickets (n=7) and Dent disease (n=4). Median blood FGF23 (measured by C-terminal ELISA) concentrations were similar in all groups (P=0.24). These levels did not correlate with phosphate, tubular maximum for phosphate, calcium, 25-hydroxyvitamin D, creatinine, and parathormone levels. Patients with distal RTA showed variable degree of proximal tubular dysfunction that resolved following alkali supplements. Blood FGF23 levels did not satisfactorily differentiate classic hypophosphatemic rickets from other causes of hypophosphatemic rickets.

DOI: 10.1007/s12098-019-02909-4
PMID: 30835073

26: Bhatt SP, Guleria R, Vikram NK, Gupta AK. Non-alcoholic fatty liver disease is an independent risk factor for inflammation in obstructive sleep apnea syndrome in obese Asian Indians. Sleep Breath. 2019 Mar;23(1):171-178. doi: 10.1007/s11325-018-1678-7. Epub 2018 Jul 22. PubMed PMID: 30032465.

INTRODUCTION: Obstructive sleep apnea (OSA) has been estimated to affect 4-11% of the population and causes systemic inflammation which leads to metabolic syndrome (MS). Non-alcoholic fatty liver disease (NAFLD) is also associated with MS whether NAFLD is an additional risk factor for the systemic inflammation that occurs in OSA is unclear.
OBJECTIVE: In this study, we aimed to analyze the association of OSA and NAFLD with MS and systemic inflammation in Asian Indians.
METHODS: Total 240 (132 males and 108 females) overweight/obese subjects [body mass index (BMI >23 kg/m2)] were recruited; of these, 124 subjects had OSA with NAFLD, 47 had OSA without NAFLD, 44 did not have OSA but had NAFLD and 25 had neither OSA nor without NAFLD. Severity of NAFLD was based on abdomen ultrasound and of OSA on overnight polysomnography. Clinical examinations, anthropometry, body composition, metabolic parameters, and inflammatory biomarkers were recorded.
RESULTS: Serum levels of leptin, macrophage migration inhibitory factor (MIF), interleukin-6 (IL-6), high sensitive C-reactive protein (Hs-CRP), and tumor necrosis factor alpha (TNF-α) were significantly higher, and adiponectin levels were significantly lower in OSA with NAFLD subjects. Prevalence of MS was significantly increased in OSA and NAFLD subjects (p=0.001). There was a strong

association and correlation between leptin, IL-6, Hs-CRP, MIF, and TNF-α in OSA and NAFLD subjects. Multivariate logistic regression showed that OSA was positively associated with the NAFLD [odds ratio (OR), (95% confidence interval (CL) 3.12 (2.58-7.72), (P=0.002)].
CONCLUSION: NAFLD is an additional risk factor in OSA subject which contributes to systemic inflammation in Asian Indians.

DOI: 10.1007/s11325-018-1678-7
PMID: 30032465

27: Bhethanabhotla S, Tiwari A, Sharma MC, Vishnubhatla S, Bakhshi S. Prognostic Significance of IL-6 in Hodgkin Lymphoma. Indian J Pediatr. 2019 Jun;86(6):551-554. doi: 10.1007/s12098-019-02902-x. Epub 2019 Mar 4. PubMed PMID: 30830568.

Elevated serum interleukin-6 (IL-6) in Hodgkin lymphoma (HL) is reported to correlate with B symptoms, response rate and survival in adult patients. The authors studied prognostic significance of IL-6 expression by immunohistochemistry on Hodgkin-Reed Sternberg cells and background reactive cells in a retrospective cohort of pediatric HL patients treated with doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) from January 2009 through December 2013. Of 142 patients, tissue blocks were retrieved in 110 patients. On logistic regression analysis, IL-6 expression on background cells alone was among the factors associated with inferior response rate (OR-9.9, 95%CI-1.2, 78.3; p=0.03). On multivariate analysis, IL-6 expression on background cells alone had significant impact on 5 y freedom from treatment failure (FFTF) (HR-7.7, 95% CI-1.2, 48.6; p=0.03). IL-6 expression by immunohistochemistry in the background cells is an independent poor predictor of response and FFTF in pediatric HL. Further prospective studies in children are needed to confirm the current findings and whether IL-6 expression can be used to stratify treatment.

DOI: 10.1007/s12098-019-02902-x
PMID: 30830568

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Diet and environment are two critical regulators that influence an individual's epigenetic profile. Besides the anterograde signaling, mitochondria act as a key regulator of epigenetic alterations in cancer either by controlling the concentration of the cofactors, activity of vital enzymes or by affecting the transcription of NF-kappaB and associated signaling molecules. As epigenetic modifications are the major drivers of aberrant gene expression, designing novel nutri-epigenomic strategies to modulate reversible epigenetic modifications will be important for effective cancer protection. In this regard, nutraceuticals such as flavonoids holds significant promise to modulate the epigenome through a network of interconnected anti-redox mechanisms. However, low solubility, rapid metabolism and poor absorption of flavonoids in gastrointestinal tract hinder their use in clinical settings. Therefore, it is imperative to develop nano-engineered systems which could considerably improve the targeted delivery of these bioactive compounds with better efficacy and pharmacokinetic properties. Concerted efforts in nano-engineering of flavonoids using polymer, lipid and complexation based approaches could provide successful bench-to-bedside translation of flavonoids as broad spectrum anti-cancer agents.

PMID: 30844733

29: Chakravarty K, Shukla G, Poornima S, Agarwal P, Gupta A, Mohammed A, Ray S, Pandey RM, Goyal V, Srivastava A, Behari M. Effect of sleep quality on memory, executive function, and language performance in patients with refractory focal epilepsy and controlled epilepsy versus healthy controls - A prospective study.

Epilepsy Behav. 2019 Mar;92:176-183. doi: 10.1016/j.yebeh.2018.12.028. Epub 2019 Jan 18. PubMed PMID: 30665125.

We aimed to evaluate the effect of sleep quality on memory, executive function, and language performance in patients with refractory focal epilepsy and controlled epilepsy and compare these with healthy individuals. We prospectively enrolled 37 adolescent and adult patients with refractory focal epilepsy (Group 1) and controlled epilepsy (Group 2) in each group. History pertaining to epilepsy and sleep were recorded, and all patients underwent overnight polysomnography. Language, memory, and executive function assessments were done using Western Aphasia Battery, Post Graduate Institute (PGI) memory scale, and battery of four executive function tests (Trail Making Test A & B, Digit symbol test, Stroop Task, and Verbal Fluency Test), respectively. Forty age- and sex-matched controls were also included in the study. Significant differences were noted in both objective and subjective sleep parameters among all the groups. On polysomnography, parameters like total sleep time, sleep efficiency, sleep latency, and rapid eye movement (REM) latency were found to be significantly worse in Group 1 as compared with Group 2. Cognitive and executive parameters were significantly impaired in Group 1. Shorter total sleep time, poorer sleep efficiency, and prolonged sleep latencies were observed to be associated with poor memory and executive function in patients with refractory epilepsy. Our study strongly suggests that sleep disturbances, mainly shorter total sleep time, poor sleep efficiency, and prolonged sleep latencies, are associated with impaired memory and executive function in patients with refractory focal epilepsy and to a lesser extent, among those with medically controlled epilepsy.

DOI: 10.1016/j.yebeh.2018.12.028
PMID: 30665125

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Background: Tuberculous meningitis (TBM) is the most devastating manifestation of extra-pulmonary tuberculosis. About 33% of TBM patients die due to very late diagnosis of the disease. Conventional diagnostic methods based on signs and symptoms, cerebrospinal fluid (CSF) smear microscopy or liquid culture suffer from either poor sensitivity or long turnaround time (up to 8 weeks). Therefore, in order to manage the disease efficiently, there is an urgent and unmet need for a rapid and reliable diagnostic test.
Methods: In the current study, to address the diagnostic challenge of TBM, a highly rapid and sensitive structural switching electrochemical aptasensor was developed by combining the electrochemical property of methylene blue (MB) with the molecular recognition ability of a ssDNA aptamer. To demonstrate the clinical diagnostic utility of the developed aptasensor, a blinded study was performed on 81 archived CSF specimens using differential pulse voltammetry.
Results: The electrochemical aptasensor developed in the current study can detect as low as 10 pg HspX in CSF background and yields a highly discriminatory response ($P<0.0001$) for TBM and not-TBM categories with ~95% sensitivity and ~97.5% specificity and has the ability to deliver sample-to-answer in ≤30 minutes.
Conclusion: In summary, we demonstrate a new aptamer-based electrochemical biosensing strategy by exploiting the target-induced structural switching of H63 SL-2 M6 aptamer and electroactivity of aptamer-tagged MB for the detection of HspX in CSF samples for the diagnosis of TBM. Further, the clinical utility of

this sensor could be extended for the diagnosis of other forms of tuberculosis in the near future.

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PMCID: PMC6440448
PMID: 30988611 [Indexed for MEDLINE]

32: Das U, Singh E, Dharavath S, Tiruttani Subhramanyam UK, Pal RK, Vijayan R, Menon S, Kumar S, Gourinath S, Srinivasan A. Structural insights into the substrate binding mechanism of novel ArgA from Mycobacterium tuberculosis. Int J Biol Macromol. 2019 Mar 15;125:970-978. doi: 10.1016/j.ijbiomac.2018.12.163. Epub 2018 Dec 18. PubMed PMID: 30576731.

The Mycobacterium tuberculosis (Mtb) Rv2747 gene encodes for a functional protein known as ArgA, which plays an important role in the first step of the l-arginine biosynthesis pathway. ArgA transfers the acetyl group from the acetyl-CoA to either l-glutamate or l-glutamine, which are the known substrates. Here, we present two crystal structures of ArgA: one complexed with CoA and product bound N-acetylglutamine and the other complexed with acetyl-CoA and the inhibitor l-arginine at 2.3 and 3.0 Å resolution respectively. The Mtb ArgA protomer was found to have a "V" cleft and a "β" bulge, archetypal of a classical GCN5-related N-acetyltransferase superfamily of proteins. The product bound form implies that ArgA can also acetylate l-glutamine like l-glutamate. The active site is strongly inhibited by l-arginine resulting in a closed conformation of ArgA and both l-arginine and N-acetylglutamine were found to occupy at the same active site. Together with structural analysis, molecular docking studies, microscale thermophoresis and enzyme inhibition assays, we conclude that l-glutamine, l-glutamate and l-arginine, all occupy at the same active site of ArgA. Furthermore in case of Mtb ArgA, l-arginine does not act as an allosteric inhibitor unlike other N-acetylglutamate synthase family of proteins.

DOI: 10.1016/j.ijbiomac.2018.12.163
PMID: 30576731 [Indexed for MEDLINE]

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Mucocele of paranasal sinuses commonly affects frontal or frontoethmoidal air cells. With the evolution of endoscopic sinus surgery, the endoscopic marsupialisation has become the standard of care for these lesions. However, the external approach still has a role in selected cases of frontal sinus mucocele. The location of the mucocele and its communication with the natural outflow tract of the frontal sinus are some of the critical factors to be considered while choosing the surgical approach. We have discussed the management of three cases of frontal mucoceles having different locations and one of them having intervening septa. We emphasise that the successful management of far laterally located mucoceles and those with laterally situated septation require an external approach in conjunction with endoscopic marsupialisation.

DOI: 10.1136/bcr-2018-226830
PMID: 30898953

34: Dhawan S, Andrews R, Kumar L, Wadhwa S, Shukla G. A Randomized Controlled Trial to Assess the Effectiveness of Muscle Strengthening and Balancing Exercises on Chemotherapy-Induced Peripheral Neuropathic Pain and Quality of Life Among Cancer Patients. Cancer Nurs. 2019 Mar 18. doi: 10.1097/NCC.0000000000000693. [Epub ahead of print] PubMed PMID: 30888982.

BACKGROUND: Chemotherapy-induced peripheral neuropathy (CIPN) is the presence of tingling, burning, itching, and unpleasant sensations in hands and feet due to nerve damage by chemotherapy. Exercise rehabilitation has potential to prevent or alleviate CIPN.
OBJECTIVE: The aim of this study was to assess the effectiveness of muscle strengthening and balancing exercises on CIPN pain and quality of life (QOL) among cancer patients.
METHODS: The randomized controlled trial included 45 cancer patients from a tertiary care hospital in India receiving chemotherapeutic drugs paclitaxel and carboplatin and found to have CIPN. Subjects were randomly allocated to exercise (n1 = 22) and usual care (n2 = 23) groups. The exercise group received home-based muscle strengthening and balancing exercise for 10 weeks. Data regarding demographic, clinical characteristics, CIPN, neuropathic pain, and QOL were collected by structured questionnaires Chemotherapy-Induced Peripheral Neuropathy Assessment Tool, nerve conduction velocity, Leeds Assessment of Neuropathic Symptoms and Signs pain scale, and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire.
RESULTS: The 2 groups were homogenous regarding demographic variables. In clinical characteristics, the exercise group had larger body surface area and received a higher dose of paclitaxel. Significant reduction in neuropathic pain scores (P < .0001) and improvement in Functional QOL (P = .0002), Symptom QOL (P = .0003), Global Health Status QOL (P = .004) scores were observed after intervention in the exercise group than the usual-care group.
CONCLUSION: Muscle strengthening and balancing exercises are effective in reducing CIPN pain and improving QOL among cancer patients.
IMPLICATIONS FOR PRACTICE: Muscle strengthening and balancing exercises can be used as a complementary therapy for effective management of CIPN.

DOI: 10.1097/NCC.0000000000000693
PMID: 30888982

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Dengue and Chikungunya are two important mosquito-borne acute febrile illnesses in children. With increased urbanization and newer strains of chikungunya virus with improved transmission with Aedes albopictus, the at-risk population for these infections has greatly increased. Dengue fever has been classified by WHO as dengue with/ without warning signs and severe dengue. Severe dengue is associated with hemorrhagic manifestations, hypovolemia and hypotension secondary to third space loss due to capillary leak or severe end organ dysfunction. NS1 antigen detection and dengue polymerase chain reaction, [polymerase chain reaction (PCR during first 5 d)] and IgM for dengue (6th day of fever onwards) are commonly utilized diagnostic tests. Appropriate fluid therapy with timely tapering of intravenous fluid rate with hematocrit, treatment of hemorrhagic manifestations and clinical monitoring are the mainstay of dengue treatment. Chikungunya has less severe course with shorter febrile phase with prominent and persistent joint symptoms. PCR and IgM against chikungunya are appropriate investigations. Treatment is supportive for chikungunya infection with appropriate joint pain relief.

DOI: 10.1007/s12098-018-2794-x
PMID: 30511272

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Chronic meningitis is a common syndrome with multiple aetiological causes. It can be associated with visionproblems as well as multifocal involvement of the central nervous system. Often it presents with constitutional symptoms as well. The intervention commonly practised in a tropical country like India is starting antitubercular therapy with corticosteroids. This practice though may be correct

in a majority of situations, may lead to diagnostic delay and may be fatal.

DOI: 10.1136/bcr-2018-228328
PMID: 30842137 [Indexed for MEDLINE]

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Haemophagocytic lymphohistiocytosis (HLH) in Human Immunodeficiency Virus (HIV) infected individuals can either be due to the disease itself or due to associated infections/malignancies. The treatment for HLH requires immunosuppressive therapy but administering immunosuppressive therapy to an already immunosuppressed patient (HIV infection) is complex. We present two such cases of HLH in patients infected with HIV. In the first case, no alternate cause for HLH was found even after extensive investigations and it was attributed to the uncontrolled HIV replication. Patient was started on dexamethasone for the same but succumbed to hospital acquired pneumonia. The second patient was diagnosed with Hodgkin's lymphoma but he succumbed to his illness before initiating immunosuppressive therapy for HLH. We report these cases to highlight the dilemma and a need for further research in this direction.

DOI: 10.11604/pamj.2019.32.105.14764
PMCID: PMC6560963
PMID: 31223395 [Indexed for MEDLINE]

39: Frullanti E, Papa FT, Grillo E, Clarke A, Ben-Zeev B, Pineda M, Bahi-Buisson N, Bienvenu T, Armstrong J, Roche Martinez A, Mari F, Nissenkorn A, Lo Rizzo C, Veneselli E, Russo S, Vignoli A, Pini G, Djuric M, Bisgaard AM, Ravn K, Bosnjak VM, Hayek J, Khajuria R, Montomoli B, Cogliati F, Pintaudi M, Hadzsiev K, Craiu D, Voinova V, Djukic A, Villard L, Renieri A. Analysis of the Phenotypes in the Rett Networked Database. Int J Genomics. 2019 Mar 27;2019:6956934. doi: 10.1155/2019/6956934. eCollection 2019. PubMed PMID: 31049350; PubMed Central PMCID: PMC6458890.

Rett spectrum disorder is a progressive neurological disease and the most common genetic cause of intellectual disability in females. MECP2 is the major causative gene. In addition, CDKL5 and FOXG1 mutations have been reported in Rett patients, especially with the atypical presentation. Each gene and different mutations within each gene contribute to variability in clinical presentation, and several groups worldwide performed genotype-phenotype correlation studies using cohorts of patients with classic and atypical forms of Rett spectrum disorder. The Rett Networked Database is a unified registry of clinical and molecular data of Rett patients, and it is currently one of the largest Rett registries worldwide with several hundred records provided by Rett expert clinicians from 13 countries. Collected data revealed that the majority of MECP2-mutated patients present with the classic form, the majority of CDKL5-mutated patients with the early-onset seizure variant, and the majority of FOXG1-mutated patients with the congenital form. A computation of severity scores further revealed significant differences between groups of patients and correlation with mutation types. The highly detailed phenotypic information contained in the Rett Networked Database allows the grouping of patients presenting specific clinical and genetic characteristics for studies by the Rett community and beyond. These data will also serve for the development of clinical trials involving homogeneous groups of patients.

DOI: 10.1155/2019/6956934
PMCID: PMC6458890
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Background: Endoscopic surgery is developing in various clinical specialties. During ear endoscopic surgery, a surgeon has to hold an endoscope with one hand and operate the surgical instruments with another hand. Therefore, the stability of the surgeon's hand affects the field of surgical view and quality of the surgery considerably. There are few techniques which are used during surgery to stabilize the endoscope. However, no study has evaluated the efficacy of such techniques in detail. This study examined the three dimensional movement of an endoscope to compare and evaluate the effect of various stabilization techniques to reduce the hand tremor while using the endoscope.
Methods: A non-randomized controlled trial involving 15 medical students was conducted in Tottori University, Japan. Subjects held an endoscope with their non-dominant hand and manipulated it using three different stabilization techniques i.e. with resting the elbow on the table, resting the endoscope on the ear canal, both with the elbow on the table and endoscope on the ear canal. For the control, subjects were made to use the endoscope without any stabilization technique. The endoscopic movement was measured with and without using the stabilization techniques.
Results: The results obtained in this study indicated that manipulating the endoscope with resting the elbow on the table restrains both vertical (Y-axis) and optical axis (Z-axis) direction of tremor, and manipulating the endoscope by resting it on the ear canal restrains both vertical (Y-axis) and horizontal axis (X-axis) direction while the combined use of both the techniques reduces the endoscope movement in all the three X, Y and Z axes.
Conclusion: In conclusion, concomitant use of both techniques appears to be clinically beneficial in endoscopic ear surgery.

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BACKGROUND: The therapeutic options for the reducing the damage caused by myocardial ischemia are limited and not devoid of adverse effects. The role of the flavanoid, fisetin, predominantly found in strawberry and apple, is yet to be explored in the heart.
STUDY DESIGN: Male Wistar rats (n = 48) were administered fisetin (10, 20 & 40 mg/kg/day, orally) or vehicle for 28 days while ISO, 85 mg/kg, subcutaneously, was also administered at 24 h interval on the 27th and 28th day. On the 29th day, rats were anaesthetized and right carotid artery was cannulated to record hemodynamic parameters. Subsequently, blood sample was collected and heart was removed to evaluate various parameters.
RESULTS: Fisetin at doses of 10 and 20 mg/kg reversed ISO induced detrimental alterations in blood pressure and left ventricular pressures and reduced the

myocardial injury markers CK-MB and LDH in the serum. These findings were supported by amelioration of ISO induced histological and ultrastructural damage by fisetin. The disequilibrium in the levels of pro and anti oxidants in the myocardial tissue caused by ISO was also normalized Furthermore, apoptosis was evident from enhanced DNA fragmentation and raised pro-apoptotic proteins (bax, caspase-3, cytochrome-c) as well as suppressed anti-apoptotic protein (Bcl-2) in case of ISO treatment which again was reversed by fisetin. A molecular mechanism for this protection was elucidated as downregulation of RAGE and NF-κB However fisetin at 40 mg/kg revealed a deteriorating effect which was similar to ISO group of rats.
CONCLUSION: Hence, through our study, the role of fisetin in cardioprotection has been uncovered via a molecular pathway.

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PURPOSE: Sentinel lymph node biopsy is an essential staging tool in patients with clinically localized oral cavity squamous cell carcinoma. The harvesting of a sentinel lymph node entails a sequence of procedures with participation of specialists in nuclear medicine, radiology, surgery, and pathology. The aim of this document is to provide guidelines for nuclear medicine physicians performing lymphoscintigraphy for sentinel lymph node detection in patients with early N0 oral cavity squamous cell carcinoma.
METHODS: These practice guidelines were written and have been approved by the European Association of Nuclear Medicine (EANM) and the International Atomic Energy Agency (IAEA) to promote high-quality lymphoscintigraphy. The final result has been discussed by distinguished experts from the EANM Oncology Committee, and national nuclear medicine societies. The document has been endorsed by the Society of Nuclear Medicine and Molecular Imaging (SNMMI). These guidelines, together with another two focused on Surgery and Pathology (and published in specialised journals), are part of the synergistic efforts developed in preparation for the "2018 Sentinel Node Biopsy in Head and Neck Consensus Conference".
CONCLUSION: The present practice guidelines will help nuclear medicine practitioners play their essential role in providing high-quality lymphatic mapping for the care of early N0 oral cavity squamous cell carcinoma patients.

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Background: Demographic transition increased the proportion of elderly in India. Elderly persons experience increased economic dependency for their day-to-day existence. The Government of India provides monetary benefit through social welfare schemes. Health outcomes of the elderly improve when they are economically independent. We aimed to assess the awareness and utilization of social welfare schemes among elderly persons in an urban resettlement colony of Delhi.
Materials and Methods: This was a community-based cross-sectional study conducted from February to May 2018. Two specially recruited interviewers administered the self-developed semi-structured interview schedule. It consisted of sociodemographic data, awareness, and utilization of various schemes.
Results: A total of 931 [416 (37.4%) males and 515 (55.3%) females] participants completed the interview. Of the total, 809 (86.9%) participants were aware of at least one social welfare scheme. Participants utilizing any of the social welfare schemes were 393 (42.2%). Females utilized the social welfare schemes almost twice as compared to males (AOR = 1.7, 95% CI: 1.1-2.6). Participants aged 75 years and above had four times higher utilization of social welfare schemes compared to 60-64 years age group (AOR = 3.9, 95% CI: 2.4-6.4).
Conclusion: Although the awareness of social welfare schemes among elderly persons was good, their utilization has scope for significant improvement. Focus is needed on elderly males and among the younger elderly persons.

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Diagnostic and Statistical Manual of mental disorder-IV (DSM-IV) TR based INCLEN Diagnostic Tool for Autism Spectrum Disorder (INDT-ASD) is an established instrument for the diagnosis of ASD in Indian subcontinent and low-middle income countries (LMIC). The introduction of DSM-5 necessitated revision of existing INDT-ASD tool to incorporate the DSM-5 related changes. This study was undertaken to develop and validate the DSM-5 based All India Institute of Medical Sciences (AIIMS)-Modified-INDT-ASD Tool. The modifications were done using Delphi method and included: (a) rearrangement of questions from the previous tool; and (b) addition of new questions on sensory symptoms. The modified tool was validated against DSM-5 diagnostic criteria. In addition, receiver operating characteristic (ROC) curves were used to determine the cut-off for total score as compared to Childhood Autism Rating Scale (CARS) score to grade the severity of ASD. Two-hundred-twenty-five children (159 boys, median age = 47months) were enrolled. The modified tool demonstrated sensitivity of 98.4% and specificity of 91.7% to diagnose ASD. A score ≥14 on the tool was suggestive of severe ASD (CARS>36.5) with a sensitivity and specificity of 80% and 80.7% respectively [Area under the curve = 0.89]. AIIMS-Modified-INDT-ASD Tool is a simple and structured instrument based on DSM-5 criteria which can facilitate diagnosis of ASD with acceptable diagnostic accuracy.

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aspiration and endoscopic ultrasound with an echobronchoscope-guided fine needle aspiration in children with mediastinal pathology. Pediatr Pulmonol. 2019 Jun;54(6):881-885. doi: 10.1002/ppul.24313. Epub 2019 Mar 19. PubMed PMID: 30891940.

BACKGROUND: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound with an echobronchoscope-guided fine needle aspiration (EUS-B-FNA) are useful modalities in the evaluation of mediastinal pathologies in adults. However, sparse data are available in children.
OBJECTIVE: To describe the utility and safety of EBUS-TBNA and EUS-B-FNA in children with mediastinal pathologies of unknown etiology.
DESIGN: Chart review.
SETTING: Pediatric Chest and Tuberculosis Clinics, Department of Pediatrics, AIIMS, New Delhi from May 2015 to March 2018.
PATIENTS: Children <18 years of age with mediastinal pathologies of undefined etiology.
METHODS: Case records of children who underwent EBUS-TBNA and EUS-B-FNA were reviewed. Data on demographic profile, clinical features, laboratory investigations, the technique of EBUS-TBNA/ EUS -B- FNA, complications, and findings were collected.
RESULTS: Thirty children (19 males) with mean (SD) age of 9.6 (±3.5) years underwent endobronchial procedures. Median (IQR) weight(kg) and height(cm) were 29 (19.5, 35) and 134 (125, 150) respectively. Tuberculosis was the most common preprocedure clinical diagnosis (73.3%), followed by lymphoma (13.3%). Presenting features were fever (80%), cough (53.3%), hepatomegaly (13%), peripheral lymphadenopathy (21.7%), and positive tuberculin skin test (63.3%). Approximately one fourth were on antitubercular therapy without definite evidence of TB. Conscious sedation was used for the procedures: midazolam and fentanyl (n=22), propofol (n=8). Transesophageal, transtracheal, and both routes were used in 20 (66.6%), 7 (23.3%), and 3 (10.1%), respectively. Lymph-nodes were sampled in 24 children (subcarinal in 16, right paratracheal in 4 and both in 4). Mean (SD) size of lymph node (in cm) on EBUS was 1.93(±0.5) and median (IQR) number of FNAC needle passes per node were 2 (2, 4). The diagnosis was confirmed in 11 (36.6%, tuberculosis in 10 by GeneXpert/ MGIT/ cytopath and lymphoma in one) patients. Only 3.3% had a minor complication.
CONCLUSION: EBUS-TBNA and EUS-B-FNA are helpful in children with undiagnosed mediastinal pathology with fair diagnostic yield and excellent patient safety profile.

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Phosphopantetheine adenylyltransferase (PPAT, EC. 2.7.7.3) catalyzes an essential step in the reaction that transfers an adenylyl group from adenosine tri phosphate (ATP) to 4'-phosphopantetheine (pPant) yielding 3'- dephospho-coenzyme A (dPCoA) and pyrophosphate (PP) in the coenzyme A (CoA) biosynthesis pathway. The enzyme PPAT from Acinetobacter baumannii (AbPPAT) was cloned, expressed and purified. The binding studies of AbPPAT were carried out with two compounds, tri-sodium citrate (TSC) and l-ascorbic acid (LAA, vitamin-C) using fluorescence spectroscopic (FS) and surface Plasmon resonance (SPR) methods. Both methods provided similar values of dissociation constants for TSC and LAA which were of the order of 10-8 M and 10-5 M respectively. The computer aided docking studies indicated fewer interactions of LAA with AbPPAT as compared to those of TSC. The freshly purified samples of AbPPAT were crystallized. The crystals of AbPPAT were soaked in the solutions containing TSC and LAA. However, the crystals of the

complex of AbPPAT with LAA did not diffract well and hence the structure of the complex of AbPPAT with LAA could not be determined. On the other hand, the crystals of the complex of AbPPAT with TSC diffracted well and the structure was determined at 1.76Å resolution. It showed that TSC bound to AbPPAT at the ATP binding site and formed several intermolecular contacts including 12 hydrogen bonds. The results of binding studies for both TSC and LAA and the structure of the complex of AbPPAT with TSC clearly indicated a potential role of TSC and LAA as antibacterial agents.

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Short stature in children is a diagnostic challenge to the physician. Bone age assessment can be done using various methods. The causes of short stature are variable; often leading to a series of investigations. The endocrine conditions have typical imaging features. This chapter provides a short overview of the methods of bone age estimation, and imaging findings and algorithmic approach towards a child with short stature.

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PURPOSE: Multiple myeloma (MM) is a hematological malignancy marked by uncontrolled proliferation and accumulation of plasma cells in bone marrow. Despite presence of numerous diagnostic markers for MM, their invasive and non-specific nature demands identification of some effective biomarker. Small non-coding RNAs, i.e., microRNAs being secreted out in circulation could depict the change in homeostasis. Earlier, we reported diagnostic potential of a proteoglycan, Versican (VCAN) in MM, hence, VCAN linked cell-free microRNAs have been explored to study their diagnostic involvement in MM.
METHODS: Biopsy proven MM patients and controls were recruited. The relative microRNA expression of VCAN linked microRNAs (miR-143, miR-144, miR-199, and miR-203) along with levels of VCAN have been investigated in bone marrow supernatant fluid (BMSF) and blood serum and their correlation were done with clinico-pathological parameters. The diagnostic potential was assessed using ROC curve.
RESULTS: Relative microRNA expression of all microRNAs was found significantly lower in MM patients in both BMSF and serum while VCAN levels were substantially higher in patients. VCAN levels showed positive trend while microRNAs expression showed negative trend with severity of disease. miR-203 showed significant correlation with myeloma-associated parameters and also showed optimum sensitivity and specificity for diagnosis of MM in serum.
CONCLUSIONS: Downregulation of cell-free microRNAs illustrates their importance in MM. The negative trend of microRNAs with disease progression suggests their diagnostic significance. Correlation of miR-203 with myeloma clinical parameters along with optimum sensitivity and specificity affirms its non-invasive diagnostic potential in MM which could further be validated in larger patient

cohort.

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A new technique of correcting tube-corneal touch is described in a case of Ahmed glaucoma valve implantation. This technique repositions the intracameral tube without externalization unlike the standard procedures which aim to correct tube-corneal touch. The technique makes use of a transscleral supracapsular anchor suture to facilitate repositioning of the tube within the ciliary sulcus. Feasible only in pseudophakic and aphakic patients, either a preexisting iridectomy or intraoperative iridectomy is an essential prerequisite to perform this procedure. The final positioning of the tube within the sulcus potentially prevents chronic rubbing of the iris by polypropylene suture as opposed to a transcameral suture.

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BACKGROUND: The Vitiligo Impact Scale (VIS)-22 is a vitiligo-specific quality-of-life instrument. Its criterion, convergent and known-groups validity, test-retest reliability and responsiveness have been studied previously in an Indian population. The clinical meaning of VIS-22 scores has not yet been analysed.
OBJECTIVES: To assign clinical meaning to VIS-22 scores using anchor-based methods.
METHODS: This was a cross-sectional study conducted in a large teaching hospital in North India. Patients with vitiligo > 15 years of age (n = 391) completed the VIS-22 and Dermatology Life Quality Index (DLQI) questionnaires, and answered a Global Question (GQ) on the effect of vitiligo on their lives on a five-point Likert scale. Multiple band sets of VIS-22 scores were devised using GQ as the anchor. A weighted kappa-coefficient was calculated to estimate the level of agreement between different band sets of VIS-22 and GQ. VIS-22 and DLQI were compared based on their degree of correlation and agreement with GQ.
RESULTS: The mean ± SD of VIS-22 scores was 24·8 ± 14·0 (range 0-61). VIS-22 scores showed good correlation with GQ (r = 0·76). Of the various VIS-22 band sets tested, the following was chosen: 0-5, 6-15, 16-25, 26-40 and 41-66

(weighted κ = 0·57), corresponding to the five categories of GQ. The degree of correlation (VIS-22, r = 0·77; DLQI, r = 0·69) and agreement (VIS-22, 51·6%; DLQI, 36·1%; P < 0·001) of VIS-22 with GQ was higher than that with DLQI.
CONCLUSIONS: VIS-22 scores can be used to stratify the impairment of vitiligo-related quality of life.

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Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired clonal stem cell disorder. Eculizumab and bone marrow transplantation are disease-modifying treatments for PNH but may not be readily available in resource-constrained settings. Of 52 pediatric patients with PNH, 20 had classical PNH and 32 had PNH/aplastic anemia (PNH/AA). Median time to diagnosis was 30 months in classical PNH patients. Renal failure was present in four patients (20%). Six (30%) achieved complete response, 10 (50%) achieved partial response with androgens in classical PNH. Two underwent allogenic stem cell transplantation. In the PNH/AA group, 16 (50%) were in CR and seven (21%) were in PR with anti-thymocyte globulin ± cyclosporine.

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RATIONALE & OBJECTIVE: Chronic kidney disease (CKD) has wide-ranging and long-term consequences for young people and their families. The omission of outcomes that are important to young people with CKD and their caregivers limits knowledge to guide shared decision making. We aimed to identify the outcomes that are important to young people with CKD and their caregivers.
STUDY DESIGN: We used the nominal group technique whereby participants identified and ranked outcomes and explained their priorities.
SETTINGS & PARTICIPANTS: Young people with CKD (stages 1-5, dialysis, or transplantation) and their caregivers were purposively sampled from 6 centers across Australia, the United States, and Canada.
ANALYTICAL APPROACH: Importance scores were calculated (scale of 0-1), and qualitative data were analyzed thematically.
RESULTS: 34 patients (aged 8-21 years) and 62 caregivers participated in 16 groups and identified 48 outcomes. The 5 highest ranked outcomes for patients were survival (importance score, 0.25), physical activity (0.24), fatigue (0.20), lifestyle restrictions (0.20), and growth (0.20); and for caregivers, kidney function (0.53), survival (0.28), infection (0.22), anemia (0.20), and growth (0.17). 12 themes were identified reflecting their immediate and current priorities (wanting to feel normal, strengthening resilience, minimizing intrusion into daily life, imminent threats to life, devastating family burdens, and seeking control over health) and considerations regarding future impacts (protecting health/development, remaining hopeful, concern for limited

opportunities, prognostic uncertainty, dreading painful and invasive procedures, and managing expectations).
LIMITATIONS: Only English-speaking participants were recruited.
CONCLUSIONS: Kidney function, infection, survival, and growth were the highest priorities for patients with CKD and their caregivers. Young people with CKD also prioritized highly the outcomes that directly affected their lifestyle and sense of normality, while caregiver's highest priorities concerned the long-term health of their child, current health problems, and the financial and family burdens of caring for a child with CKD.

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PURPOSE: Aromatic antiepileptic drugs (AEDs) are frequently implicated in cutaneous adverse drug reactions (cADRs), a few of which are associated with certain human leukocyte antigen (HLA) alleles in some populations. We aimed to find HLA-associations with AED-related cADRs among North Indians.
METHODS: North Indian subjects with cADR due to an AED, and those who were AED-tolerant were recruited as cases and controls, respectively. Genotyping for HLA-A, B and DRB1 were performed. Statistical analysis to compare carrier-rates and allele-frequencies between cases and controls (and healthy population, where necessary), was done for HLA-alleles occurring more than twice in either group.
RESULTS: 120 cases {11 - Lamotrigine (LTG), 14 -Valproic acid (VPA), 8 -Levetiracetam (LEV), 35 -Carbamazepine (CBZ) and 52 - Phenytoin (PHT)}, and 250 controls were recruited. Presence of HLA-A*31:01 and HLA-B*51:01 were found to increase the risk of Maculopapular exanthema (MPE) due to CBZ and PHT (OR=6.38; 95% CI: 1.46-27.75; OR=4.60; 95% CI: 1.54-13.72, respectively). Among the severe cADRs, HLA-B*57:01(OR=11.00 95% CI: 1.41-85.81) and HLA-DRB1*07:01 (OR=7.25; 95% CI: 1.09-48.18) were noted to be significantly associated with CBZ-induced Stevens Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN); HLA-B *51:01 was associated with drug reaction eosinophilia and systemic symptoms (DRESS) caused by PHT (OR=6.90; 95% CI: 1.38-34.29).
CONCLUSIONS: We found significant associations of some HLA alleles with specific cADRs to CBZ and PHT in North Indians, which may need to be tested before AED-initiation; only screening for HLA-B*15:02 may not help in this population.

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PURPOSE: Cardiac changes accompanying seizures may be responsible for sudden unexpected death in epilepsy (SUDEP), and drugs with antiseizure and favorable cardiovascular profile could be beneficial. The effect of losartan and enalapril alone and in combination with sodium valproate on seizures, cognition, cardiac histopathology, and serum brain-derived neurotropic factor (BDNF) levels were determined.
METHODS: Male "Wistar" rats (200-250 g) were administered enalapril (20 mg/kg, intraperitoneally (i.p.)) and losartan (10 mg/kg, i.p.) daily and simultaneously subjected to pentylenetetrazole (PTZ)-kindling (PTZ 30 mg/kg, i.p., every alternate day). Enalapril and losartan were injected 45 & 120 min before seizure stimuli. In another set of experiments, sodium valproate (150 mg/kg, i.p.) alone or in combination with enalapril (20 mg/kg, i.p.) and losartan (10 mg/kg, i.p.) were administered daily during induction of kindling. The effect on seizures and behavior were noted; rats were sacrificed, and blood and hearts were collected for further analysis, i.e., BDNF levels, heart weight-body weight (HWBW) ratio, and cardiac histopathology.
RESULTS: Losartan, but not enalapril, suppressed the seizure score in PTZ kindling. Sodium valproate alone or in combination with losartan or enalapril prevented kindled seizures. Sodium valproate per se caused cognitive impairment, which was prevented on combining with losartan or enalapril. A decrease in HWBW ratio was observed only in enalapril group (p value = 0.02). Kindling led to cardiac ischemic changes, which could be prevented by losartan and sodium valproate. Serum BDNF level was decreased in PTZ (p value = 0.02) and sodium valproate per se group (p value = 0.04), but sodium valproate could reverse the PTZ-induced decrease in serum BDNF level.
CONCLUSION: The use of losartan with sodium valproate in epilepsy may prevent the cognitive and cardiac sequelae of seizures. The BDNF levels as a marker for cardiovascular risk in persons with epilepsy (PWE) needs to be explored further.

DOI: 10.1016/j.yebeh.2018.12.019
PMID: 30658894

67: Kakkar A, Guleria P, Madan K, Kumar R, Kumar S, Jain D. Immunohistochemical Assessment of BAP1 Protein in Mucoepidermoid Carcinomas. Indian J Otolaryngol Head Neck Surg. 2019 Mar;71(1):33-37. doi: 10.1007/s12070-018-1549-3. Epub 2018 Dec 19. PubMed PMID: 30906710; PubMed Central PMCID: PMC6401040.

Mucoepidermoid carcinomas are common malignant salivary gland tumors. Despite recent advances in diagnosis and treatment, there has not been much improvement in outcome of these patients, necessitating identification of novel targeted therapeutic agents. Genomic profiling of mucoepidermoid carcinomas has recently revealed aberrations in BAP1 gene. Therefore, we conducted this study to identify BAP1 loss by immunohistochemistry in these tumors. Mucoepidermoid carcinoma cases were retrieved; hematoxylin-and-eosin stained sections were reviewed. Immunohistochemistry for BAP1 was performed. Forty cases were assessed, including 25 salivary gland and 15 pulmonary mucoepidermoid carcinomas. There were 19 cases in the parotid (76%), two in submandibular gland (8%), and remaining 16% from minor salivary gland locations. Ten (40%) were low grade, nine (36%) were intermediate grade, and six (24%) were high grade mucoepidermoid carcinomas.

Thirteen (86.7%) pulmonary mucoepidermoid carcinomas were tracheobronchial, while two (13.3%) were intraparenchymal; all were low grade mucoepidermoid carcinomas. On immunohistochemistry, BAP1 nuclear staining was retained in all cases (100%), irrespective of tumor location or grade. Therapeutic connotations necessitate the identification of readily applicable techniques to detect BAP1 loss in mucoepidermoid carcinomas. Using immunohistochemistry, loss of BAP1 staining was not seen in any of our cases, suggesting insensitivity of BAP1 IHC to detect aberrations at genomic level in these tumors. Analysis of BAP1 alterations by targeted sequencing may therefore be performed prior to excluding the possibility of response to BAP1-targeted therapeutics based on immunohistochemistry alone.

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PMCID: PMC6401040 [Available on 2020-03-01]
PMID: 30906710

68: Kalasova I, Hanzlikova H, Gupta N, Li Y, AltmÃ¼ller J, Reynolds JJ, Stewart GS, Wollnik B, Yigit G, Caldecott KW. Novel PNKP mutations causing defective DNA strand break repair and PARP1 hyperactivity in MCSZ. Neurol Genet. 2019 Mar 25;5(2):e320. doi: 10.1212/NXG.0000000000000320. eCollection 2019 Apr. PubMed PMID: 31041400; PubMed Central PMCID: PMC6454307.

Objective: To address the relationship between novel mutations in polynucleotide 5'-kinase 3'-phosphatase (PNKP), DNA strand break repair, and neurologic disease.
Methods: We have employed whole-exome sequencing, Sanger sequencing, and molecular/cellular biology.
Results: We describe here a patient with microcephaly with early onset seizures (MCSZ) from the Indian sub-continent harboring 2 novel mutations in PNKP, including a pathogenic mutation in the fork-head associated domain. In addition, we confirm that MCSZ is associated with hyperactivation of the single-strand break sensor protein protein poly (ADP-ribose) polymerase 1 (PARP1) following the induction of abortive topoisomerase I activity, a source of DNA strand breakage associated previously with neurologic disease.
Conclusions: These data expand the spectrum of PNKP mutations associated with MCSZ and show that PARP1 hyperactivation at unrepaired topoisomerase-induced DNA breaks is a molecular feature of this disease.

DOI: 10.1212/NXG.0000000000000320
PMCID: PMC6454307
PMID: 31041400

69: Kalsi AK, Halder A, Jain M, Chaturvedi PK, Mathew M, Sharma JB. Association of raised levels of IL-4 and anti-TPO with hyperprolactinemia. Am J Reprod Immunol. 2019 Mar;81(3):e13085. doi: 10.1111/aji.13085. Epub 2019 Jan 30. PubMed PMID: 30614113.

BACKGROUND AND OBJECTIVE: The modulatory role of prolactin in autoimmune regulation is well established. Hyperprolactinemia is often associated with autoimmune disease like systemic lupus erythematosus and autoimmune thyroid diseases. The objective was to compare levels of direct and indirect autoimmune factors in different categories of hyperprolactinemia cases and predict the direction of association between hyperprolactinemia and autoimmune factors, if any.
METHODS: A total of 102 hyperprolactinemia cases (>100 ng/mL serum prolactin level) were included along with 24 controls. Among 102 hyperprolactinemia cases, there were 36 idiopathic cases, 19 pituitary adenoma cases, 36 drug-induced cases, and 11 cases associated with other secondary/systemic diseases (chronic renal failure, chronic hepatic failure, etc).
MEASUREMENTS: Direct autoimmune markers, IL-2, IFN-γ, IL-4, and IL-5, were measured in serum by ELISA. Indirect autoimmune markers, anti-TPO, anti-tg, anti-CCP, VDRL, platelet count, and aPTT, were measured as per laboratory-defined protocol.
RESULTS: Serum levels of IL-4 and anti-TPO were significantly high in idiopathic hyperprolactinemia cases. Serum IL-4 levels were also significantly high in pituitary adenoma cases, drug-induced cases, and in cases with other secondary

causes of hyperprolactinemia. Serum anti-TPO levels were also significantly high in drug-induced hyperprolactinemia cases.
CONCLUSION: No significant difference in autoimmune factors is observed between macroprolactinemia and true hyperprolactinemia. Serum IL-4 and anti-TPO were high in all categories of hyperprolactinemia. This suggests a possible association of hyperprolactinemia with autoimmune conditions (high IL-4 and anti-TPO), mostly subclinical. Thus, hyperprolactinemia case with serum prolactin level >100 ng/mL may require long-term follow-up for the development of autoimmune disease in future.

DOI: 10.1111/aji.13085
PMID: 30614113

70: Kant K, Tomar AK, Sharma P, Kundu B, Singh S, Yadav S. Human epididymis protein 4 quantification and interaction network analysis in seminal plasma. Protein Pept Lett. 2019 Mar 27. doi: 10.2174/0929866526666190327124919. [Epub ahead of print] PubMed PMID: 30919767.

BACKGROUND: A well-known tissue marker of ovarian cancer, human epididymis protein 4 (HE4) is the member of whey acidic four-disulfide core proteins family. Purified from human seminal plasma and characterized as a cross-class protease inhibitor, HE4 was proposed to shield spermatozoa against proteolytic factors. However, its exact biological function is unknown. Proteins usually function in conjunction with other proteins in the system and thus, identification and analysis of protein networks become essential to decode protein functions.
OBJECTIVE: This study was performed to explore possible role(s) of HE4 in reproductive physiology via identification of its interactome in human seminal plasma.
METHOD: HE4 binding proteins were identified through co-immunoprecipitation and MALDI-TOF/MS analysis. Also, HE4 was quantified by ELISA in fertile and infertile human seminal plasma samples.
RESULTS: Ten HE4 binding proteins were identified, viz. protein phosphatase 1 regulatory subunit 21, protein kinase CLK3, Ankyrin repeat domain-containing protein36A, prostatic acid phosphatase, KIF5C, Spectrin repeat containing, nuclear envelope 1, isoform CRAf, tropomyosin 4, vezatin, utrophin and fibronectin1. This interaction network suggests that HE4 plays multiple roles, specifically in capacitation, sperm motility and maturation. Further, HE4 concentration in human seminal plasma samples was determined by Elisa. Higher HE4 expression in normozoospermia compared to azoospermia and asthenozoospermia affirms its importance in fertilization.
CONCLUSION: Based on identified interactome, it is plausible that HE4 plays a crucial role in fertilization, specifically in sperm maturation, motility and capacitation.

DOI: 10.2174/0929866526666190327124919
PMID: 30919767

71: Kapoor D, Gupta Y, Desai A, Praveen D, Joshi R, Rozati R, Bhatla N, Prabhakaran D, Reddy P, Patel A, Tandon N. Lifestyle intervention programme for Indian women with history of gestational diabetes mellitus. Glob Health Epidemiol Genom. 2019 Mar 11;4:e1. doi: 10.1017/gheg.2018.18. eCollection 2019. PubMed PMID: 30891248; PubMed Central PMCID: PMC6415123.

Aim: To evaluate the feasibility and potential effectiveness of a lifestyle intervention (diet and physical activity) among women with history of gestational diabetes mellitus (GDM), delivered by trained facilitators.
Methods: Fifty-six normoglycaemic or prediabetic women with prior GDM were recruited at mean of 17 months postpartum. Socio-demographic, medical and anthropometric data were collected. Six sessions on lifestyle modification were

delivered in groups (total four groups, with 12-15 women in each group). Pre and post intervention (6 months) weight, body mass index (BMI), waist circumference, 75 g oral glucose tolerance test, blood pressure (BP) and lipid parameters were compared.
Results: The intervention was feasible, with 80% of women attending four or more sessions. Post-intervention analyses showed a significant mean reduction of 1.8 kg in weight, 0.6 kg/m2 in BMI and 2 cm in waist circumference. There was also a significant drop of 0.3 mmol/L in fasting plasma glucose, 0.9 mmol/L in 2 h post glucose load value of plasma glucose, 3.6 mmHg in systolic BP, and 0.15 mmol/L in triglyceride levels. Changes in total cholesterol, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol and diastolic BP were non-significant.
Conclusions: This study showed feasibility of the lifestyle intervention delivered in group sessions to women with prior gestational diabetes.

DOI: 10.1017/gheg.2018.18
PMCID: PMC6415123
PMID: 30891248

72: Khosla R, Vyas AK, Trehanpati N. Dichotomy of Notch signalling in regulating tumour immune surveillance. Scand J Immunol. 2019 Mar;89(3):e12744. doi: 10.1111/sji.12744. Epub 2019 Jan 15. Review. PubMed PMID: 30548971.

Notch signalling is an evolutionarily conserved multifaceted pathway that controls diverse cellular processes. Its role in regulating development and tissue homeostasis is well established. Aberrant activation of the Notch pathway has been implicated in the initiation and progression of many types of cancers. However, although in some cancers Notch signalling acts as a tumour-promoter, in others it is reported to suppress tumour growth and progression. Accumulating evidence suggests the involvement of both the innate and adaptive immune system in the development of various tumours. Currently, extensive studies on investigating the effects of Notch signalling in tumour immune surveillance are being carried out. Interestingly, recent literature shows how the changing expression of Notch genes in different T cell subsets like CD4 and CD8 helps in controlling anti-tumour immune responses. In this review, we discuss in depth the roles of Notch signalling molecules and different immune cells in the context of the tumour microenvironment. We also outline how current knowledge can be exploited to develop novel therapies in order to control the propagation of cancer stem cells.

DOI: 10.1111/sji.12744
PMID: 30548971 [Indexed for MEDLINE]

73: Khurana C, Tandon S, Chand S, Chinmaya BR. Effectiveness of oral health education program using braille text in a group of visually impaired children-before and after comparison trial. J Educ Health Promot. 2019 Mar 14;8:50. doi: 10.4103/jehp.jehp_233_18. eCollection 2019. PubMed PMID: 31008117; PubMed Central PMCID: PMC6442267.

CONTEXT: Vision is the most important sense for interpreting the world and when sight is impaired, especially in childhood it can have detrimental effects on one's life. To maintain the oral health status of such group requires special approach.
AIM: The aim of this study is to evaluate the impact of Braille text and verbal, oral hygiene instructions on the oral health status of visually impaired children.
SETTINGS AND DESIGN: A prospective nonrandomized before and after comparison trial without any control group was conducted among 165 children aged 7-19 years residing in one of the blind schools in Delhi.
MATERIALS AND METHODS: A questionnaire was developed to record the source of oral health knowledge and practices. Oral health status of the children was evaluated by recording plaque index (PI) and gingival index (GI) scores at 1, 3, and 5

months intervals. Periodic reinforcement of oral health education was performed with the help of instructions in Braille language.
STATISTICAL ANALYSIS: Paired t-test and McNemar tests were used to assess the difference between the scores before and after oral health education.
RESULTS: Among completely blind children, the mean difference of PI and GI score from baseline to the last evaluation was found to be 0.56 and 0.28, whereas among partially blind children, it was found to be 0.58 and 0.25, respectively. All the above values were statistically significant ($P < 0.001$).
CONCLUSION: Visually impaired children irrespective of the degree of blindness could maintain an acceptable level of oral hygiene when taught using Braille text for instructions. However, continuous motivation and reinforcement at regular intervals are required for the maintenance of oral health status.

DOI: 10.4103/jehp.jehp_233_18
PMCID: PMC6442267
PMID: 31008117

74: Krishnappa D, Sharma SK, Singh AD, Sinha S, Ammini AC, Soneja M. Impact of tuberculosis on glycaemic status: A neglected association. Indian J Med Res. 2019 Mar;149(3):384-388. doi: 10.4103/ijmr.IJMR_1927_17. PubMed PMID: 31249204.

Background & objectives: Diabetes mellitus (DM) is an important risk factor for tuberculosis and has received increasing emphasis. However, the reverse association of tuberculosis impacting blood sugar levels has not been well studied. The present study was conducted to evaluate the prevalence of hyperglycemia in patients with tuberculosis and assess its resolution following successful treatment of tuberculosis.
Methods: In this prospective study, a total of 582 patients with tuberculosis were evaluated for hyperglycaemia [DM or impaired glucose tolerance (IGT)] with random blood sugar (RBS) and all patients with RBS >100 mg/dl were subjected to a 75 g oral glucose tolerance test (OGTT). All patients received thrice weekly intermittent Directly Observed Treatment Short Course (DOTS) for tuberculosis. Patients with hyperglycaemia were re-evaluated at the end of anti-tuberculosis treatment with an OGTT and glycated hemoglobin (HbA1c) levels to assess for glycaemic status.
Results: In the present study, 41 of the 582 patients were found to have DM [7%, 95% confidence interval (CI) (5.2, 9.4)] while 26 patients were found to have IGT [4.5%, 95% CI (3, 6.5)]. Three patients were lost to follow up. Of the 26 patients with IGT, 17 [65.4%, 95% CI (46.1, 80.7)] reverted to euglycaemic status following successful treatment of tuberculosis, while the blood sugar levels improved in all patients with DM following treatment of tuberculosis.
Interpretation & conclusions: Our study results show that tuberculosis adversely impacts glycaemic status with improvement in blood sugar levels at the end of successful treatment of tuberculosis. Longitudinal studies with large sample size are required to confirm these findings.

DOI: 10.4103/ijmr.IJMR_1927_17
PMID: 31249204

75: Kumar K, Sharma R. Over-the-counter Use of Glucocorticoids causing Severe Stunting in Siblings. Indian Pediatr. 2019 Mar 15;56(3):251. PubMed PMID: 30955003.

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Recently conducted human phase- I trials showed protective effect of anti-HIV-1 broadly neutralizing antibodies (bnAbs). The V3 region of the HIV-1 envelope is highly conserved as it is the co-receptor binding site, and is highly immunogenic. Recombinant single-chain antibody fragments (scFvs) can serve as potential tools for construction of chimeric/bispecific antibodies that can

target different epitopes on the HIV-1 envelope. Previously, we have constructed a V3 specific human scFv phage recombinant library by a combinational approach of Epstein-Barr virus (EBV) transformation and antigen (V3) preselection, using peripheral blood mononuclear cells (PBMCs), from a subtype C HIV-1 infected antiretroviral naive donor. In the present study, by biopanning this recombinant scFv phage library with V3B (subtype B) and V3C (subtype C) peptides, we identified unique cross reactive anti-V3 scFv monoclonals. These scFvs demonstrated cross-neutralizing activity when tested against subtype A, subtype B, and subtype C viruses. Further, molecular modeling of the anti-V3 scFvs with V3C and V3B peptides predicted their sites of interaction with the scFvs, providing insights for future immunogen design studies. A large collection of such monoclonal antibody fragments with diverse epitope specificities can be useful immunotherapeutic reagents along with antiretroviral drugs to prevent HIV-1 infection and disease progression.

DOI: 10.1007/s12010-018-2862-8
PMID: 30151637 [Indexed for MEDLINE]

77: Kumar S. Infrared spectroscopy could be a diagnostic tool in dermatology. Br J Dermatol. 2019 Mar;180(3):459-460. doi: 10.1111/bjd.17410. PubMed PMID: 30821375.

78: Kumar V, Kumawat D, Kumar P. Swept source optical coherence tomography analysis of choroidal thickness in macular telangiectasia type 2: a case-control study. Graefes Arch Clin Exp Ophthalmol. 2019 Mar;257(3):567-573. doi: 10.1007/s00417-018-04215-9. Epub 2018 Dec 17. PubMed PMID: 30560414.

PURPOSE: There has been a recent interest in the association of macular telangiectasia (MacTel) type 2 with central serous choroidopathy and other pachychoroid disorders. This study was performed to assess the subfoveal choroidal thickness (SFCT) in patients with MacTel type 2 and compare it with healthy controls using swept source optical coherence tomography (SS-OCT).
METHODS: It was a retrospective case-control study performed at a tertiary eye care center. The cases constituted patients with MacTel type 2 detected over the last 2 years (April 2016 to March 2018). The controls were healthy adults with no posterior segment pathology. The patients were evaluated with color fundus photography, SS-OCT (Triton, Topcon Inc., Oakland, New Jersey, USA) and fundus fluorescein angiography. The cases were staged based on Gass and Blodi classification. SFCT was compared between the two groups.
RESULTS: Sixty-five eyes of 33 patients with MacTel were included. The controls consisted of 61 eyes of 33 healthy age-matched ($p = 0.81$) and sex-matched ($p = 0.31$) adults. The mean SFCT in cases (353.0 ± 91.2 µm) was higher than controls (289.2 ± 69.0 µm), and this difference was statistically significant ($p = 0.0001$). The mean SFCT was different in various stages: 346.6 ± 86.3 µm (stage 2), 334.6 ± 90.2 µm (stage 3), 374.6 ± 94.0 µm (stage 4), and 294.8 ± 68.8 µm (stage 5), though this was not statistically significant ($p = 0.28$).
CONCLUSIONS: The choroid in MacTel type 2 patients was significantly thickened as compared to controls. SFCT may vary as the structural changes worsen over time.

DOI: 10.1007/s00417-018-04215-9
PMID: 30560414 [Indexed for MEDLINE]

79: Kumar V, Kumar P, Ravani R, Gupta P. Macular telangiectasia type II with pachychoroid spectrum of macular disorders. Eur J Ophthalmol. 2019 Mar;29(2):216-222. doi: 10.1177/1120672118769527. Epub 2018 Apr 20. PubMed PMID: 29676172.

PURPOSE:: To report the cases with features of macular telangiectasia type II and pachychoroid spectrum of macular disorders simultaneously.
METHODS:: It is a retrospective case series from a tertiary eye care center. Multimodal imaging features of these eyes including color fundus photographs, red free imaging, short-wave autofluorescence, fundus fluorescein angiography,

indocyanine green angiography, and optical coherence tomography were studied.
RESULTS:: Six eyes of three patients having combination of macular telangiectasia type II and pachychoroid group of disorders were found. Three eyes showed features of central serous chorioretinopathy, one eye had polypoidal choroidal vasculopathy, one eye had pachychoroid pigment epitheliopathy and one had thickened choroid.
CONCLUSION:: This is the first report of macular telangiectasia type II in association with the pachychoroid spectrum of macular disorders and provides insight into possible common etiopathogenetic mechanisms.

DOI: 10.1177/1120672118769527
PMID: 29676172 [Indexed for MEDLINE]

80: Kumar Vimal A, Kant Godiyal A, Singh U, Bhasin S, Joshi D. Transfemoral amputee's limit of stability and sway analysis during weight shifting exercise with a vibrotactile feedback system. Somatosens Mot Res. 2019 Mar;36(1):31-41. doi: 10.1080/08990220.2019.1572602. Epub 2019 Mar 14. PubMed PMID: 30870060.

Amputation in the transfemoral amputee (TFA) results in loss of sensory feedback of the amputated limb and therefore results in the poor postural stability. To assess the postural stability, the limit of stability (LOS) is a reliable parameter. In this study, we have investigated the effect of vibrotactile feedback (VF) on the LOS during the weight shifting exercise (WSE) for a TFA. The data of centre of pressure (COP) during WSE was collected from five TFA and five healthy individuals using a zebris force plate. The VF was provided on the amputated/healthy limb's anterior and posterior part of the stump/thigh during forward and backward WSE, respectively. A customized foot insole with 24 embedded dielectric sensors was used to drive the vibratory motor. The effect of VF was analyzed by pre and post-test. Results show that with the use of VF, TFA significantly improved (t-test, $p < .05$) the sound limb's LOS during forward WSE. Also, ANOVA analysis between WSE divisions shows that the prosthetic limb does not follow the path of WSE. We further examine the spectral power using the Welch method to determine the dominant sway frequency of COP. It shows a decreased frequency between 0.5-2 Hz in the healthy and decreased frequency between 0-0.5 Hz and >2 Hz in the amputee with VF. It concluded that VF could improve the LOS of TFA during WSE which ultimately leads to postural stability enhancement.

DOI: 10.1080/08990220.2019.1572602
PMID: 30870060

81: Kumarasinghe SPW, Pandya A, Chandran V, Rodrigues M, Dlova NC, Kang HY, Ramam M, Dayrit JF, Goh BK, Parsad D. A global consensus statement on ashy dermatosis, erythema dyschromicum perstans, lichen planus pigmentosus, idiopathic eruptive macular pigmentation, and Riehl's melanosis. Int J Dermatol. 2019 Mar;58(3):263-272. doi: 10.1111/ijd.14189. Epub 2018 Sep 3. Review. PubMed PMID: 30176055.

Ashy dermatosis (AD), lichen planus pigmentosus (LPP), erythema dyschromicum perstans (EDP), and idiopathic eruptive macular pigmentation are several acquired macular hyperpigmentation disorders of uncertain etiology described in literature. Most of the published studies on these disorders are not exactly comparable, as there are no clear definitions and different regions in the world describe similar conditions under different names. A consensus on the terminology of various morphologies of acquired macular pigmentation of uncertain etiology was a long-felt need. Several meetings of pigmentary disorders experts were held to address this problem. A consensus was reached after several meetings and collation of e-mailed questionnaire responses and e-mail communications among the authors of publications on the above conditions. This was achieved by a global consensus forum on AD, LPP, and EDP, established after the 22nd International Pigment Cell Conference held in Singapore in 2014. Thirty-nine experts representing 18 countries participated in the deliberations. The main focus of the deliberations was terminology of the conditions; as such, we present here the consensus statement of the forum and briefly review the available literature on the subject. We have not attempted to discuss treatment modalities in detail.

DOI: 10.1111/ijd.14189
PMID: 30176055 [Indexed for MEDLINE]

82: Kumari N, Yadav S. Modulation of protein oligomerization: An overview. Prog Biophys Mol Biol. 2019 Mar 11. pii: S0079-6107(18)30196-2. doi: 10.1016/j.pbiomolbio.2019.03.003. [Epub ahead of print] Review. PubMed PMID: 30872157.

A large section of cellular proteins in both prokaryotic and eukaryotic systems have oligomeric property. Intently, oligomerization of protein is an invaluable phenomenon from the point of view of protein evolution. This review comprises an overview on modulation of protein oligomerization. The comprehensive modulation of protein oligomerization can be supportive for effective drug designing in the future. The common mechanisms of protein oligomerization are domain swapping and ligand induced dimerization. Infrequent mechanism of protein oligomerization involves point mutations at the dimer interface, post-translational modification and insertion/deletion at the interface. Predominantly, ligand induced oligomerization is the most useful method to regulate the protein oligomerization that can act as a modulator. Thus, functional modulation of oligomeric proteins can be done, both in-vitro and in-vivo, using various artificial and natural modulators, respectively. Though, the biophysical methods, like microscopy and spectroscopy, have strong potential to characterize the oligomeric proteins. Oligomeric proteins can be characterized biochemically too. Hence, this review illustrates the regulation of protein oligomerization using several modulators, in the future, these can be used for effective drug designing to cure several diseases associated with oligomeric proteins.

DOI: 10.1016/j.pbiomolbio.2019.03.003
PMID: 30872157

83: Kusuma YS, Burman D, Kumari R, Lamkang AS, Babu BV. Impact of health education based intervention on community's awareness of dengue and its prevention in Delhi, India. Glob Health Promot. 2019 Mar;26(1):50-59. doi: 10.1177/1757975916686912. Epub 2017 Mar 28. PubMed PMID: 28349734.

Dengue is endemic in India. The capital, Delhi, continues to witness a higher number of cases due to urbanization-related factors. This study is intended to implement health education towards prevention of dengue, and to assess its impact on people's knowledge and practices related to causes and prevention of dengue among urban poor in Delhi. Pre- (n = 484) and post- (n = 496) intervention surveys from 15 sub-clusters from five slums/slum-like settlements in Delhi were carried out. Health education based intervention was carried out through partnership with the municipal bodies and non-governmental organizations. Socio-demographic characteristics of participants were similar in both surveys. Intervention resulted in significant increase in knowledge on cause, symptom perception and mosquito behaviour in terms of breeding and biting habits. Practice of personal protection measures increased significantly. The participation of people increased during intervention compared to the routine programme. Health education based interventions are instrumental in improving people's knowledge and behaviour. Hence, routine health educational activities as a supportive strategy in the health system need to be strengthened. New integrated approaches such as eco-bio-social approaches with community participation are to be developed and tested in endemic settings like Delhi.

DOI: 10.1177/1757975916686912
PMID: 28349734

84: Lopes BA, Meyer C, Barbosa TC, Poubel CP, Mansur MB, Duployez N, Bashton M, Harrison CJ, Zur Stadt U, Horstmann M, Pombo-de-Oliveira MS, Palmi C, Cazzaniga

G, Venn NC, Sutton R, Alonso CN, Tsaur G, Gupta SK, Bakhshi S, Marschalek R, Emerenciano M. IKZF1 Deletions with COBL Breakpoints Are Not Driven by RAG-Mediated Recombination Events in Acute Lymphoblastic Leukemia. Transl Oncol. 2019 May;12(5):726-732. doi: 10.1016/j.tranon.2019.02.002. Epub 2019 Mar 13. PubMed PMID: 30877974; PubMed Central PMCID: PMC6423364.

IKZF1 deletion (ΔIKZF1) is an important predictor of relapse in both childhood and adult B-cell precursor acute lymphoblastic leukemia (B-ALL). Previously, we revealed that COBL is a hotspot for breakpoints in leukemia and could promote IKZF1 deletions. Through an international collaboration, we provide a detailed genetic and clinical picture of B-ALL with COBL rearrangements (COBL-r). Patients with B-ALL and IKZF1 deletion (n = 133) were included. IKZF1 Δ1-8 were associated with large alterations within chromosome 7: monosomy 7 (18%), isochromosome 7q (10%), 7p loss (19%), and interstitial deletions (53%). The latter included COBL-r, which were found in 12% of the IKZF1 Δ1-8 cohort. Patients with COBL-r are mostly classified as intermediate cytogenetic risk and frequently harbor ETV6, PAX5, CDKN2A/B deletions. Overall, 56% of breakpoints were located within COBL intron 5. Cryptic recombination signal sequence motifs were broadly distributed within the sequence of COBL, and no enrichment for the breakpoint cluster region was found. In summary, a diverse spectrum of alterations characterizes ΔIKZF1 and they also include deletion breakpoints within COBL. We confirmed that COBL is a hotspot associated with ΔIKZF1, but these rearrangements are not driven by RAG-mediated recombination.

DOI: 10.1016/j.tranon.2019.02.002
PMCID: PMC6423364
PMID: 30877974

85: M K MA, Kumaresan A, Yadav S, Mohanty TK, Datta TK. Comparative proteomic analysis of high- and low-fertile buffalo bull spermatozoa for identification of fertility-associated proteins. Reprod Domest Anim. 2019 May;54(5):786-794. doi: 10.1111/rda.13426. Epub 2019 Mar 23. PubMed PMID: 30820981.

The present study identified few potential proteins in the spermatozoa of buffalo bulls that can be used as an aid in fertility determination through comparative proteomics. The sperm proteome of high-fertile buffalo bulls was compared with that of low-fertile buffalo bulls using two-dimensional difference gel electrophoresis (2D-DIGE), and the differentially expressed proteins were identified through mass spectrometric method. The protein interaction network and the functional bioinformatics analysis of differentially expressed proteins were also carried out. In the spermatozoa of high-fertile bulls, 10 proteins were found overexpressed and 15 proteins were underexpressed at the level of twofold or more ($p \leq 0.05$). The proteins overexpressed in high-fertile spermatozoa were PDZD8, GTF2F2, ZNF397, KIZ, LOH12CR1, ACRBP, PRSS37, CYP11B2, F13A1 and SPO11, whereas those overexpressed in low-fertile spermatozoa were MT1A, ATP5F1, CS, TCRB, PRODH2, HARS, IDH3A, SRPK3, Uncharacterized protein C9orf9 homolog isoform X4, TUBB2B, GPR4, PMP2, CTSL1, TPPP2 and EGFL6. The differential expression ranged from 2.0- to 6.1-fold between the two groups, where CYP11B2 was high abundant in high-fertile spermatozoa and MT1A was highly abundant in low-fertile spermatozoa. Most of the proteins overexpressed in low-fertile spermatozoa were related to energy metabolism and capacitation factors, pointing out the possible role of pre-mature capacitation and cryo-damages in reducing the fertility of cryopreserved buffalo spermatozoa.

DOI: 10.1111/rda.13426
PMID: 30820981 [Indexed for MEDLINE]

86: Mahajan S, Suri V, Sharma MC, Kedia S, Sardana H, Nakra T. Primary intracranial malignant ectomesenchymoma in an adult: Report of a rare case and review of the literature. Neuropathology. 2019 Jun;39(3):200-206. doi:

10.1111/neup.12547. Epub 2019 Mar 25. PubMed PMID: 30907031.

Malignant ectomesenchymoma (MEM) is an exceedingly rare rapidly progressing tumor of soft tissues of the central nervous system, believed to be derived from neural crest cells. The majority of cases have been observed in young children or adolescents. So far only 11 patients with intracranial manifestations (with confirmed clinicopathological data) have been documented. We report the first case of adult intracranial MEM in a 54-year-old man who presented with a 4 months history of headache and weakness of right side of the body. Magnetic resonance imaging showed a homogenously enhanced dural-based lesion in the left fronto-temporo-parietal lobe with significant perilesional edema and mass effect. No metastatic disease was identified and the lesion was grossly resected. Histopathological and immunohistochemical examination revealed mature and immature neurons and bizarre astrocytes admixed with a mesenchymal spindle cell (rhabdomyoblastic) component. Specific risk factors that contribute toward the development of MEM are unknown. Due to the scarcity of reported cases the role of adjuvant therapy is unclear.

DOI: 10.1111/neup.12547
PMID: 30907031

87: Majumdar A, Wilkinson E, Rinu PK, Maung TM, Bachani D, Punia JS, Jain S, Yadav T, Jarhyan P, Mohan S, Kumar AMV. Tuberculosis-diabetes screening: how well are we doing? A mixed-methods study from North India. Public Health Action. 2019 Mar 21;9(1):3-10. doi: 10.5588/pha.18.0048. PubMed PMID: 30963036; PubMed Central PMCID: PMC6436489.

Setting: Public health care facilities in Sonipat District, Haryana State, India.
Objectives: To assess 1) the proportion of tuberculosis (TB) patients screened for diabetes mellitus (DM) and vice versa, 2) factors associated with screening, and 3) the enablers, barriers and solutions related to screening.
Design: A mixed-methods study with quantitative (cohort study involving record reviews of patients registered between November 2016 and April 2017) and qualitative (interviews of patients, health care providers [HCPs] and key district-level staff) components.
Results: Screening for TB among DM patients was not implemented, despite documents indicating that it had been. Of 562 TB patients, only 137 (24%) were screened for DM. TB patients registered at tertiary and secondary health centres were more likely to be screened than primary health centres. Low patient awareness, poor knowledge of guidelines among HCPs, lack of staff and inadequate training were barriers to screening. Enablers were the positive attitude of HCPs and programme staff. The key solutions suggested were to improve awareness of HCPs and patients regarding the need for screening, training of HCPs and wider availability of DM testing facilities.
Conclusion: The implementation of bidirectional screening was poor. Adequate staffing, regular training, continuous laboratory supplies for DM diagnosis and widespread publicity should be ensured.

Publisher: Structures de santé publiques du district de Sonipat, état d'Haryana, Inde.1) Evaluer la proportion de patients avec la tuberculose (TB) ayant eu une recherche de diabète (DM) et vice-versa, 2) les facteurs associés à ce dépistage ; et 3) les facilitateurs, les contraintes et les solutions relatifs au dépistage.Une étude à méthodes mixtes comportant des composants quantitatifs (étude de cohorte basée sur une revue des dossiers des patients enregistrés entre novembre 2016 et avril 2017) et qualitatifs (entretiens avec des patients, des prestataires de soins de santé [HCP] et du personnel clé du district).Le dépistage de la TB parmi les patients DM n'a pas été mis en œuvre, malgré les documents indiquant qu'il l'avait été. Sur 562 patients TB, seulement 137 (24%) ont été dépistés à la recherche de DM. Les patients TB enregistrés dans des centres de santé tertiaires et secondaires ont été plus susceptibles d'être dépistés, comparés à ceux des centres de santé primaires. La faible sensibilisation des patients, une connaissance médiocre des directives parmi les

HCP, le manque de personnel et une formation insuffisante ont été les contraintes au dépistage. L'attitude positive des HCP et du personnel du programme a favorisé le dépistage. Les solutions principales suggérées ont été d'améliorer la sensibilisation des HCP et des patients en matière de nécessité du dépistage, de la formation des HCP et de la plus grande disponibilité des structures de recherche du DM.La mise en œuvre du dépistage bidirectionnel a été médiocre. Il faut assurer suffisamment de personnel, une formation régulière, des fournitures de laboratoire continues pour le diagnostic du DM ainsi qu'une vaste propagande.Publisher: Establecimientos de atención de salud en el distrito Sonipat, del estado de Haryana en la India.1) Evaluar la proporción de pacientes con tuberculosis (TB) en quienes se practica el tamizaje de la diabetes (DM) y vice versa; 2) los factores asociados con la práctica del tamizaje; y 3) los factores facilitadores, los obstáculos y las soluciones en materia de detección sistemática.Fue este un estudio de métodos mixtos con componentes cuantitativos (estudio de cohortes a partir de las historias clínicas de los pacientes registrados de noviembre del 2016 a abril del 2017) y componentes cualitativos (entrevistas a los pacientes, los proveedores de atención de salud [HCP] y miembros clave del personal distrital).La detección sistemática de la TB en los pacientes con diagnóstico de DM no se practicaba, pese a los documentos que afirmaban lo contrario. De los 562 pacientes con TB, solo en 137 (24%) se practicó el tamizaje de la DM. La probabilidad de recibir el tamizaje fue mayor en los pacientes con TB registrados en los centros de atención terciaria y secundaria, que en los registrados en centros de atención primaria. Los obstáculos al tamizaje fueron la escasa sensibilización de los pacientes, el desconocimiento de las directrices por parte de los HCP, la escasez de personal y la capacitación deficiente. Los factores que facilitaron la práctica del tamizaje fueron la actitud positiva de los HCP y del personal del programa. Las principales soluciones propuestas fueron reforzar la sensibilización de los HCP y los pacientes con respecto a la necesidad del tamizaje, la capacitación de los HCP y una mayor disponibilidad de establecimientos que practiquen las pruebas de la DM.La ejecución de la detección sistemática recíproca era deficiente. Es necesario procurar una dotación adecuada de personal, realizar capacitaciones periódicas y velar por un abastecimiento continuo de suministros de laboratorio para el diagnóstico de la DM, además de realizar extensas campañas de comunicación.
DOI: 10.5588/pha.18.0048
PMCID: PMC6436489
PMID: 30963036

88: Makharia GK, Catassi C. Celiac Disease in Asia. Gastroenterol Clin North Am. 2019 Mar;48(1):101-113. doi: 10.1016/j.gtc.2018.09.007. Epub 2018 Dec 13. Review. PubMed PMID: 30711203.

Celiac disease, once thought to be very uncommon in Asia, is now emerging in many Asian countries. Although the absolute number of patients with celiac disease at present is not very high, this number is expected to increase markedly over the next few years/decades owing to increasing awareness. It is now that the medical community across the Asia should define the extent of the problem and prepare to handle the impending epidemic of celiac disease in Asia.

DOI: 10.1016/j.gtc.2018.09.007
PMID: 30711203 [Indexed for MEDLINE]

89: Malhotra R, Kumar V, Wahal N, ClavÃ© A, Kennedy JA, Murray DW, Pandit H. New Instrumentation Improves Patient Satisfaction and Component Positioning for Mobile-Bearing Medial Unicompartmental Knee Replacement. Indian J Orthop. 2019 Mar-Apr;53(2):289-296. doi: 10.4103/ortho.IJOrtho_172_17. PubMed PMID: 30967699; PubMed Central PMCID: PMC6415557.

Background: The Oxford unicompartmental knee replacement (OUKR) has achieved excellent functional outcomes and long term survivorship in many single center and single surgeon series. However, in national registries, the failure rates are

up to three times higher than total knee replacement. This is at least in part due to difficulty experienced by low-volume surgeons in implanting the prosthesis accurately. A new instrumentation system (Microplasty) was introduced to help surgeons achieve better component positioning, however, it is not known whether the new instruments achieve that goal. This study investigates whether the new system achieves better component positioning and whether it improves the clinical outcomes when compared to the existing instruments.
Materials and Methods: This retrospective cohort study compared 50 consecutive OUKR implanted using the conventional Phase 3 instrumentation with 100 consecutive OUKR implanted using the new Microplasty instrumentation. Component orientation was measured on postoperative radiographs, and the percentage outside the recommended range was identified. Intraoperative data and retrospectively collected clinical data were also analyzed.
Results: Femoral component alignment improved significantly, and there were no outliers in the Microplasty group. Although there were fewer tibial component alignment outliers with Microplasty, the difference was not significant. The intraoperative incidence of tibial recut, patient satisfaction and patient expectations was significantly better in the Microplasty group. The Oxford Knee Scores were also better with Microplasty, however, the difference was not significant.
Conclusion: Microplasty instrumentation helps the surgeon achieve optimal component positioning and reduces the need for tibial recut. The clinical outcomes are also better with the Microplasty instrumentation.

DOI: 10.4103/ortho.IJOrtho_172_17
PMCID: PMC6415557
PMID: 30967699

90: Malhotra R, Gaba S, Wahal N, Kumar V, Srivastava DN, Pandit H. Femoral Component Sizing in Oxford Unicompartmental Knee Replacement: Existing Guidelines Do Not Work for Indian Patients. J Knee Surg. 2019 Mar;32(3):205-210. doi: 10.1055/s-0038-1635113. Epub 2018 Feb 28. PubMed PMID: 29490403.

Oxford unicompartmental knee replacement (OUKR) has shown excellent long-term clinical outcomes as well as implant survival when used for correct indications with optimal surgical technique. Anteromedial osteoarthritis is highly prevalent in Indian patients, and OUKR is the ideal treatment option in such cases. Uncertainty prevails about the best method to determine femoral component size in OUKR. Preoperative templating has been shown to be inaccurate, while height- and gender-based guidelines based on European population might not apply to the Indian patients. Microplasty instrumentation introduced in 2012 introduced the sizing spoon, which has the dual function of femoral component sizing and determining the level of tibia cut. We aimed to check the accuracy of sizing spoon and also to determine whether the present guidelines are appropriate for use in the Indian patients. A total of 130 consecutive Oxford mobile bearing medial cemented UKR performed using the Microplasty instrumentation were included. The ideal femoral component size for each knee was recorded by looking for overhang and underhang in post-operative lateral knee radiograph. The accuracy of previous guidelines was determined by applying them to our study population. Previously published guidelines (which were based on Western population) proved to be accurate in only 37% of cases. Hence, based on the demographics of our study population, we formulated modified height- and gender-based guidelines, which would better suit the Indian population. Accuracy of modified guidelines was estimated to be 74%. The overall accuracy of sizing spoon (75%), when used as an intraoperative guide, was similar to that of modified guidelines. Existing guidelines for femoral component sizing do not work in Indian patients. Modified guidelines and use of intraoperative spoon should be used to choose the optimal implant size while performing OUKR in Indian patients.

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DOI: 10.1055/s-0038-1635113
PMID: 29490403 [Indexed for MEDLINE]

91: Mandal P, Parmar A, Ambekar A, Dhawan A. Substance use among treatment seeking Indian adolescent girls: Are they unique? Asian J Psychiatr. 2019 Mar;41:17-19. doi: 10.1016/j.ajp.2019.03.007. Epub 2019 Mar 6. PubMed PMID: 30870647.

INTRODUCTION: Substance use among adolescents is on the rise across the globe along with a diminution of gender gap observed earlier posing a huge public health burden. Unfortunately, there is a paucity of literature on adolescent substance use. The literature is even sparse about substance use among adolescent girls. The current study aims to provide a glimpse of the profile and pattern of substance use among Indian adolescent girls seeking treatment for substance use problems in a specialty addiction treatment centre in India.
MATERIALS AND METHODS: This study is retrospective in design. Information regarding socio-demographics and substance use were extracted from the medical records of adolescent girls (≤ 19 years) who sought treatment for substance use problems during 2004-2018, at the adolescent clinic of a tertiary addiction treatment centre located in north India was retrieved carried out. The data was statistically analysed using SPSS.
RESULTS: A total of 28 girls sought treatment during this period. The mean age of the girls was 15.89 ± 2.72 years. Most of the girls were students (6/28) or had never started working (12/28). Majority of them were coming from an urban background (89.3%) and were educated up to 10th class (85.5%). A total of 17 (60.7%) girls sought treatment for opioids use of which 11 were using illicit opioids like heroin and five (29.9%) of them reported taking opioids by injecting route primarily. History of past abstinence attempts, and treatment attempt were present in very few of them (10.7% and 14.3%).
CONCLUSION: Our study suggests a distinct substance use profile of adolescent girls. There is a need for further systematic studies to assess their clinical needs.

DOI: 10.1016/j.ajp.2019.03.007
PMID: 30870647

92: Mantoo MR, Tripathy SK, Phulware RH, Bagri NK, Hari P, Barwad A. Juvenile dermatomyositis with IgA nephropathy: case-based review. Rheumatol Int. 2019 Mar;39(3):577-581. doi: 10.1007/s00296-018-4229-4. Epub 2018 Dec 14. Review. PubMed PMID: 30552457.

Juvenile dermatomyositis (JDM) is the most common childhood idiopathic inflammatory myopathy (IIM). It is characterized by the classic skin rash in the form of Gottron papules and heliotrope rash, and symmetric proximal muscle weakness. Renal involvement in JDM is rare which includes acute kidney injury and glomerulonephritis. We report a 10-year-old boy with juvenile dermatomyositis and IgA nephropathy. Child responded dramatically to the conventional therapy with steroids and methotrexate for the primary disease, and did not require any additional treatment for his renal disease. Child's primary disease is in remission and has normal urinalysis with normal renal function at 6-month follow-up. We reviewed the literature and found 11 cases of IIMs with renal involvement. Four patients (one JDM, two polymyositis, and one dermatomyositis) had IgA nephropathy out of which three patients responded to the conventional therapy of primary disease and only one patient with polymyositis needed hiking immunosuppression targeted for renal condition. Therapy targeting the underlying disorder is usually sufficient in patients with JDM and secondary IgA nephropathy.

DOI: 10.1007/s00296-018-4229-4
PMID: 30552457

93: Marwaha RK, Garg MK, Dang N, Mithal A, Narang A, Chadha A, Gupta N, Kumar MR. Reference range of random urinary calcium creatinine ratio in North Indian children and adolescents. Ann Pediatr Endocrinol Metab. 2019 Mar;24(1):34-40. doi: 10.6065/apem.2019.24.1.34. Epub 2019 Mar 31. PubMed PMID: 30943678; PubMed

Central PMCID: PMC6449613.

PURPOSE: Urinary calcium creatinine ratio (UCaCrR) is a reliable indicator for monitoring hypercalciuria following vitamin D supplementation. However, the reference range varies from region to region. Previous studies did not take vitamin D and parathyroid hormone status into account while evaluating UCaCrR. Hence, we undertook this study to establish the 95th percentile of UCaCrR as an indicator of hypercalciuria in North Indian children and adolescents.
METHODS: Four hundred seventy-three participants (boys 62.2%, girls 37.8%) with adequate dietary calcium intake, normal serum levels of 25-hydroxy-vitamin D (>20 ng/mL), and without secondary hyperparathyroidism following supplementation were selected for evaluation of UCaCrR.
RESULTS: The mean age and body mass index of subjects were 11.2±2.6 years and 18.0±3.6 kg/m2, respectively. The 95th percentile of UCaCrR in the study population was 0.126. The mean, median, and 95th percentile of UCaCrR was significantly higher in prepubertal children (age ≤10 years) (0.0586±0.0374, median=0.0548, 95th percentile=0.136) compared to those >10 years old (0.0503±0.0363, median=0.0407, 95th percentile=0.123, P=0.02). No significant difference in UCaCrR was observed between genders and different weight categories.
CONCLUSION: UCaCrR of 0.13 defines the cutoff value for hypercalciuria in North Indian children and adolescents with adequate dietary intake of calcium and sufficient serum vitamin D levels.

DOI: 10.6065/apem.2019.24.1.34
PMCID: PMC6449613
PMID: 30943678

94: Meena JP, Gupta AK. Neuroblastoma in a Developing Country: Miles to Go. Indian J Pediatr. 2019 May;86(5):403-405. doi: 10.1007/s12098-019-02930-7. Epub 2019 Mar 26. Review. PubMed PMID: 30915646.

95: Meena RK, Doddamani RS, Sharma R. Contiguous Diastematomyelia with Lipomyelomeningocele in Each Hemicord-an Exceptional Case of Spinal Dysraphism. World Neurosurg. 2019 Mar;123:103-107. doi: 10.1016/j.wneu.2018.11.225. Epub 2018 Dec 6. PubMed PMID: 30529523.

BACKGROUND: Split cord malformation (SCM) is a rare congenital anomaly of the spinal cord. Rarely, SCM coexists with a variety of dysraphic pathologies that occur at the same or different spinal level in a patient. Exceptionally rare is the occurrence of SCM type 1 and lipomeningomyelocele of each hemicord.
CASE DESCRIPTION: A 15-month-old girl presented with gradually progressive, painless swelling in the lower back since birth. Spinal imaging showed the presence of type I SCM associated with lipomeningomyelocele of each hemicord. Surgical exploration and detethering was done.
CONCLUSIONS: Management of such complex cases of spinal dysraphism is challenging. Delineating their embryologic basis, detailed radiologic assessment, and meticulous microneurosurgical techniques are the cornerstone for successful management.

DOI: 10.1016/j.wneu.2018.11.225
PMID: 30529523 [Indexed for MEDLINE]

96: Mittal P, Agarwal SK, Singh G, Bhowmik D, Mahajan S, Dinda A, Bagchi S. Spectrum of biopsy-proven renal disease in northern India: A single-centre study. Nephrology (Carlton). 2019 Mar 4. doi: 10.1111/nep.13582. [Epub ahead of print] PubMed PMID: 30834630.

AIM: Pattern of kidney diseases varies across geographies due to multiple factors. There is a paucity of information from South Asia due to the absence of nationwide/regional biopsy registries. This study aimed to delineate the spectrum of renal parenchymal diseases in our region.

METHODS: Records of kidney biopsies done in our nephrology department between 2006 and 2016 were analysed. Clinico-pathological correlation was done from the available records.
RESULTS: Of the 3275 biopsy evaluated, 61.9% were males, and mean age was 33.2 ± 14.2 years. 6.2% patients were elderly (age ≥ 60 years). Nephrotic syndrome (60.3%) was the commonest indication for biopsy. On histology, 73.0% patients had primary glomerulonephritis (GN), 15.5% secondary GN, 5.3% tubulo-interstitial and 3.7% vascular disease. Focal segmental glomerulosclerosis (FSGS) was the commonest primary GN accounting for 18.2% of all GNs, followed by minimal change disease (16.8%), membranous nephropathy (MN) (16.0%) and IgA nephropathy (10.4%). Lupus nephritis (10.6%) and amyloidosis (3.7%) were the commonest secondary GN. The commonest cause of nephrotic syndrome was minimal change disease (22.9%), acute nephritic syndrome was lupus nephritis (30.6%), rapidly progressive renal failure was pauci-immune crescentic GN (24.5%). IgA nephropathy was the commonest etiology of asymptomatic urinary abnormalities (26.3%) and gross haematuria (50%). About 60.9% patients of undetermined chronic kidney disease had glomerular diseases, and 13.6% had chronic tubulointerstitial nephritis. Lupus nephritis and acute cortical necrosis were significantly more common in females compared with males.
CONCLUSION: This is one of the largest cohorts of kidney biopsies from India, and it delineates the unique features and differences in the pattern of kidney disease in our population.

DOI: 10.1111/nep.13582
PMID: 30834630

97: Mittal S, Mohan A, Hadda V, Madan K. Endobronchial ultrasound elastography in mediastinal lymphadenopathy: Report of two cases and systematic review of literature. Lung India. 2019 Mar-Apr;36(2):149-153. doi: 10.4103/lungindia.lungindia_349_17. PubMed PMID: 30829250; PubMed Central PMCID: PMC6410580.

Endobronchial ultrasound elastography is new ultrasound technology that is being reported recently for the evaluation of mediastinal lymphadenopathy during endobronchial ultrasound-guided (EBUS) transbronchial needle aspiration. This modality is based on the assessment of tissue stiffness that may be useful in differentiating benign from malignant lesions. Image generation leads to colored images with different colors signifying varying degrees of stiffness. The utility of this technique has been studied to differentiate between benign and malignant lymph nodes and various methods for representation of results which include visual color estimation, quantitative color estimation, and strain ratios have been described. Herein, we report two patients with mediastinal lymphadenopathy wherein EBUS elastography was employed. We also systemically review the studies describing this technique in differentiating benign from malignant lymph nodes.

DOI: 10.4103/lungindia.lungindia_349_17
PMCID: PMC6410580
PMID: 30829250

98: Monga N, Kharbanda OP. A Pristine Approach for the Prominent Premaxilla in Bilateral Cleft Lip and Palate (BCLP) Cases. Cleft Palate Craniofac J. 2019 Mar 13:1055665619833865. doi: 10.1177/1055665619833865. [Epub ahead of print] PubMed PMID: 30866673.

OBJECTIVE:: The neonate premaxilla in bilateral cleft lip and palate is often protruding and displaced laterally. Surgeons prefer the premaxilla to be repositioned and centralized to allow a tension-free primary lip repair. This report describes the fabrication of a premaxillary bonnet appliance with silicone material and its successful use in 2 cases of bilateral cleft lip and palate (BCLP).
PATIENTS, PARTICIPANTS:: Two male BCLP patients of ages 34 days and 10 days, respectively.

INTERVENTIONS:: Nonsurgical repositioning of the premaxillary segment using silicone cup-bonnet appliance.
RESULTS:: The duration of active treatment by silicone appliance was 36 days in case 1 and 75 days in case 2. The retention period was 2 months and 3 months, respectively. The appliance made of room temperature vulcanizing (RTV) silicone is flexible and softer in comparison to the rigid conventional acrylic appliance and is therefore almost atraumatic. A gentler appliance resulted in enhanced compliance and acceptance by the neonates. There was a noticeable change in the position of the discernible asymmetric premaxilla. Analysis of frontal facial photographs revealed an angular change in the position of the premaxilla (C) by 12° in case 1 and 6° in case 2 in reference to the midfacial plane.
CONCLUSION:: This silicone appliance provides enhanced compliance and improved retention compared to acrylic appliance since it is a more gentle, flexible, and less traumatic alternative to a rigid acrylic appliance. Further, the RTV silicone appliance can be 3-dimensionally printed for better accuracy following intraoral scanning and thus eliminating the need for impression making in cleft newborns.

DOI: 10.1177/1055665619833865
PMID: 30866673

99: Mukherjee A, Lodha R, Kabra SK. Pharmacokinetics of First-Line Anti-Tubercular Drugs. Indian J Pediatr. 2019 May;86(5):468-478. doi: 10.1007/s12098-019-02911-w. Epub 2019 Mar 26. Review. PubMed PMID: 30915644.

Determining the optimal dosages of isoniazid, rifampicin, pyrazinamide and ethambutol in children is necessary to obtain therapeutic serum concentrations of these drugs. Revised dosages have improved the exposure of 1st line anti-tubercular drugs to some extent; there is still scope for modification of the dosages to achieve exposures which can lead to favourable outcome of the disease. High dose of rifampicin is being investigated in clinical trials in adults with some benefit; studies are required in children. Inter-individual pharmacokinetic variability and the effect of age, nutritional status, Human immunodeficiency virus (HIV) infection, acetylator genotype may need to be accounted for in striving for the dosages best suited for an individual.

DOI: 10.1007/s12098-019-02911-w
PMID: 30915644

100: Mylliemngap B, Swain S, Vyas S, Kumar P. Myxedema Coma, Pancytopenia, and Hypocoagulopathy: A Rare Presentation of Sheehan's Syndrome. Indian J Endocrinol Metab. 2019 Mar-Apr;23(2):268-269. doi: 10.4103/ijem.IJEM_120_19. PubMed PMID: 31161117; PubMed Central PMCID: PMC6540897.

Fenestrations are rare but well-known arterial anatomic variations in which a segment of artery divides into two parallel channels that reunite distally. Although fenestrations as such are asymptomatic, they have gained clinical significance because of their association with aneurysms and other intracranial vascular pathologies. Here we present a 35-year-old woman with history of sudden severe occipital headache and vomiting. Imaging revealed a ruptured aneurysm in the distal posterior inferior cerebellar artery arising from one of the limbs of the fenestration. The aneurysm was successfully managed by coiling, and the patient made complete recovery without neurological sequelae.

DOI: 10.1177/1591019919838194
PMID: 30922197

101: Nadarajah J, Jain N, Sebastian LJD, Gaikwad SB, Garg A, Prabhakar A. Endovascular management of a ruptured aneurysm associated with distal PICA fenestration. Interv Neuroradiol. 2019 Aug;25(4):430-433. doi: 10.1177/1591019919838194. Epub 2019 Mar 28. PubMed PMID: 30922197.

102: Nag TC. Accessory structures that originate from photoreceptor bundles in

the retina of the teleost Notopterus notopterus (Pallas). Tissue Cell. 2019 Jun;58:8-11. doi: 10.1016/j.tice.2019.03.003. Epub 2019 Mar 27. PubMed PMID: 31133250.

The teleost species Notopterus notopterus (Pallas) possess bundled photoreceptors in their retina. It was found that the margin of the inner portion (the vitreal half) of photoreceptor bundles emits thin processes. Each process terminates on the contralateral photoreceptor bundle, or the processes from adjacent photoreceptor bundle may fuse. The site of the inner half of the photoreceptor bundles from where they arise shows minimal support of the photoreceptor bundles by retinal pigment epithelium, and so it is likely that those accessory structures may aid to hold the photoreceptor bundles in correct orientation.

DOI: 10.1016/j.tice.2019.03.003
PMID: 31133250

103: Nayyar R, Kumar P. Spontaneous appendico-renal fistula: clinical presentation and management of a previously unreported entity. BMJ Case Rep. 2019 Mar 22;12(3). pii: e228278. doi: 10.1136/bcr-2018-228278. PubMed PMID: 30904895.

Entero-urinary fistulas are uncommon in urological practice and may have widely varying aetiologies ranging from benign to malignant or iatrogenic in nature. All permutations of entero-urinary fistulas have been reported in the literature except an appendico-renal fistula. Here, we present one such case, presenting with urinary tract infections and perineal urethrocutaneous fistulae. He was ultimately diagnosed to have a spontaneous appendico-renal fistula as underlying pathology behind the symptoms.

DOI: 10.1136/bcr-2018-228278
PMID: 30904895

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105: O'Callaghan-Gordo C, Shivashankar R, Anand S, Ghosh S, Glaser J, Gupta R, Jakobsson K, Kondal D, Krishnan A, Mohan S, Mohan V, Nitsch D, P A P, Tandon N, Narayan KMV, Pearce N, Caplin B, Prabhakaran D. Prevalence of and risk factors for chronic kidney disease of unknown aetiology in India: secondary data analysis of three population-based cross-sectional studies. BMJ Open. 2019 Mar 7;9(3):e023353. doi: 10.1136/bmjopen-2018-023353. Erratum in: BMJ Open. 2019 Mar 18;9(3):e023353corr1. PubMed PMID: 30850400; PubMed Central PMCID: PMC6429742.

OBJECTIVES: To assess whether chronic kidney disease of unknown aetiology (CKDu) is present in India and to identify risk factors for it using population-based data and standardised methods.
DESIGN: Secondary data analysis of three population-based cross-sectional studies conducted between 2010 and 2014.
SETTING: Urban and rural areas of Northern India (states of Delhi and Haryana) and Southern India (states of Tamil Nadu and Andhra Pradesh).
PARTICIPANTS: 12 500 individuals without diabetes, hypertension or heavy proteinuria.
OUTCOME MEASURES: Mean estimated glomerular filtration rate (eGFR) and prevalence of eGFR below 60 mL/min per 1.73 m2 (eGFR <60) in individuals without diabetes, hypertension or heavy proteinuria (proxy definition of CKDu).
RESULTS: The mean eGFR was 105.0±17.8 mL/min per 1.73 m2. The prevalence of eGFR <60 was 1.6% (95% CI=1.4 to 1.7), but this figure varied markedly between areas, being highest in rural areas of Southern Indian (4.8% (3.8 to 5.8)). In Northern India, older age was the only risk factor associated with lower mean eGFR and

eGFR <60 (regression coefficient (95% CI)=-0.94 (0.97 to 0.91); OR (95% CI)=1.10 (1.08 to 1.11)). In Southern India, risk factors for lower mean eGFR and eGFR <60, respectively, were residence in a rural area (-7.78 (-8.69 to -6.86); 4.95 (2.61 to 9.39)), older age (-0.90 (-0.93 to -0.86); 1.06 (1.04 to 1.08)) and less education (-0.94 (-1.32 to -0.56); 0.67 (0.50 to 0.90) for each 5 years at school).
CONCLUSIONS: CKDu is present in India and is not confined to Central America and Sri Lanka. Identified risk factors are consistent with risk factors previously reported for CKDu in Central America and Sri Lanka.

DOI: 10.1136/bmjopen-2018-023353
PMCID: PMC6429742
PMID: 30850400

106: Ojha V, Chandrashekhara S, Vadher A, Malhi AS, Nayak S, Kumar S. A rare association of mitral atresia and double outlet right ventricle (MA-DORV) with unicuspid pulmonary valve. Acta Cardiol. 2019 Mar 29:1-2. doi: 10.1080/00015385.2019.1572961. [Epub ahead of print] PubMed PMID: 30925228.

107: Ojha V, Sh C, Ganga KP, Saxena A, Gulati G. Congenital left ventricular diverticulum in Pentalogy of Cantrell: Puzzle solved on dual source CT. Ann Thorac Surg. 2019 Mar 25. pii: S0003-4975(19)30406-0. doi: 10.1016/j.athoracsur.2019.02.050. [Epub ahead of print] PubMed PMID: 30922822.

108: Ooi CJ, Hilmi I, Banerjee R, Chuah SW, Ng SC, Wei SC, Makharia GK, Pisespongsa P, Chen MH, Ran ZH, Ye BD, Park DI, Ling KL, Ong D, Ahuja V, Goh KL, Sollano J, Lim WC, Leung WK, Ali RAR, Wu DC, Ong E, Mustaffa N, Limsrivilai J, Hisamatsu T, Yang SK, Ouyang Q, Geary R, De Silva JH, Rerknimitr R, Simadibrata M, Abdullah M, Leong RWL; Asia-Pacific Association of Gastroenterology (APAGE) Working Group on Inflammatory Bowel Disease and Asian Organization for Crohn's and Colitis. Best practices on immunomodulators and biologic agents for ulcerative colitis and Crohn's disease in Asia. J Gastroenterol Hepatol. 2019 Mar 8. doi: 10.1111/jgh.14648. [Epub ahead of print] Review. PubMed PMID: 30848854.

The Asia-Pacific Working Group on Inflammatory Bowel Disease was established in Cebu, Philippines, under the auspices of the Asia-Pacific Association of Gastroenterology with the goal of improving inflammatory bowel disease care in Asia. This consensus is carried out in collaboration with Asian Organization for Crohn's and Colitis. With biologic agents and biosimilars becoming more established, it is necessary to conduct a review on existing literature and establish a consensus on when and how to introduce biologic agents and biosimilars in conjunction with conventional treatments for ulcerative colitis and Crohn's disease in Asia. These statements also address how pharmacogenetics influences the treatments of ulcerative colitis and Crohn's disease and provides guidance on response monitoring and strategies to restore loss of response. Finally, the review includes statements on how to manage treatment alongside possible hepatitis B and tuberculosis infections, both common in Asia. These statements have been prepared and voted upon by members of inflammatory bowel disease workgroup employing the modified Delphi process. These statements do not intend to be all-encompassing, and future revisions are likely as new data continue to emerge.

DOI: 10.1111/jgh.14648
PMID: 30848854

109: Padmapriyadarsini C, Bhavani PK, Natrajan M, Ponnuraja C, Kumar H, Gomathy SN, Guleria R, Jawahar SM, Singh M, Balganesh T, Swaminathan S. Evaluation of metformin in combination with rifampicin containing antituberculosis therapy in

patients with new, smear-positive pulmonary tuberculosis (METRIF): study protocol for a randomised clinical trial. BMJ Open. 2019 Mar 1;9(3):e024363. doi: 10.1136/bmjopen-2018-024363. PubMed PMID: 30826761; PubMed Central PMCID: PMC6429929.

INTRODUCTION: Shorter duration of treatment for the management of drug-susceptible pulmonary tuberculosis (TB) would be a significant improvement in the care of patients suffering from the disease. Besides newer drugs and regimens, other modalities like host-directed therapy are also being suggested to reach this goal. This study's objective is to assess the efficacy and safety of metformin-containing anti-TB treatment (ATT) regimen in comparison to the standard 6-month ATT regimen in the treatment of patients with newly diagnosed sputum smear-positive drug-sensitive pulmonary TB.
METHODS AND ANALYSIS: We are conducting a multicentric, randomised open-label controlled clinical trial to achieve the study objective. The intervention group will receive isoniazid (H), rifampicin (R), ethambutol (E) and pyrazinamide (Z) along with 1000 mg of daily metformin (Met) for the first 2 months while the control group will receive only HRZE. After 2 months, both the groups will receive HRE daily for 4 months. The primary endpoint is time to sputum culture conversion. Secondary endpoints will include time to detection of Mycobacterium tuberculosis in sputum, pharmacokinetics and pharmacogenomics of study drugs, drug-drug interactions, safety and tolerability of the various combinations and measurement of autophagy and immune responses in the study participants.
ETHICS AND DISSEMINATION: The ethics committee of the participating institutes have approved the study. Results from this trial will contribute to evidence towards constructing a shorter, effective and safe regimen for patients with TB. The results will be shared widely with the National Programme managers, policymakers and stakeholders through open access publications, dissemination meetings, conference abstracts and policy briefs. This is expected to provide a new standard of care for drug-sensitive patients with pulmonary TB who will not only reduce the number of clinic visits and lost to follow-up of patients from treatment but also reduce the burden on the healthcare system.
TRIAL REGISTRATION NUMBER: CTRI/2018/01/011176; Pre-results.

DOI: 10.1136/bmjopen-2018-024363
PMCID: PMC6429929
PMID: 30826761

110: Pal I, Paltati CRB, Kaur C, Shubhi Saini, Kumar P, Jacob TG, Bhardwaj DN, Roy TS. Morphological and neurochemical changes in GABAergic neurons of the aging human inferior colliculus. Hear Res. 2019 Jun;377:318-329. doi: 10.1016/j.heares.2019.02.005. Epub 2019 Mar 5. PubMed PMID: 30878270.

It is well known that quality of hearing decreases with increasing age due to changes in the peripheral or central auditory pathway. Along with the decrease in the number of neurons the neurotransmitter profile is also affected in the various parts of the auditory system. Particularly, changes in the inhibitory neurons in the inferior colliculus (IC) are known to affect quality of hearing with aging. To date, there is no information about the status of the inhibitory neurotransmitter GABA in the human IC during aging. We have collected and processed inferior colliculi of persons aged 11-97 years at the time of death for morphometry and immunohistochemical expression of glutamic acid decarboxylase (GAD67) and parvalbumin. We used unbiased stereology to estimate the number of cresyl-violet and immunostained neurons. Quantitative real-time PCR was used to measure the relative expression of the GAD67 mRNA. We found that the number of total, GABAergic and PV-positive neurons significantly decreased with increasing age ($p < 0.05$). The proportion of GAD67-ir neurons to total number of neurons was also negatively associated with increasing age ($p = 0.004$), but there was no change observed in the proportion of PV-ir neurons relative to GABAergic neurons ($p = 0.25$). Further, the fold change in the levels of GAD67 mRNA was negatively

correlated to age (p = 0.024). We conclude that the poorer quality of hearing with increasing age may be due to decreased expression of inhibitory neurotransmitters and the decline in the number of inhibitory neurons in the IC.

DOI: 10.1016/j.heares.2019.02.005
PMID: 30878270

111: Pal R, Ghosh A, Kumar R, Galwankar S, Paul SK, Pal S, Sinha D, Jaiswal AK, Moscote-Salazar LR, Agrawal A. Public health crisis of road traffic accidents in India: Risk factor assessment and recommendations on prevention on the behalf of the Academy of Family Physicians of India. J Family Med Prim Care. 2019 Mar;8(3):775-783. doi: 10.4103/jfmpc.jfmpc_214_18. PubMed PMID: 31041200; PubMed Central PMCID: PMC6482791.

Roads are considered a sign of development bringing colossal benefits to community as socioeconomic and logistic facilitator. Yet, growth of road network has brought road crashes leading to civic pain from premature deaths of productive age group. In 2017, 16 citizens were killed and 53 injured every hour on Indian roads as per officially reported data, while a fair number go unreported. This is unacceptably high when compared with international standards. Risk correlates of road traffic injuries (RTIs) need to be redefined so as to form a continuum with other confounding factors that impact to take lives on road. Risk factors impacting RTIs vary from human components to the roles and responsibilities of healthcare stakeholders. We should have made roads safer for all citizens because a large percentage of population - children, pedestrians, cyclists, motorcyclists, and the elderly - are most vulnerable. A taskforce was set up by the Academy of Family Physicians of India to scientifically analyze the literature available to assess risks and put forward appropriate recommendations.

DOI: 10.4103/jfmpc.jfmpc_214_18
PMCID: PMC6482791
PMID: 31041200

112: Pal R, Hameed S, Kumar P, Singh S, Fatima Z. Understanding lipidomic basis of iron limitation induced chemosensitization of drug-resistant Mycobacterium tuberculosis. 3 Biotech. 2019 Apr;9(4):122. doi: 10.1007/s13205-019-1645-4. Epub 2019 Mar 5. PubMed PMID: 30863701; PubMed Central PMCID: PMC6401079.

Under limited micronutrients condition, Mycobacterium tuberculosis (MTB) has to struggle for acquisition of the limited micronutrients available in the host. One such crucial micronutrient that MTB requires for the growth and sustenance is iron. The present study aimed to sequester the iron supply of MTB to control drug resistance in MTB. We found that iron restriction renders hypersensitivity to multidrug-resistant MTB strains against first-line anti-TB drugs. To decipher the effect of iron restriction on possible mechanisms of chemosensitization and altered cellular circuitry governing drug resistance and virulence of MTB, we explored MTB cellular architecture. We could identify non-intact cell envelope, tampered MTB morphology and diminished mycolic acid under iron restricted MDR-MTB cells. Deeper exploration unraveled altered lipidome profile observed through conventional TLC and advanced mass spectrometry-based LC-ESI-MS techniques. Lipidome analysis not only depicted profound alterations of various lipid classes which are crucial for pathogenecity but also exposed leads such as indispensability of iron to sustain metabolic, genotoxic and oxidative stresses. Furthermore, iron deprivation led to inhibited biofilm formation and capacity of MTB to adhere buccal epithelial cells. Lastly, we demonstrated enhanced survival of Mycobacterium-infected Caenorhabditis elegans model under iron limitation. The present study offers evidence and proposes alteration of lipidome profile and affected virulence traits upon iron chelation. Taken together, iron deprivation could be a potential strategy to rescue MDR and enhance the effectiveness of existing anti-TB drugs.

DOI: 10.1007/s13205-019-1645-4

PMCID: PMC6401079 [Available on 2020-04-01]
PMID: 30863701

113: Pandav CS. Iodized Salt Consumption. Indian J Pediatr. 2019 Mar;86(3):218-219. doi: 10.1007/s12098-019-02893-9. Epub 2019 Feb 12. Review. PubMed PMID: 30756286.

114: Pangti R, Dixit A, Gupta S. Bipolar forceps of a high-power electrosurgical unit for precise removal of small benign skin lesions. J Am Acad Dermatol. 2019 Mar 15. pii: S0190-9622(19)30440-2. doi: 10.1016/j.jaad.2019.03.026. [Epub ahead of print] PubMed PMID: 30885755.

115: Pathak D, Srivastava AK, Gulati S, Rajeswari MR. Assessment of cell-free levels of iron and copper in patients with Friedreich's ataxia. Biometals. 2019 Apr;32(2):307-315. doi: 10.1007/s10534-019-00186-4. Epub 2019 Mar 14. PubMed PMID: 30874991.

Friedreich's ataxia (FRDA), a progressive neurodegenerative disorder caused by trinucleotide (GAA) repeat expansion in frataxin (fxn) gene which results in decreased levels of frataxin protein. Insufficient frataxin levels leads to iron and copper deposits in the brain and cardiac cells. A total of hundred and twenty patients, suspected of FRDA were screened for the (GAA) repeats in the fxn gene and only confirmed patients (n = 25) were recruited in the study. The total Iron and total copper concentrations were measured in blood plasma using Nitro PAPS and Dibrom PAESA method, respectively both in patients and age, sex matched healthy controls. The iron levels mean ± SD (6.2 ± 3.8) in plasma of FRDA patients were found to be significantly decreased as compared to healthy controls mean ± SD (15.2 ± 4.2). A similar trend was observed in case of plasma copper levels in FRDA patient (8.15 ± 4.6) as compared to controls (17.5 ± 3.40). Present results clearly prove abnormal distribution of extra-cellular iron in FRDA patients, which is in accordance with the well established fact of intracellular iron overload, which is the key feature of the pathogenesis of this disease. This can be of importance in understanding the pathophysiology of the disease in association with frataxin/iron. It appears that intracellular sequestration of trace metals in FRDA patients (due to low frataxin) results in their sub-optimal levels in blood plasma (extra-cellular) an observation that can find prognostic application in clinical trials.

DOI: 10.1007/s10534-019-00186-4
PMID: 30874991

116: Patra S, Khaitan BK, Sharma VK, Khanna N. A randomized comparative study of the effect of betamethasone oral mini-pulse therapy versus oral azathioprine in progressive non-segmental vitiligo. J Am Acad Dermatol. 2019 Mar 16. pii: S0190-9622(19)30439-6. doi: 10.1016/j.jaad.2019.03.025. [Epub ahead of print] PubMed PMID: 30890339.

117: Pentakota N, Ramaswamy G, Thekkur P, Nair D, Chinnakali P, Kumar Saya G. Is a smartphone application effective in improving physical activity among medical school students? Results from a quasi-experimental study. Int J Adolesc Med Health. 2019 Mar 28. pii: /j/ijamh.ahead-of-print/ijamh-2018-0192/ijamh-2018-0192.xml. doi: 10.1515/ijamh-2018-0192. [Epub ahead of print] PubMed PMID: 30920953.

Introduction Physical activity (PA) is proven to be an effective strategy to avert the life threatening cardiovascular diseases. There is need for developing feasible aids to improve compliance to PA. Hence, we conducted a study among medical college students a) to assess the prevalence of recommended PA level and b) to assess the effectiveness of installing a smartphone application (app) in improving PA. Methodology A quasi-experimental study was conducted among medical

college students in Puducherry, India. The baseline PA was assessed using the Global Physical Activity Questionnaire (GPAQ) and anthropometric measurements such as height and weight were measured as per World Health Organization (WHO) standards. A smartphone app (Runtastic) was installed on the mobile phones of all study participants. At the end of 1 month, the end line PA and anthropometric measurements were captured using same scales. Results Of the total 350 students who were included, the mean age of the participants was 18.9 (0.9) years and 58% of them were male. The proportion of participants with the WHO recommended level of PA increased from 81% at the baseline to 91% after 1 month of installation of the mobile app ($p < 0.001$). There was also a statistically significant increase in the leisure time PA [median (interquartile range - IQR) of metabolic equivalents (METS): 0 (0-1600) vs. 1260.0 (0-1920)]. Clinically significant change was not seen in body mass index (BMI) though the reduction was statistically significant [(mean (standard deviation - SD) of BMI: 22.54 (2.49) vs. after intervention 22.46 (2.47); $p = 0.018$]. Conclusion This quasi-experimental study conducted among medical college students reported significant improvement in total and leisure time PA.

DOI: 10.1515/ijamh-2018-0192
PMID: 30920953

118: Prajapati C, Singh MB, Padma Srivastava MV, Sreenivas V, Bhatia R, Goyal V, Shukla G, Vishnu VY, Gursahani R, Patterson V, Bajpai S, Jain P. Comparing long-term outcomes of epilepsy patients from a single-visit outreach clinic with a conventional epilepsy clinic: A cross-sectional observational study from India. Seizure. 2019 Apr;67:5-10. doi: 10.1016/j.seizure.2019.02.008. Epub 2019 Mar 2. PubMed PMID: 30849714.

PURPOSE: To compare long-term treatment outcomes in epilepsy patients from a single-visit outreach clinic on the Lifeline Express (LLE) with a conventional hospital (AIIMS) based epilepsy clinic in India.
METHODS: Using a cross-sectional observational study design, consecutive epilepsy patients from fifteen LLE clinics conducted from 2009 to 2014 were compared to epilepsy patients registered in the same duration at the AIIMS epilepsy clinic. The primary outcome was to determine if patients were still taking AEDs. To determine current AED status, patients from the LLE clinic were contacted telephonically. For the AIIMS patients, hospital records were reviewed and phone calls made to those patients who had not followed-up for more than a year.
RESULTS: In the 5 years under review, 1923 and 1257 patients had consulted at the LLE and AIIMS clinics respectively. Long-term outcomes were available for analysis in 688 AIIMS and 531 LLE clinic patients. Of the AIIMS patients, 581(87%) were continuing AEDs, 49(7%) had discontinued AEDs after being seizure-free for at least 5 years, 39(6%) had discontinued AEDs without medical advice and 19(2.8%) were dead. Outcomes in 531 LLE patients revealed that 351(72%) continued to be on AEDs, 34(7%) had discontinued AEDs on advice, 106 (22%) had discontinued AEDs without any medical advice and 40 (7.5%) were dead. The treatment gap in the LLE patients was reduced from 49% at first contact to 22% at follow-up 2-8 years later.
CONCLUSIONS: Even single-visit epilepsy clinics may be an effective option for reducing treatment gap in limited-resource regions of the world.

DOI: 10.1016/j.seizure.2019.02.008
PMID: 30849714 [Indexed for MEDLINE]

119: Pujari A, Chawla R, Agarwal D, Gagrani M, Kapoor S, Kumar A. Pathomechanism of traumatic indirect choroidal rupture. Med Hypotheses. 2019 Mar;124:64-66. doi: 10.1016/j.mehy.2019.02.010. Epub 2019 Feb 2. PubMed PMID: 30798919.

The probable chain of events responsible for choroidal rupture is as follows. During high-speed orbital injuries, the protective ocular reflexes position the eye in an elevated, and abducted position. At this point in time, the

anteroposterior compressive forces on to the globe create an eccentrically positioned circle of damaging currents along the posterior ocular coats against a relatively static optic nerve. Because of this eccentricity, a longer radius of curvature is expected to lie along the temporal half of the globe leading to an elastic recoil of the retinal and scleral layers and a fracture along the RPE-Bruch's-Choriocapillaris complex manifesting clinically as choroidal rupture.

DOI: 10.1016/j.mehy.2019.02.010
PMID: 30798919

120: Pujari A, Behera A, Mukhija R, Chawla R, Yadav S, Sharma N. Ocular toxicity due to colours used during holi celebration in India: correlation of clinical findings with the anterior segment OCT. Cutan Ocul Toxicol. 2019 Mar;38(1):1-4. doi: 10.1080/15569527.2018.1495225. Epub 2018 Sep 10. PubMed PMID: 29985058.

PURPOSE: To correlate the anatomical extent of ocular surface toxicity due to colours using anterior segment optical coherence tomography (ASOCT) with the clinical findings.
METHODS: Patients presenting to our emergency department with ocular colour toxicity during the Holi festival celebrations from March 2 2018 to March 5 2018 were assessed for any adnexal, conjunctival, corneal, and anterior chamber findings, as well as findings on anterior segment optical coherence tomography.
RESULTS: A total of 21 patients were observed. The average age was 23 years with 16 patients being male (76.19%). Bilateral ocular involvement was more common (13 patients, 61.90%). Clinically, the corneal changes included localized punctate epitheliopathy (type I) in 12 patients (57.14%) and diffuse punctate epitheliopathy admixed with a variable sized epithelial defect (type II) in the other 9 patients (42.85%). The visual acuity among the former group varied from 6/6 to 6/9, whereas for the latter, it ranged from 6/12 to 6/24. On ASOCT in both the types, the superficial stromal involvement was noted up to 60 microns. Interestingly in two patients with type II corneal involvement, anterior segment involvement was noted in the form of staining of the lens capsule and dense anterior chamber inflammation.
CONCLUSIONS: Ocular toxicity due to colours used during Holi mainly involves the surface epithelium and the superficial stroma. This was observed clinically and also confirmed on ASOCT. The colour can rarely diffuse into the anterior chamber causing an inflammatory reaction and staining of the lens capsule. However, if managed appropriately, vision-threatening complications can be averted.

DOI: 10.1080/15569527.2018.1495225
PMID: 29985058 [Indexed for MEDLINE]

121: Purkayastha S, Patil V, Sahu A. Use of Stimulants in Patients with Psychosis Having Past History of or Co-occurring Attention Deficit Hyperactivity Disorder: Is it Safe? Indian J Psychol Med. 2019 Mar-Apr;41(2):195-196. doi: 10.4103/IJPSYM.IJPSYM_262_18. PubMed PMID: 30983674; PubMed Central PMCID: PMC6436421.

122: Pushpam D, Chopra A, Sreenivas V, Kumar R, Bakhshi S. Absolute Lymphocyte Count at the End of Induction as a Surrogate Marker for Minimal Residual Disease in T-cell Acute Lymphoblastic Leukemia. Indian Pediatr. 2019 May 15;56(5):381-383. Epub 2019 Mar 17. PubMed PMID: 30898988.

OBJECTIVE: The relation of absolute lymphocyte count (ALC) with minimal residual disease (MRD) in T cell - acute lymphoblastic leukemia (T-ALL) is not known. The objective of the study was to correlate ALC with MRD, steroid-response and complete remission (CR).
METHODS: De-novo T- ALL patients (age 1-18 y) recruited prospectively; 52 enrolled, 9 excluded, and 43 analyzed. 39 achieved CR and MRD was available for 28 patients; 23 were MRD negative.
RESULTS: ALC did not correlate with steroid response and CR. Median (range) ALC

at the end of induction was significantly higher in patients who were MRD negative compared to MRD positive [1.24 (0.12, 6.69) vs 0.62 (0.15, 0.87); P=0.03], respectively. Patients having ALC ≥700 ×109 /L were significantly more likely to be MRD negative than those with lower values (P= 0.028).
CONCLUSION: Our study suggests that ALC is a favorable factor, and may act as surrogate marker for MRD.

123: Raheja A, Suri A, Sreenivasan SA, Singla R. Insurance and Flow-Alteration Superficial Temporal Artery to Middle Cerebral Artery (STA-MCA) Bypass in Management of Complex Anterior Intracranial Circulation Aneurysms in Postendovascular Era. World Neurosurg. 2019 Mar 19. pii: S1878-8750(19)30777-6. doi: 10.1016/j.wneu.2019.03.109. [Epub ahead of print] PubMed PMID: 30902771.

BACKGROUND: Optimal management of complex anterior circulation aneurysms is an enigmatic challenge because of frequent involvement of major vessel bifurcation, choroidal vessels, and lenticulostriate/thalamostriate perforators. Cerebral ischemia associated with prolonged clipping time is a major concern pertinent to their surgical management, especially in patients with poor cross-flow. To circumvent this hurdle, single/double-barrel low-flow superficial temporal artery (STA) to middle cerebral artery (M3/M4-MCA) can be performed, which can maintain distal cerebral perfusion while facilitating safe clip reconstruction of complex MCA and supraclinoidal internal carotid artery (ICA) aneurysms involving ICA bifurcation or supraclinoidal ICA aneurysms with poor cross-circulation-insurance bypass, as well as supplement/alter blood flow after MCA aneurysm trapping-flow-alteration bypass.
METHODS: A retrospective chart review of consecutive neurosurgical patients operated over 2 years at this center was performed. Patients with complex MCA and ICA aneurysms who were treated with STA-MCA bypass were included. The clinical profile, pre- and postoperative images, intraoperative imaging, and patient outcomes were recorded. Surgical reconstruction of aneurysm was the treatment of choice due to involvement of choroidal/thalamostriate perforators, MCA/ICA bifurcation, complex aneurysm morphology, or dissecting/thrombosed nature of aneurysm. STA-MCA low-flow bypass was performed using M3/M4 segment of MCA as the recipient in anticipation of prolonged temporary clipping time on M1-MCA, supraclinoidal ICA aneurysms with suspected ICA terminus involvement, or need for possible trapping of fusiform MCA aneurysm. The saccular/fusiform part of aneurysm was clip reconstructed and the partially thrombosed dissecting segment was opened for thrombectomy and trapped using proximal and distal clips after good patency of bypass was confirmed. The distal MCA flow was restored adequately and confirmed intraoperatively using indocyanine green angiography and micro-Doppler ultrasonography.
RESULTS: MCA (n = 4) and supraclinoid-ICA (n = 1) aneurysms were managed successfully using this strategy, which involved 6 STA-MCA bypass procedures (insurance and flow-alteration bypass, 3 each). Postoperative check angiograms demonstrated patent bypass in all 5 patients. Four patients had favorable outcome (modified Rankin Scale score 0/1); one had recovering hemiparesis and aphasia (modified Rankin Scale score 4).
CONCLUSIONS: This series highlights the surgical strategy and safety for successfully managing complex MCA and ICA aneurysms using low-flow STA-MCA revascularization procedures.

DOI: 10.1016/j.wneu.2019.03.109
PMID: 30902771

124: Rahman S, Archana A, Jan AT, Dutta D, Shankar A, Kim J, Minakshi R. Molecular Insights Into the Relationship Between Autoimmune Thyroid Diseases and Breast Cancer: A Critical Perspective on Autoimmunity and ER Stress. Front Immunol. 2019 Mar 1;10:344. doi: 10.3389/fimmu.2019.00344. eCollection 2019. Review. PubMed PMID: 30881358; PubMed Central PMCID: PMC6405522.

The etiopathologies behind autoimmune thyroid diseases (AITDs) unravel misbehavior of immune components leading to the corruption of immune homeostasis

where thyroid autoantigens turn foe to the self. In AITDs lymphocytic infiltration in the thyroid shows up a deranged immune system charging the follicular cells of the thyroid gland (thyrocytes) leading to the condition of either hyperthyroidism or hypothyroidism. The inflammation in AITDs consistently associate with ER function due to which disturbances in the ER protein homeostasis leads to unfolded protein response (UPR) that promotes pathogenesis of autoimmunity. The roles of ER stress in the instantaneous downregulation of MHC class I molecules on thyrocytes and the relevance of IFN γ in the pathogenesis of AITD has been well-documented. Thyroglobulin being the major target of autoantibodies in most of the AITDs is because of its unusual processing in the ER. Autoimmune disorders display a conglomeration of ER stress-induced UPR activated molecules. Several epidemiological data highlight the preponderance of AITDs in women as well as its concurrence with breast cancer. Both being an active glandular system displaying endocrine activity, thyroid as well as breast tissue show various commonalities in the expression pattern of heterogenous molecules that not only participate in the normal functioning but at the same time share the blame during disease establishment. Studies on the development and progression of breast carcinoma display a deranged and uncontrolled immune response, which is meticulously exploited during tumor metastasis. The molecular crosstalks between AITDs and breast tumor microenvironment rely on active participation of immune cells. The induction of ER stress by Tunicamycin advocates to provide a model for cancer therapy by intervening glycosylation. Therefore, this review attempts to showcase the molecules that are involved in feeding up the relationship between breast carcinoma and AITDs.

DOI: 10.3389/fimmu.2019.00344
PMCID: PMC6405522
PMID: 30881358

125: Ramos A, Planchat M, Vieira Melo AR, Raposo M, Shamim U, Suroliya V, Srivastava AK, Faruq M, Morino H, Ohsawa R, Kawakami H, Bannach Jardim L, Saraiva-Pereira ML, Vasconcelos J, Santos C, Lima M. Mitochondrial DNA haplogroups and age at onset of Machado-Joseph disease/spinocerebellar ataxia type 3: a study in patients from multiple populations. Eur J Neurol. 2019 Mar;26(3):506-512. doi: 10.1111/ene.13860. Epub 2018 Dec 7. PubMed PMID: 30414314.

BACKGROUND AND PURPOSE: Mitochondrial dysfunction has been implicated in the pathogenesis of several neurodegenerative disorders, including Machado-Joseph disease (MJD), an autosomal dominant late-onset polyglutamine ataxia that results from an unstable expansion of a CAG tract in the ATXN3 gene. The size of the CAG tract only partially explains age at onset (AO), highlighting the existence of disease modifiers. Mitochondrial DNA (mtDNA) haplogroups have been associated with clinical presentation in other polyglutamine disorders, constituting potential modifiers of MJD phenotype.
METHODS: A cross-sectional study, using 235 unrelated patients from Portugal, Brazil, India and Japan, was performed to investigate if mtDNA haplogroups contribute to AO of MJD. mtDNA haplogroups were obtained after sequencing the mtDNA hypervariable region I. Patients were classified in 15 phylogenetically related haplogroup clusters.
RESULTS: The AO was significantly different among populations, implying the existence of other non-CAG factors, which seem to be population specific. In the Portuguese population, patients classified as belonging to haplogroup JT presented the earliest onset (estimated onset 34.6 years of age). Haplogroups W and X seem to have a protective effect, causing a delay in onset (estimated onset 47 years of age). No significant association between haplogroup clusters and AO was detected in the other populations or when all patients were pooled. Although haplogroup JT has already been implicated in other neurodegenerative disorders, no previous reports of an association between haplogroups W and X and disease were found.
CONCLUSIONS: These findings suggest that haplogroups JT, W and X modify AO in MJD. Replication studies should be performed in European populations, where the

frequency of the candidate modifiers is similar.

DOI: 10.1111/ene.13860
PMID: 30414314

126: Ramot R, Kachhawa G, Kulshreshtha V, Varshney S, Sankar MJ, Devasenathipathy K, Sreenivas V, Khadgawat R. Bone Mass in Newborns Assessed by DXA - A Systematic Review and Meta-analysis. Indian J Endocrinol Metab. 2019 Mar-Apr;23(2):198-205. doi: 10.4103/ijem.IJEM_681_18. PubMed PMID: 31161103; PubMed Central PMCID: PMC6540894.

Purpose: Peak bone mass - a key determinant of osteoporotic fractures result from bone accretion starting form intrauterine life to early adulthood. Optimal skeletal growth in-utero and infancy may offer protection against osteoporosis in adult life. We attempted to pool the data from available literature to get a consensus on average bone mass among healthy newborns (age ≤30 days after birth).
Methods: Systematic review was conducted (PRISMA guidelines) to generate pooled estimates of bone mass parameters at whole body (WB) and lumbar spine (LS), based on both fixed and random effect models of meta-analyses. Two investigators independently carried out a comprehensive literature search using PubMed, Google Scholar and Embase. Meta-regression was applied to further explore causes of heterogeneity.
Results: Out of a total 2703 studies, 2682 was excluded leaving 21 studies for final analysis. Thirteen studies reported bone mass by Hologic® and eight by Lunar®. The pooled WBBMC was 66.2g (95% CI 65.4 to 67.05 by fixed effect model, while the corresponding parameter for LS was 2.3g (95% CI 2.2 to 2.4). The subgroup and meta-regression analyses done for controlling potential confounders did not significantly affect heterogeneity.
Conclusion: We generated the pooled estimate of bone mass (WBBMC) among healthy newborn subjects. There was high degree of heterogeneity among studies.

DOI: 10.4103/ijem.IJEM_681_18
PMCID: PMC6540894
PMID: 31161103

127: Ranjan R, Sud A, Kanojia RK, Goel L, Chand S, Sinha A. Results of Supracondylar "V" Osteotomy for the Correction of Genu Valgum Deformity. Indian J Orthop. 2019 Mar-Apr;53(2):366-373. doi: 10.4103/ortho.IJOrtho_547_17. PubMed PMID: 30967710; PubMed Central PMCID: PMC6415553.

Background: Medial close wedge, lateral open wedge, dome and "V" osteotomies are the commonly to correct the genu valgum (GV) deformity. However, the ideal method for the correction of coronal plane deformity is controversial. This prospective study is to evaluate the functional and radiological result of supracodylar "V" osteotomy to correct GV deformity.
Materials and Methods: "V" osteotomy was done in all patients with clinically significant GV deformity and was fixed with crossed K-wires. Weight-bearing mobilization was started after radiological union. Patients were evaluated for correction in different clinical and radiological parameters. The function of the knee was assessed by Bostman's score. The subjective score was used to assess the parent's satisfaction after the procedure.
Results: 187 limbs with genu valgum deformity (47 males and 71 females) were included in this study. We observed a significant improvement in the mean intermalleolar distance, clinical and radiological tibiofemoral angle and lateral distal femoral angle, from 17.3 to 3.9 cm, 23.8°to-4.5°, 25.6° to 6.1°, 76.6° to 88.4°, respectively. The mean Bostman score improved from 20.6 to 28.1. The parent's satisfaction assessed subjectively was 95.3 points.
Conclusion: This osteotomy along with the fixation with K-wires is a safe, effective, reproducible technique with a short learning curve and a procedure requiring no repeat surgery for implant removal, with good functional results, and without major complications.

DOI: 10.4103/ortho.IJOrtho_547_17
PMCID: PMC6415553
PMID: 30967710

128: Rao R, Varshney M, Singh S, Agrawal A, Ambekar A. Mental Healthcare Act, 2017, and addiction treatment: Potential pitfalls and trepidations. Indian J Psychiatry. 2019 Mar-Apr;61(2):208-212. doi: 10.4103/psychiatry.IndianJPsychiatry_463_18. PubMed PMID: 30992618; PubMed Central PMCID: PMC6425793.

The Mental Healthcare Act (MHCA), 2017, is enacted with an aim to promote and protect the rights of and improve the care and treatment for people affected by mental illness in India. The Act purportedly includes substance use disorder (SUD) specifically in the definition of mental illness itself. However, some of the phrases used in the definition such as "abuse" are not clear, as the current classificatory systems of mental illnesses do not have any diagnostic category termed "abuse." Another important issue is the lack of clarity on which categories of SUD would be covered under MHCA. Simple reading of the text of the Act seems to suggest that SUD is a single entity for the purpose of this law. In such case, many provisions of the act such as supported admission that are meant for the treatment of people with severe mental illnesses with gross impairment may become applicable to all types of SUD. This can create potential problems for addiction treatment providers. On the other hand, certain other provisions of the Act are good news for patients suffering from SUD. The Act lays down various rights that include, among others, protection from cruel, inhuman, or degrading treatment in any mental health establishment. This is very important from the perspective of treatment of SUD in the context of India, where human rights violations in the name of addiction treatment are often reported. The inclusion of SUD in MHCA, 2017, slots SUD as a health issue, rather than a law-and-order issue alone. This displays the intent of policymakers toward SUD, which, in itself, is laudable. There are certain ways in which the potential pitfalls mentioned earlier can be addressed, which is discussed in the article.

DOI: 10.4103/psychiatry.IndianJPsychiatry_463_18
PMCID: PMC6425793
PMID: 30992618

129: Rout G, Nayak B, Patel AH, Gunjan D, Singh V, Kedia S, Shalimar. Therapy with Oral Directly Acting Agents in Hepatitis C Infection Is Associated with Reduction in Fibrosis and Increase in Hepatic Steatosis on Transient Elastography. J Clin Exp Hepatol. 2019 Mar-Apr;9(2):207-214. doi: 10.1016/j.jceh.2018.06.009. Epub 2018 Jun 21. PubMed PMID: 31024203; PubMed Central PMCID: PMC6477071.

Background/Aims: Direct-Acting Antivirals (DAAs) are now the standard of care for management of Chronic Hepatitis C (CHC) infection. The aim of this study was to evaluate change in Liver Stiffness Measurement (LSM) and Controlled Attenuation Parameter (CAP) by transient elastography (FibroScan®) after completion of DAA therapy.
Methods: LSM and CAP were measured serially (baseline pre-treatment, at 12 weeks post therapy, and one year after completion of therapy) in a prospective cohort of 372 CHC patients treated with DAAs. Patients with at least two FibroScan measurements were included.
Results: The mean age was 38.1 ± 12.6 years; 58.3% males. Cirrhosis as defined by biopsy or fibroscan measurement (≥12.5) kPa was found in 25.5%. On paired analysis (n = 317), LSM (IQR) decreased from a baseline value 7.1 (5.3-13.8) kPa to 6.2 (4.8-11.2) kPa 12 weeks post therapy with a median decline 0.7 (-0.6-2.6) kPa, P < 0.001. Similarly, on paired analysis (n = 160), LSM decreased from baseline 6.9 (5.1-12.7) kPa to 6.1 (4.8-9.4) kPa after one year of treatment with median decline 0.9 (-0.6-3.2) kPa, P < 0.001. In contrast, on paired analysis (n = 317), CAP increased from baseline of 213.0 (180.0-254.5) dB/m to 225.0 (190.0-269.0) dB/m at 12 weeks post therapy with median increase 7.0 (-23.5-45.5), P = 0.001. Similarly, on paired analysis (n = 160), CAP increased from baseline of 210.0 (180.3-260.8) dB/m to 234.0 (204.0-282.0) dB/m at one year

post therapy with median increase 25.0 (-12.5-61.5) dB/m, P < 0.001. On multivariate linear regression analysis, low baseline CAP value and low albumin were significantly associated with increase in CAP values.
Conclusion: Treatment with DAAs reduces liver stiffness, but is associated with increase in hepatic steatosis.

DOI: 10.1016/j.jceh.2018.06.009
PMCID: PMC6477071 [Available on 2020-03-01]
PMID: 31024203

130: Rout G, Sharma S, Gunjan D, Kedia S, Saraya A, Nayak B, Singh V, Kumar R, Shalimar. Development and Validation of a Novel Model for Outcomes in Patients with Cirrhosis and Acute Variceal Bleeding. Dig Dis Sci. 2019 Mar 4. doi: 10.1007/s10620-019-05557-y. [Epub ahead of print] PubMed PMID: 30830520.

BACKGROUND: Acute variceal bleeding (AVB) in patients with cirrhosis is associated with high mortality, ranging from 12 to 20% at 6 weeks. The existing prognostic models for AVB lack precision and require further validation.
AIM: In this prospective study, we aimed to develop and validate a new prognostic model for AVB, and compared it with the existing models.
METHODS: We included 285 patients from March 2017 to November 2017 in the derivation cohort and 238 patients from December 2017 to June 2018 in the validation cohort. Two prognostic models were developed from derivation cohort by logistic regression analysis. Discrimination was assessed using area under the receiver operator characteristic curve (AUROC).
RESULTS: The 6-week mortality was 22.1% in derivation cohort and 22.3% in validation cohort, P = 0.866. Model for end-stage liver disease (MELD) [odds ratio (OR) 1.106] and encephalopathy (E) (OR 4.658) in one analysis and Child-Pugh score (OR 1.379) and serum creatinine (OR 1.474) in another analysis were significantly associated with 6-week mortality. MELD-E model (AUROC 0.792) was superior to Child-creatinine model (AUROC) in terms of discrimination. The MELD-E model had highest AUROC; as compared to other models-MELD score (AUROC 0.751, P = 0.036), Child-Pugh score (AUROC 0.737, P = 0.037), D'Amico model (AUROC 0.716, P = 0.014) and Augustin model (AUROC 0.739, P = 0.018) in derivation cohort. In validation cohort, the discriminatory performance of MELD-E model (AUROC 0.805) was higher as compared to other models including MELD score (AUROC 0.771, P = 0.048), Child-Pugh score (AUROC 0.746, P = 0.011), Augustin model (AUROC 0.753, P = 0.039) and D'Amico model (AUROC 0.736, P = 0.021).
CONCLUSION: In cirrhotic patients with AVB, the novel MELD-Encephalopathy model predicts 6 weeks mortality with higher accuracy than the existing prognostic models.

DOI: 10.1007/s10620-019-05557-y
PMID: 30830520

131: Rout G, Sharma S, Gunjan D, Kedia S, Nayak B, Shalimar. Comparison of various prognostic scores in variceal and non-variceal upper gastrointestinal bleeding: A prospective cohort study. Indian J Gastroenterol. 2019 Apr;38(2):158-166. doi: 10.1007/s12664-018-0928-8. Epub 2019 Mar 4. PubMed PMID: 30830583.

BACKGROUND AND AIMS: Various prognostic scores like Glasgow-Blatchford bleeding score (GBS), modified Glasgow-Blatchford bleeding score (mGBS), full Rockall score (FRS) including endoscopic findings, clinical Rockall score (CRS), and albumin, international normalized ratio (INR), mental status, systolic blood pressure, age >65 (AIMS65) are used for risk stratification in patients with upper gastrointestinal bleeding (UGIB). The utility of these scores in variceal UGIB (VUGIB) is not well defined. In this prospective study, we aimed to assess the performance of these scores in patients with non-variceal (NVUGIB) and VUGIB.
METHODS: We included 1011 patients (during March 2017 and August 2018) including 439 with NVUGIB and 572 VUGIB. Performance of GBS, mGBS, FRS, CRS, and AIMS65 for various outcome measures was analyzed using the area under receiver operator characteristic curve (AUROC).

RESULTS: The accuracy of prognostic scores in predicting the composite outcome including the need of hospital-based intervention and 42-day mortality was higher in NVUGIB as compared with VUGIB, AUROC: CRS: 0.641 vs. 0.537; FRS: 0.669 vs. 0.625; GBS: 0.719 vs. 0.587; mGBS: 0.711 vs. 0.594; AIMS65: 0.567 vs. 0.548. GBS and mGBS at a cut-off score of 1 had the highest negative predictive value, 91.7% and 91.3%, respectively, for predicting composite outcome in NVUGIB. Similarly, these scores had better accuracy for predicting 42-day rebleeding in NVUGIB as compared to VUGIB, AUROC: CRS: 0.680 vs. 0.537; FRS: 0.698 vs. 0.565; GBS: 0.661 vs. 0.543; mGBS: 0.627 vs. 0.540; AIMS65: 0.695 vs. 0.606.
CONCLUSION: The prognostic scores such as CRS, FRS, GBS, mGBS, and AIMS65 predict the need for hospital-based management, rebleeding, and mortality better among patients with NVUGIB than VUGIB.

DOI: 10.1007/s12664-018-0928-8
PMID: 30830583

132: Sahay P, Nair S, Maharana PK, Sharma N. Pseudomembranous conjunctivitis: unveil the curtain. BMJ Case Rep. 2019 Mar 15;12(3). pii: e228538. doi: 10.1136/bcr-2018-228538. PubMed PMID: 30878958.

133: Sakthivel P, Sikka K, Kakkar A, Kavutharapu S, Thakar A. Polypoidal Trachea: A Clinician's Predicament. Am J Med. 2019 Mar;132(3):e523-e524. doi: 10.1016/j.amjmed.2018.11.012. Epub 2018 Nov 30. PubMed PMID: 30503880.

134: Sandhyamani S, Tandon PN. Dr. Sriramachari, founder neuropathologist of India. Neurol India. 2019 Mar-Apr;67(2):356-363. doi: 10.4103/0028-3886.257995. PubMed PMID: 31085836.

135: Sankar J, Dhochak N, Kumar K, Singh M, Sankar MJ, Lodha R. Comparison of International Pediatric Sepsis Consensus Conference Versus Sepsis-3 Definitions for Children Presenting With Septic Shock to a Tertiary Care Center in India: A Retrospective Study. Pediatr Crit Care Med. 2019 Mar;20(3):e122-e129. doi: 10.1097/PCC.0000000000001864. PubMed PMID: 30640887.

OBJECTIVES: To evaluate the proportion of children fulfilling "Sepsis-3" definition and International Pediatric Sepsis Consensus Conference definition among children diagnosed to have septic shock and compare the mortality risk between the two groups.
DESIGN: Retrospective chart review.
SETTING: PICU of a tertiary care teaching hospital from 2014 to 2017.
PATIENTS: Children (≤ 17 yr old) with a diagnosis of septic shock at admission or during PICU stay.
INTERVENTIONS: None.
MEASUREMENTS AND MAIN RESULTS: We applied both International Pediatric Sepsis Consensus Conference and the new "Sepsis-3" definition (sepsis with hypotension requiring vasopressors and a lactate value of ≥ 2 mmol/L) to identify cases of septic shock by these definitions. Key outcomes such as mortality, proportion attaining shock reversal at 24 hours and organ dysfunction were compared between those fulfilling "Sepsis-3" definitions ("Sepsis-3" group) and those fulfilling "International Pediatric Sepsis Consensus Conference" definition ("International Pediatric Sepsis Consensus Conference" group). A total of 216 patients fulfilled International Pediatric Sepsis Consensus Conference definitions of septic shock. Of these, only 104 (48%; 95% CI, 42-55) fulfilled "Sepsis-3" definition. Children fulfilling "Sepsis-3 plus International Pediatric Sepsis Consensus Conference definitions" ("Sepsis-3 and International Pediatric Sepsis Consensus Conference" group) had lower proportion with shock resolution (61% vs 82%; relative risk, 0.73; 95% CI, 0.62-0.88) and higher risk of multiple organ dysfunction (85% vs 68%; 1.24; 1.07-1.45) at 24 hours. The mortality was 48.5% in "Sepsis-3 and International Pediatric Sepsis Consensus Conference" group as compared with 37.5% in the "International Pediatric Sepsis Consensus Conference only" group (relative risk, 1.3; 95% CI, 0.94-1.75).
CONCLUSIONS: Less than half of children with septic shock identified by International Pediatric Sepsis Consensus Conference definitions were observed to fulfill the criteria for shock as per "Sepsis-3" definitions. Lack of difference

in the risk of mortality between children who fulfilled "Sepsis-3" definition and those who did not fulfill the definition raises questions on the appropriateness of using this definition for diagnosis of septic shock in children.

DOI: 10.1097/PCC.0000000000001864
PMID: 30640887

136: Santoshi JA, Jain S, Popalwar HJ, Pakhare AP. Musculoskeletal disorders and associated risk factors in coaching students: A cross-sectional study. J Family Med Prim Care. 2019 Mar;8(3):929-933. doi: 10.4103/jfmpc.jfmpc_54_19. PubMed PMID: 31041227; PubMed Central PMCID: PMC6482780.

Background: Coaching institutes attract students aspiring for admission to professional courses and jobs. Physical stress during coaching includes poor study posture and sitting on chairs improperly in overcrowded classes for prolonged periods. Many students attending the coaching institutes report to outpatient clinics of multiple specialties with musculoskeletal disorders (MSD).
Materials and Methods: We carried out a cross-sectional study of 500 coaching students. We ascertained the 12-month MSD (period prevalence) and last 7-day MSD (point prevalence) using the Nordic Musculoskeletal Questionnaire. The duration of attending classes, hours of daily study, and duration of sitting continuously at a stretch were also enquired.
Results: A total of 488 responses were retrieved. Males and females accounted for 63.9% and 36.1%, respectively. The respondents' mean age was 18.6 ± 1.06 years; mean body mass index was 21.4; mean duration of attending classes was 15.6 ± 7.66 months; mean hours of daily study were 4.78 ± 1.71 hours; mean duration of sitting continuously at a stretch was 2.2 hours. The overall prevalence of MSD was 87.1%. The mean frequency of MSD per participant was 2.6. Most participants reported pain in the neck region and lower back (43%), followed by ankle/foot (36%), followed by upper back (32%), followed by shoulder (28%); knee, elbow, and wrist/hand were lesser than 20%, while hip/thigh pain was the least common symptom (8%).
Conclusion: This study serves to sensitize the medical community to this largely under-reported problem in young individuals who are in the phase of life preparing for their future career while inadvertently risking their long-term health in the process.

DOI: 10.4103/jfmpc.jfmpc_54_19
PMCID: PMC6482780
PMID: 31041227

137: Sarkar S, Chawla N. Clinical staging model in bipolar disorder: A few considerations. Bipolar Disord. 2019 May;21(3):278-279. doi: 10.1111/bdi.12750. Epub 2019 Mar 5. PubMed PMID: 30725501.

138: Selvan H, Gupta S. Cyclodialysis cleft repair: A multi-centred, retrospective case series-Comment. Clin Exp Ophthalmol. 2019 Mar;47(2):303. doi: 10.1111/ceo.13422. Epub 2018 Nov 28. PubMed PMID: 30345581.

139: Selvan H, Singh A, Tandon R. Deep blue dot corneal degeneration: confocal characteristics. Int Ophthalmol. 2019 Mar;39(3):667-669. doi: 10.1007/s10792-018-0849-7. Epub 2018 Feb 8. PubMed PMID: 29423782.

PURPOSE: To discuss the clinical features, differential diagnosis and the novel confocal microscopic findings noted in the rare 'deep blue dot corneal degeneration'.
METHODS: Observational case report.
RESULTS: Slit-lamp biomicroscopic examination revealed bilateral, numerous, circular to oval discrete blue opacities at the level of deep stroma and fine grey linear opacities at the level of mid to deep stroma. Confocal microscopy demonstrated two types of corresponding hyper-reflective extracellular lesions: oval deposit-like, most concentrated at a depth of 430-480 µ and needle-like at the depth 330-370 µ.
CONCLUSIONS: Deep blue dot corneal degeneration is a rare entity where blue

deposits of amyloid are seen in the deep corneal stroma. It should be considered as a differential diagnosis when an old-aged person presents with good vision and the above mentioned findings.

DOI: 10.1007/s10792-018-0849-7
PMID: 29423782 [Indexed for MEDLINE]

140: Seth R, Xess I, Jana M. Diagnosis of Invasive Fungal Infections in Children. Indian Pediatr. 2019 Mar 15;56(3):229-236. PubMed PMID: 30954996.

Invasive fungal infections are important causes of morbidity and mortality particularly in high-risk patients. Recognizing such infections is often difficult because of non-specific symptoms and clinical signs. Timely diagnosis is also a challenge due to difficulty in obtaining adequate volume of samples, need for anaesthesia to perform certain diagnostic procedures, and insufficient data and experience related to fungal biomarkers and molecular detection tests. This results in widespread use of empiric broad spectrum antifungal agents with the consequent emergence of drug-resistant strains. This review focusses on the definition, clinical and microbial profile and diagnostic modalities for invasive fungal infections.

PMID: 30954996

141: Shakrawal J, Selvan H, Sharma A, Angmo D. Double trouble: Microspherophakia with Axenfeld-Rieger anomaly. Indian J Ophthalmol. 2019 Mar;67(3):394-395. doi: 10.4103/ijo.IJO_978_18. PubMed PMID: 30777961; PubMed Central PMCID: PMC6407397.

142: Sharma A, Dadhwal V, Rana A, Chawla J. Isolated large bilateral choroid plexus cysts associated with trisomy 18. BMJ Case Rep. 2019 Mar 1;12(3). pii: e229216. doi: 10.1136/bcr-2019-229216. PubMed PMID: 30826785.

143: Sharma A, Biradar B, Malhi AS, Kumar S. Subtotal Cor Triatriatum on Dual-Source Computed Tomography. Ann Thorac Surg. 2019 Mar;107(3):e213. doi: 10.1016/j.athoracsur.2018.09.029. Epub 2018 Oct 31. PubMed PMID: 30391251.

144: Sharma P, Kumari B, Dahiya S, Kulsum U, Kumar S, Manral N, Pandey S, Kaur P, Sood S, Das BK, Kapil A. Azithromycin resistance mechanisms in typhoidal salmonellae in India: A 25 years analysis. Indian J Med Res. 2019 Mar;149(3):404-411. doi: 10.4103/ijmr.IJMR_1302_17. PubMed PMID: 31249207.

Background & objectives: : Azithromycin has been in use as an alternate treatment option for enteric fever even when the guidelines on the susceptibility testing were not available. There is lack of data on susceptibility and mechanisms of resistance of azithromycin in Salmonella Typhi and S. Paratyphi A. The aim of the present study was to determine the azithromycin susceptibility and resistance mechanisms in typhoidal salmonellae isolates archived in a tertiary care centre in north India for a period of 25 years.
Methods: : Azithromycin susceptibility was determined in 602 isolates of S. Typhi (469) and S. Paratyphi A (133) available as archived collection isolated during 1993 to 2016, by disc diffusion and E-test method.PCR was done for ereA, ermA, ermB, ermC, mefA, mphA and msrA genes from plasmid and genomic DNA and sequencing was done to detect mutations in acrR, rplD and rplV genes.
Results: : Azithromycin susceptibility was seen in 437/469 [93.2%; 95% confidence interval (CI), 90.5 to 95.1%] isolates of S. Typhi. Amongst 133 isolates of S. Paratyphi A studied, minimum inhibitory concentration (MIC) of ≤16 mg/l was found in 102 (76.7%; 95% CI, 68.8 to 83.0). MIC value ranged between 1.5 and 32 mg/l with an increasing trend in MIC50and MIC90with time. Mutations were found in acrR in one and rplV in two isolates of S. Typhi. No acquired mechanism for macrolide resistance was found.
Interpretation & conclusions: : Azithromycin could be considered as a promising agent against typhoid fever on the basis of MIC distribution in India. However, due to emergence of resistance in some parts, there is a need for continuous surveillance of antimicrobial susceptibility and resistance mechanisms. There is

also a need to determine the breakpoints for S. Paratyphi A.

DOI: 10.4103/ijmr.IJMR_1302_17
PMID: 31249207

145: Shewade HD, Gupta V, Satyanarayana S, Pandey P, Bajpai UN, Tripathy JP, Kathirvel S, Pandurangan S, Mohanty S, Ghule VH, Sagili KD, Prasad BM, Nath S, Singh P, Singh K, Singh R, Jayaraman G, Rajeswaran P, Srivastava BK, Biswas M, Mallick G, Bera OP, Sahai KN, Murali L, Kamble S, Deshpande M, Kumar N, Kumar S, Jaisingh AJJ, Naqvi AJ, Verma P, Ansari MS, Mishra PC, Sumesh G, Barik S, Mathew V, Lohar MRS, Gaurkhede CS, Parate G, Bale SY, Koli I, Bharadwaj AK, Venkatraman G, Sathiyanarayanan K, Lal J, Sharma AK, Rao R, Kumar AMV, Chadha SS. Patient characteristics, health seeking and delays among new sputum smear positive TB patients identified through active case finding when compared to passive case finding in India. PLoS One. 2019 Mar 13;14(3):e0213345. doi: 10.1371/journal.pone.0213345. eCollection 2019. PubMed PMID: 30865730; PubMed Central PMCID: PMC6415860.

BACKGROUND: Axshya SAMVAD is an active tuberculosis (TB) case finding (ACF) strategy under project Axshya (Axshya meaning 'free of TB' and SAMVAD meaning 'conversation') among marginalized and vulnerable populations in 285 districts of India.
OBJECTIVES: To compare patient characteristics, health seeking, delays in diagnosis and treatment initiation among new sputum smear positive TB patients detected through ACF and passive case finding (PCF) under the national TB programme in marginalized and vulnerable populations between March 2016 and February 2017.
METHODS: This observational analytic study was conducted in 18 randomly sampled Axshya districts. We enrolled all TB patients detected through ACF and an equal number of randomly selected patients detected through PCF in the same settings. Data on patient characteristics, health seeking and delays were collected through record review and patient interviews (at their residence). Delays included patient level delay (from eligibility for sputum examination to first contact with any health care provider (HCP)), health system level diagnosis delay (from contact with first HCP to TB diagnosis) and treatment initiation delays (from diagnosis to treatment initiation). Total delay was the sum of patient level, health system level diagnosis delay and treatment initiation delays.
RESULTS: We included 234 ACF-diagnosed and 231 PCF-diagnosed patients. When compared to PCF, ACF patients were relatively older (≥65 years, 14% versus 8%, p = 0.041), had no formal education (57% versus 36%, p<0.001), had lower monthly income per capita (median 13.1 versus 15.7 USD, p = 0.014), were more likely from rural areas (92% versus 81%, p<0.002) and residing far away from the sputum microscopy centres (more than 15 km, 24% versus 18%, p = 0.126). Fewer patients had history of significant loss of weight (68% versus 78%, p = 0.011) and sputum grade of 3+ (15% versus 21%, p = 0.060). Compared to PCF, HCP visits among ACF patients was significantly lower (median one versus two HCPs, p<0.001). ACF patients had significantly lower health system level diagnosis delay (median five versus 19 days, p = 0.008) and the association remained significant after adjusting for potential confounders. Patient level and total delays were not significantly different.
CONCLUSION: Axshya SAMVAD linked the most impoverished communities to TB care and resulted in reduction of health system level diagnosis delay.

DOI: 10.1371/journal.pone.0213345
PMCID: PMC6415860
PMID: 30865730

146: Shi T, Denouel A, Tietjen AK, Campbell I, Moran E, Li X, Campbell H, Demont C, Nyawanda BO, Chu HY, Stoszek SK, Krishnan A, Openshaw P, Falsey AR, Nair H; RESCEU Investigators . Global Disease Burden Estimates of Respiratory Syncytial Virus-Associated Acute Respiratory Infection in Older Adults in 2015: A Systematic Review and Meta-Analysis. J Infect Dis. 2019 Mar 18. pii: jiz059. doi: 10.1093/infdis/jiz059. [Epub ahead of print] PubMed PMID: 30880339.

Respiratory syncytial virus-associated acute respiratory infection (RSV-ARI) constitutes a substantial disease burden in older adults aged ≥65 years. We aimed to identify all studies worldwide investigating the disease burden of RSV-ARI in this population. We estimated the community incidence, hospitalization rate, and in-hospital case-fatality ratio (hCFR) of RSV-ARI in older adults, stratified by industrialized and developing regions, using data from a systematic review of studies published between January 1996 and April 2018 and 8 unpublished population-based studies. We applied these rate estimates to population estimates for 2015 to calculate the global and regional burdens in older adults with RSV-ARI in the community and in hospitals for that year. We estimated the number of in-hospital deaths due to RSV-ARI by combining hCFR data with hospital admission estimates from hospital-based studies. In 2015, there were about 1.5 million episodes (95% confidence interval [CI], .3 million-6.9 million) of RSV-ARI in older adults in industrialized countries (data for developing countries were missing), and of these, approximately 14.5% (214 000 episodes; 95% CI, 100 000-459 000) were admitted to hospitals. The global number of hospital admissions for RSV-ARI in older adults was estimated at 336 000 hospitalizations (uncertainty range [UR], 186 000-614 000). We further estimated about 14 000 in-hospital deaths (UR, 5000-50 000) related to RSV-ARI globally. The hospital admission rate and hCFR were higher for those aged ≥65 years than for those aged 50-64 years. The disease burden of RSV-ARI among older adults is substantial, with limited data from developing countries. Appropriate prevention and management strategies are needed to reduce this burden.

DOI: 10.1093/infdis/jiz059
PMID: 30880339

147: Shrivastava N, Singh P, Nayak B, Garg B. The Spectrum of Clinical and Urodynamic Findings in Patients with Spinal Tuberculosis Exhibiting Lower Urinary Tract Symptoms, before and after Spinal Surgical Intervention with Antitubercular Treatment: A Prospective Study. Asian Spine J. 2019 Mar 26. doi: 10.31616/asj.2018.0217. [Epub ahead of print] PubMed PMID: 30909676.

Study Design: Observational study.
Purpose: This study aims to assess the clinical and urodynamic parameters in patients with spinal tuberculosis (TB) exhibiting lower urinary tract symptoms (LUTS) at the time of presentation and after spinal surgical intervention.
Overview of Literature: Variable urodynamic findings in patients with spinal TB.
Methods: We prospectively evaluated 10 patients with spinal TB exhibiting LUTS. Urinary symptoms were assessed by the American Urological Association (AUA) symptom score. We performed a urodynamic study (UDS), including electromyography, in all patients before and 3 months after spinal surgery.
Results: The mean age of patients was 29.7 years (range, 15-52 years), and the mean AUA symptom score was 12.5 and 11.8 before and after spinal surgery, respectively. Overall, five patients exhibited improvement in the AUA symptom score, and three showed no change, while two patients' condition worsened. We observed detrusor overactivity (DO) in two patients, and detrusor sphincter dyssynergia (DSD) in four patients. In addition, high-pressure voiding (HPV) was noted in two patients. On follow-up after spinal surgery, DO and DSD exhibited no improvement. Although HPV resolved, two patients developed new-onset poor compliance with worsening DO and DSD. Furthermore, two patients had bilateral hydronephrosis before surgery, which resolved on follow-up.
Conclusions: Patients with spinal TB exhibiting LUTS can display a spectrum of clinical presentations and variable UDS findings. As two patients exhibited new onset poor compliance with bilateral hydronephrosis in one of them, this study concludes that a close follow-up for upper tracts in these patients is required despite successful spinal surgery.

DOI: 10.31616/asj.2018.0217
PMID: 30909676

148: Singh D, Reeta KH, Sharma U, Jagannathan NR, Dinda AK, Gupta YK. Neuro-protective effect of monomethyl fumarate on ischemia reperfusion injury in rats: Role of Nrf2/HO1 pathway in peri-infarct region. Neurochem Int. 2019 Jun;126:96-108. doi: 10.1016/j.neuint.2019.03.010. Epub 2019 Mar 14. PubMed PMID: 30880045.

Post stroke recanalization has been associated with increased risk of oxidative stress. Stimulating endogenous antioxidant pathway by activation of nuclear factor erythroid-2-related factor-2 (Nrf2) plays a key role in neuronal defense against inflammation and oxidative stress in penumbra. Here, we explored whether monomethyl fumarate (MMF) could produce neuro-protection after ischemia/reperfusion (I/R) injury via Nrf2/HO1 activation. In male SD rats, middle cerebral artery was occluded for 90 min and confirmed using Laser Doppler flowmeter. MMF (10, 20 and 40 mg/kg) was administered in two divided doses at 30 min post ischemia and 5-10 min after reperfusion. After 24 h, effect on neurobehavioral parameters, infarct damage by TTC staining and MRI, oxidative stress and inflammatory cytokines were assessed. Expression studies of nuclear Nrf2 and cytoplasmic HO1 were performed in peri-infarct cortex and striatum; followed by dual immunofluorescence study to check the specific cell type. I/R induced neurobehavioral deficits and infarct damage were significantly ($p < 0.05$) attenuated by MMF (20 and 40 mg/kg). MMF, 20 mg/kg, significantly normalized I/R induced altered redox status and increased levels of TNF-α, IL-1β in the ipsilateral cortex. MRI data showed significantly reduced infarct in cortex but not in striatum after MMF treatment. Expression of nuclear Nrf2 and cytoplasmic HO1 were significantly ($p < 0.05$) increased in peri-infarct cortex after treatment with MMF. Additionally, dual immunofluorescence showed increased Nrf2 expression in neurons and HO1 expression in neurons as well as astrocytes in peri-infarct cortex after MMF treatment. Our results show the neuro-protective potential of MMF probably by restricting the progression of damage from striatum to cortex through activation of Nrf2/HO1 pathway in peri-infarct cortex.

DOI: 10.1016/j.neuint.2019.03.010
PMID: 30880045

149: Singh K, Patel SA, Biswas S, Shivashankar R, Kondal D, Ajay VS, Anjana RM, Fatmi Z, Ali MK, Kadir MM, Mohan V, Tandon N, Narayan KMV, Prabhakaran D. Multimorbidity in South Asian adults: prevalence, risk factors and mortality. J Public Health (Oxf). 2019 Mar 1;41(1):80-89. doi: 10.1093/pubmed/fdy017. PubMed PMID: 29425313.

BACKGROUND: We report the prevalence, risk factors and mortality associated with multimorbidity in urban South Asian adults.
METHODS: Hypertension, diabetes, heart disease, stroke and chronic kidney disease were measured at baseline in a sample of 16 287 adults ages ≥20 years in Delhi, Chennai and Karachi in 2010-11 followed for an average of 38 months. Multimorbidity was defined as having ≥2 chronic conditions at baseline. We identified correlates of multimorbidity at baseline using multinomial logistic models, and we assessed the prospective association between multimorbidity and mortality using Cox proportional hazards models.
RESULTS: The adjusted prevalence of multimorbidity was 9.4%; multimorbidity was highest in adults who were aged ≥60 years (37%), consumed alcohol (12.3%), body mass index ≥25 m/kg2 (14.1%), high waist circumference (17.1%) and had family history of a chronic condition (12.4%). Compared with adults with no chronic conditions, the fully adjusted relative hazard of death was twice as high in adults with two morbidities (hazard ratio [HR] = 2.3; 95% confidence interval [CI]: 1.6, 3.3) and thrice as high in adults with ≥3 morbidities (HR = 3.1; 95% CI: 1.9, 5.1).
CONCLUSION: Multimorbidity affects nearly 1 in 10 urban South Asians, and each additional morbidity carries a progressively higher risk of death. Identifying locally appropriate strategies for prevention and coordinated management of multimorbidity will benefit population health in the region.

DOI: 10.1093/pubmed/fdy017
PMID: 29425313

150: Singh K, Ali MK, Devarajan R, Shivashankar R, Kondal D, Ajay VS, Menon VU, Varthakavi PK, Viswanathan V, Dharmalingam M, Bantwal G, Sahay RK, Masood MQ, Khadgawat R, Desai A, Prabhakaran D, Narayan KMV, Phillips VL, Tandon N; CARRS Trial Group. Rationale and protocol for estimating the economic value of a multicomponent quality improvement strategy for diabetes care in South Asia. Glob Health Res Policy. 2019 Mar 18;4:7. doi: 10.1186/s41256-019-0099-x. eCollection 2019. PubMed PMID: 30923749; PubMed Central PMCID: PMC6421672.

Background: Economic dimensions of implementing quality improvement for diabetes care are understudied worldwide. We describe the economic evaluation protocol within a randomised controlled trial that tested a multi-component quality improvement (QI) strategy for individuals with poorly-controlled type 2 diabetes in South Asia.
Methods/design: This economic evaluation of the Centre for Cardiometabolic Risk Reduction in South Asia (CARRS) randomised trial involved 1146 people with poorly-controlled type 2 diabetes receiving care at 10 diverse diabetes clinics across India and Pakistan. The economic evaluation comprises both a within-trial cost-effectiveness analysis (mean 2.5 years follow up) and a microsimulation model-based cost-utility analysis (life-time horizon). Effectiveness measures include multiple risk factor control (achieving HbA1c < 7% and blood pressure < 130/80 mmHg and/or LDL-cholesterol < 100 mg/dl), and patient reported outcomes including quality adjusted life years (QALYs) measured by EQ-5D-3 L, hospitalizations, and diabetes related complications at the trial end. Cost measures include direct medical and non-medical costs relevant to outpatient care (consultation fee, medicines, laboratory tests, supplies, food, and escort/accompanying person costs, transport) and inpatient care (hospitalization, transport, and accompanying person costs) of the intervention compared to usual diabetes care. Patient, healthcare system, and societal perspectives will be applied for costing. Both cost and health effects will be discounted at 3% per year for within trial cost-effectiveness analysis over 2.5 years and decision modelling analysis over a lifetime horizon. Outcomes will be reported as the incremental cost-effectiveness ratios (ICER) to achieve multiple risk factor control, avoid diabetes-related complications, or QALYs gained against varying levels of willingness to pay threshold values. Sensitivity analyses will be performed to assess uncertainties around ICER estimates by varying costs (95% CIs) across public vs. private settings and using conservative estimates of effect size (95% CIs) for multiple risk factor control. Costs will be reported in US$ 2018.
Discussion: We hypothesize that the additional upfront costs of delivering the intervention will be counterbalanced by improvements in clinical outcomes and patient-reported outcomes, thereby rendering this multi-component QI intervention cost-effective in resource constrained South Asian settings.
Trial registration: ClinicalTrials.gov: NCT01212328.

DOI: 10.1186/s41256-019-0099-x
PMCID: PMC6421672
PMID: 30923749

151: Singh N, Goyal V. Rituximab as induction therapy in refractory myasthenia gravis: 18Â month follow-up study. J Neurol. 2019 Jul;266(7):1596-1600. doi: 10.1007/s00415-019-09296-y. Epub 2019 Mar 27. PubMed PMID: 30919039.

BACKGROUND: Myasthenia gravis is an immune-mediated disorder characterized by easy fatigability and diurnal variation in skeletal muscle weakness. Aim of therapy is to prevent crisis and maintain remission. However, despite standard

therapy, some remain refractory to treatment.
AIMS AND OBJECTIVES: To look for efficacy of rituximab in treating refractory myasthenia gravis (MG) in the form of MGFA-PIS score, number of crisis, and dose reduction in immunotherapies.
MATERIAL AND METHODS: A retrospective study was performed in patients with myasthenia gravis (MG) referred to the All India Institute of Medical Sciences (AIIMS) from January 2012 to December 2017 with follow-up of at least 6 months.
RESULTS: Eight refractory MG patients (six AchR positive and two Musk-positive) were identified on oral corticosteroids and azathioprine. After four cycles of rituximab, all patients showed a dose reduction of whom seven were completely tapered off prednisone and there was a 53.8% dose reduction in azathioprine. All patients were continued on AZA after RTX infusion unless contraindicated. Seven achieved minimal manifestation (MM)-2 status as per the MGFA-PIS scale. None of the patients had infusion associated reactions or cytopenia post-RTX infusion.
CONCLUSION: In this small retrospective study, we used RTX as induction therapy and results suggest that repeated RTX infusions may not be necessary as it adds to cost of therapy, especially in LMIC like India.

DOI: 10.1007/s00415-019-09296-y
PMID: 30919039

152: Singh RK, Kumar S, Tomar MS, Verma PK, Singh SP, Gautam PK, Acharya A. Classical Protein Kinase C: a novel kinase target in breast cancer. Clin Transl Oncol. 2019 Mar;21(3):259-267. doi: 10.1007/s12094-018-1929-x. Epub 2018 Jul 30. Review. PubMed PMID: 30062522.

Classical protein kinase C (cPKC) enzymes are ser/thr protein kinases that have been an important factor in regulating a variety of cellular functions required for both in terms of health and disease. Therefore, precise control of cPKC-mediated signal is necessary for cellular homeostasis; however, their dysregulation leads to the development of several pathophysiological conditions including cancer. In cellular microenvironment, cPKC-mediated signaling is accompanied by multiple molecular mechanisms including phosphorylation, second messenger binding, and scaffold proteins. Functional cPKC interacts with a number of cellular proteins involved in the regulation of multiple biological functions such as cell growth, survival, migration, and adhesion. Further, the role of cPKC varies from cell to cell, substrate to substrate and, therefore, it is plausible to assume that the dysregulation of cPKC activity causes cellular transformation. Currently, there is no sufficient literature available to provide better understating to develop an effective therapeutic regimen to reverse pathophysiological condition caused by functionally dysregulated cPKC. Therefore, in the present review, we have focused on to provide a better and detail information on the various aspects of cPKC such as structure, mode of activation, regulation, and distinct cellular functions useful for the development of an effective therapeutic regimen against the breast cancer.

DOI: 10.1007/s12094-018-1929-x
PMID: 30062522 [Indexed for MEDLINE]

153: Singh S, Sahni K, Arava S. Speckled Acral Hypopigmentation: A New Pigmentary Disorder or an Unknown Presentation of a Known Disorder? Indian Dermatol Online J. 2019 Mar-Apr;10(2):182-183. doi: 10.4103/idoj.IDOJ_139_18. PubMed PMID: 30984599; PubMed Central PMCID: PMC6434748.

154: Singh S, Kumar S, Deep R. Patients with deliberate self-harm attended in emergency setting at a tertiary care hospital: A 13-month analysis of clinical-psychiatric profile. Int J Psychiatry Med. 2019 Mar 25:91217419837052. doi: 10.1177/0091217419837052. [Epub ahead of print] PubMed PMID: 30909765.

OBJECTIVES: To describe the pattern and clinical-psychiatric profile of patients presenting with deliberate self-harm attempt to an emergency setting.
METHODS: The study involves the analysis of the case records of 109 consecutive patients with deliberate self-harm evaluated by the psychiatric emergency team at a premier, tertiary care hospital in India over a period of 13 months (January

2015-January 2016).
RESULTS: Deliberate self-harm had a clinical prevalence of 16.4% (109/666) among total mental and behavioral emergencies attended in the same period. A large majority of attempters were in the age range of 18-39 years (84.4%), and females (58.7%) outnumbered males in total sample. Married females and unmarried males had significantly higher chances of attempting deliberate self-harm ($\chi 2 = 6.57$, $p = 0.01$). More than half (52.3%) of patients were found to have a diagnosable psychiatric illness at the time of presentation, most common being depressive disorder in 19.3% of overall sample. Past history of a psychiatric illness was evident in only 12.5% of patients. Common methods of deliberate self-harm were prescription drug/psychotropic overdose, poisoning with ingestion of phenyl cleaner or rat-killer poison. Significant gender differences were observed in the nature of precipitating events for deliberate self-harm, with interpersonal relationship problems being significantly more common in women ($p = 0.03$).
CONCLUSION: This study adds relevant and useful information on cross-cutting as well as gender-specific characteristics of patients presenting with deliberate self-harm attempt, from a developing country context. The study findings bear implications for designing interventions for primary and secondary prevention of such behavioral emergencies at a community level.

DOI: 10.1177/0091217419837052
PMID: 30909765

155: Singhal D, Sahay P, Nagpal R, Maharana PK. Re: Sun etÂ al.: Determining subclinical edema in Fuchs endothelial corneal dystrophy: revised classification using Scheimpflug tomography for preoperative assessment (Ophthalmology. 2019;2:195-204). Ophthalmology. 2019 Mar;126(3):e21-e22. doi: 10.1016/j.ophtha.2018.10.010. PubMed PMID: 30803526.

156: Singhal R, Rathore DK, Bhakuni T, Seth T, Guchhait P. Absence of Nonclassical Monocytes in Hemolytic Patients: Free Hb and NO-Mediated Mechanism. J Immunol Res. 2019 Mar 27;2019:1409383. doi: 10.1155/2019/1409383. eCollection 2019. PubMed PMID: 31032371; PubMed Central PMCID: PMC6458887.

In a recent work, we have described the kinetics among the monocyte subsets in the peripheral blood of hemolytic patients including paroxysmal nocturnal hemoglobinuria (PNH) and sickle cell disease (SCD). After engulfing Hb-activated platelets, classical monocytes (CD14+CD16-) significantly transformed into highly inflammatory (CD14+CD16hi) subsets in vitro. An estimated 40% of total circulating monocytes in PNH and 70% in SCD patients existed as CD14+CD16hi subsets. In this study, we show that the nonclassical (CD14dimCD16+) monocyte subsets are nearly absent in patients with PNH or SCD, compared to 10-12% cells in healthy individuals. In mechanism, we have described the unique role of both free Hb and nitric oxide (NO) in reducing number of nonclassical subsets more than classical monocytes. After engulfing Hb-activated platelets, the monocytes including nonclassical subsets acquired rapid cell death within 12 h in vitro. Further, the treatment to monocytes either with the secretome of Hb-activated platelets containing NO and free Hb or purified free Hb along with GSNO (a physiological NO donor) enhanced rapid cell death. Besides, our data from both PNH and SCD patients exhibited a direct correlation between intracellular NO and cell death marker 7AAD in monocytes from the peripheral blood. Our data together suggest that due to the immune surveillance nature, the nonclassical or patrolling monocytes are encountered frequently by Hb-activated platelets, free Hb, and NO in the circulation of hemolytic patients and are predisposed to die rapidly.

DOI: 10.1155/2019/1409383
PMCID: PMC6458887
PMID: 31032371

157: Singla V, Gattu T, Aggarwal S, Bhambri A, Agarwal S. Evaluation of Epworth Sleepiness Scale to Predict Obstructive Sleep Apnea in Morbidly Obese Patients and Increasing Its Utility. J Laparoendosc Adv Surg Tech A. 2019

Mar;29(3):298-302. doi: 10.1089/lap.2018.0329. Epub 2018 Aug 15. PubMed PMID: 30109974.

INTRODUCTION: Studies have shown that Epworth sleepiness scale (ESS) is not a good tool to predict obstructive sleep apnea (OSA). However, data regarding the accuracy of ESS in the prediction of OSA among morbidly obese patients are scarce.
METHODS: The study involved a retrospective review of the charts of the consecutive patients who underwent bariatric surgery at a tertiary care teaching hospital. All the patients underwent polysomnography (PSG) and undertook the ESS questionnaire. The sensitivity and specificity of ESS were calculated based on its correlation with the PSG findings. Furthermore, a new score was devised to improve the utility of ESS to predict OSA.
RESULTS: A total of 232 consecutive patients from January 2014 to July 2017 were included in the study. The mean age and body mass index (BMI) were 40.5±11.8 years and 47.6±7.3 kg/m2, respectively. Among the 162 patients who had an ESS <10, 57.4% had moderate-to-severe OSA. The sensitivity of ESS to predict moderate-to-severe OSA was found to be 38.8% and the positive predictive value was 84.2% (positive likelihood ratio 2.82, 95% confidence interval = 1.57-5.06). A predictive score was identified as 0.031Age (years) +0.039BMI (kg/m2) + 0.038ESS + Gender (1 for male, 0 for female). The score had a sensitivity of 80% at a cutoff of 3.3.
CONCLUSIONS: Among the morbidly obese, ESS is a poor predictor of OSA. Its utility as a tool for prediction of moderate-to-severe OSA can be improved by use of a new formula incorporating age, gender, and BMI beside ESS.

DOI: 10.1089/lap.2018.0329
PMID: 30109974 [Indexed for MEDLINE]

158: Sinha M, Pandey NN, Rajagopal R, Kumar S. Anomalous Superior Caval Drainage of the Great Cardiac Vein. Ann Thorac Surg. 2019 Mar;107(3):e211. doi: 10.1016/j.athoracsur.2018.09.042. Epub 2018 Nov 4. PubMed PMID: 30403978.

159: Somashekar PH, Girisha KM, Nampoothiri S, Gowrishankar K, Devi RR, Gupta N, Narayanan DL, Kaur A, Bajaj S, Jagadeesh S, Lewis LES, Shailaja S, Shukla A. Locus and allelic heterogeneity and phenotypic variability in Waardenburg syndrome. Clin Genet. 2019 Mar;95(3):398-402. doi: 10.1111/cge.13468. Epub 2018 Nov 27. PubMed PMID: 30394532.

Waardenburg syndrome (WS) is a disorder of neural crest cell migration characterized by auditory and pigmentary abnormalities. We investigated a cohort of 14 families (16 subjects) either by targeted sequencing or whole-exome sequencing. Thirteen of these families were clinically diagnosed with WS and one family with isolated non-syndromic hearing loss (NSHL). Intra-familial phenotypic variability and non-penetrance were observed in families diagnosed with WS1, WS2 and WS4 with pathogenic variants in PAX3, MITF and EDNRB, respectively. We observed gonosomal mosaicism for a variant in PAX3 in an asymptomatic father of two affected siblings. For the first time, we report a biallelic pathogenic variant in MITF in a subject with WS2 and a biallelic variant in EDNRB was noted in a subject with WS2. An individual with isolated NSHL carried a pathogenic variant in MITF. Blended phenotype of NSHL and albinism was observed in a subject clinically diagnosed to have WS2. A phenocopy of WS1 was observed in a subject with a reported pathogenic variant in GJB2, known to cause isolated NSHL. These novel and infrequently reported observations exemplify the allelic and genetic heterogeneity and show phenotypic diversity of WS.

DOI: 10.1111/cge.13468
PMID: 30394532

160: Sood S, Agarwal SK, Singh R, Gupta S, Sharma VK. In vitro assessment of gentamicin and azithromycin-based combination therapy against Neisseria gonorrhoeae isolates in India. J Med Microbiol. 2019 Apr;68(4):555-559. doi:

10.1099/jmm.0.000953. Epub 2019 Mar 14. PubMed PMID: 30869583.

PURPOSE: The public health burden of infections caused by Neisseria gonorrhoeae is magnified due to high rates of resistance to traditional antimicrobials. The aim of this study was to evaluate the in vitro efficacy of an alternative dual therapy comprising gentamicin and azithromycin.
METHODOLOGY: The E-test method was used to determine the minimum inhibitory concentrations (MICs) of gentamicin and azithromycin individually prior to testing in combination using the cross or 90o angle formation method. A total of 70 clinical isolates of N.gonorrhoeae displaying varying ceftriaxone MICs along with 2 reference strains (WHO K and P) and 1 ceftriaxone-resistant QA isolate were examined. The fractional inhibitory concentration index (FICI) was calculated and the results were interpreted using the following criteria: synergy, FICI ≤0.5; indifference or additive, FICI >0.5 to ≤4.0; and antagonism, FICI >4.0.
RESULTS: A total of 54 (77.1%) isolates displayed indifference, while 16 (22.9%) demonstrated synergy. When azithromycin was tested alone, the MICs ranged from 0.016 to 2 µg ml-1 . However, in combination with gentamicin, the mean MIC value of all isolates decreased from 0.275 µg ml-1 to 0.090 µg ml-1 (P=0.05).When gentamicin was tested alone, the MICs ranged from 0.25 to 8 µg ml-1, with a mean MIC of 4.342 µg ml-1, whereas in combination with azithromycin it decreased significantly to 2.042 µg ml-1 (P=0.04).
CONCLUSION: No antagonism was observed in this combination, suggesting that it could be a future treatment option as we prepare for a post-cephalosporin era. However, comprehensive in vivo evaluations are warranted and recommendations should be made based on clinical trials.

DOI: 10.1099/jmm.0.000953
PMID: 30869583 [Indexed for MEDLINE]

161: Srivastava MVP, Vishnu VY. The infamous story of incident stroke and inflamed gall bladder! Neurol India. 2019 Mar-Apr;67(2):389-390. doi: 10.4103/0028-3886.258025. PubMed PMID: 31085841.

162: Subhadarshani S, Abhishek GN. Imatinib-induced Melasma-like Pigmentation. Indian J Dermatol. 2019 Mar-Apr;64(2):158-159. doi: 10.4103/ijd.IJD_302_17. PubMed PMID: 30983616; PubMed Central PMCID: PMC6440189.

163: Takkar B, Khokhar S, Agarwal D, Venkatesh P. Ultra-wide field imaging of giant circumferential chorioretinal fold following post-operative hypotony. Indian J Ophthalmol. 2019 Mar;67(3):407. doi: 10.4103/ijo.IJO_1483_18. PubMed PMID: 30777970; PubMed Central PMCID: PMC6407375.

164: Talwar S, Siddharth CB, Rajashekar P, Sengupta S, Sharma S, Gharde P, Choudhary SK, Airan B. An alternative technique for completion of the total cavopulmonary connection. J Card Surg. 2019 May;34(5):236-238. doi: 10.1111/jocs.14037. Epub 2019 Mar 29. PubMed PMID: 30924563.

BACKGROUND: Total Cavopulmonary connection (Fontan) is the final palliation for patients with a functionally univentricular heart. This is commonly accomplished after a prior bidirectional Glenn on cardiopulmonary bypass (CPB) with separate cannulation of the aorta, superior vena cava (SVC), and inferior vena cava. We describe an alternative technique of Fontan completion that eliminates the need for cannulation and dissection of the SVC, and pulmonary artery dissection.
METHODS: Between January and October 2018, 17 patients underwent completion Fontan using an alternate technique at our institute. All operations were conducted on CPB at normothermia without cannulating the SVC RESULTS: Mean CPB time was 60 ± 16.8 minutes (range, 39-102 minutes). There were no early deaths. Mean postoperative Fontan pressures were 15.6 ± 1.2 mm Hg with no gradient between the SVC and IVC pressures. Mean duration of hospital stay was 15.6 ± 3.6 days (range, 10-22 days). No patient developed phrenic nerve paresis or palsy.
CONCLUSIONS: Completion without cannulating the SVC is simple, reproducible, and

easy to teach. It avoids the disadvantages associated with routine techniques.

DOI: 10.1111/jocs.14037
PMID: 30924563

165: Talwar S, Arora Y, Gupta SK, Kothari SS, Ramakrishnan S, Saxena A, Choudhary SK. Total Anomalous Pulmonary Venous Connection Beyond the First Decade of Life. World J Pediatr Congenit Heart Surg. 2019 Mar;10(2):185-191. doi: 10.1177/2150135118822792. PubMed PMID: 30841831.

OBJECTIVE: We report our experience with surgery for total anomalous pulmonary venous connection (TAPVC) beyond first decade of life.
METHODS: Between January 1987 and July 2017, 98 patients ≥ten years underwent TAPVC repair. Their detailed case-records were analyzed.
RESULTS: Mean age was 19.05 (± 12.8; median 18) years. Anatomic subtypes were supracardiac (n = 62), cardiac (n = 20), and mixed (n = 16). An atrial septal defect (ASD) was present in all. Severe tricuspid valve regurgitation was present in four patients and severe rheumatic mitral regurgitation was present in one. On preoperative cardiac catheterization, mean pulmonary artery pressure was 67 ± 15.6 mm Hg (median 58; range 37-96). Mean pulmonary vascular resistance was 5.6 ± 3.9 Woods units·m2 (median 4.7, range 2.9-11.8). Twenty-five patients had moderate and eight had severe pulmonary arterial hypertension. Right ventricular dysfunction was present in eight patients. At repair, a small ASD was left open in 87 patients while in 11 patients, the ASD was closed using a unidirectional valved patch. Follow-up was available for 90 (92%) patients. There were no late deaths over a mean follow-up of 163 ± 103.98 months (median 163, range 1-362). Eighty-two patients were in NYHA class I and eight were in class II. Right ventricular function normalized in 82 patients while 80 patients had reduction in pulmonary artery pressure. Event-free survival was 94.2% at 5 years, 92.3% at 10 years, and 90% at 20 and 30 years.
CONCLUSIONS: Outcomes of surgical repair for TAPVC beyond first decade of life are satisfactory. Close follow-up, however, is necessary for possible persistence of pulmonary arterial hypertension.

DOI: 10.1177/2150135118822792
PMID: 30841831 [Indexed for MEDLINE]

166: Titiyal JS, Kaur M, Bharti N, Singhal D, Saxena R, Sharma N. Optimal near and distance stereoacuity after binocular implantation of extended range of vision intraocular lenses. J Cataract Refract Surg. 2019 Jun;45(6):798-802. doi: 10.1016/j.jcrs.2018.12.024. Epub 2019 Mar 12. PubMed PMID: 30876785.

PURPOSE: To evaluate stereopsis and visual quality after bilateral implantation of extended range of vision intraocular lenses (ERV IOLs).
SETTING: R.P. Centre for Ophthalmic Sciences, AIIMS, New Delhi, India.
DESIGN: Prospective interventional study.
METHODS: Patients underwent phacoemulsification with bilateral implantation of ERV IOLs. The primary outcome measures were stereopsis (distance and near Randot) and visual quality (ray-tracing aberrometry). The secondary outcome measures were visual acuity and patient satisfaction. Follow-up was performed on day 1 and at 1, 3, 6, and 12 months postoperatively.
RESULTS: The study comprised 50 patients (100 eyes). The mean age of the patients was 58.9 years ± 8.9 (SD). At 1 year, the mean distance stereopsis was 103.6 ± 49.1 seconds of arc (arcsec) and near stereopsis was 21.1 ± 2.3 arcsec. Perfect near stereopsis of 20 arcsec was present in 80% of cases, and 82% had good distance stereopsis of 100 arcsec or better. Stereopsis correlated well with the patient satisfaction score ($P < .001$) and average internal modulation transfer function (MTF) ($P < .015$). The mean Strehl ratio was 0.029 ± 0.021, MTF was 0.24 ± 0.08, total higher-order aberrations were 0.62 ± 0.41 μm, and coma was 0.25 ± 0.18 μm. The mean binocular uncorrected decimal visual acuities were 0.98 ± 0.07 (distance), 0.82 ± 0.09 (intermediate) and 0.64 ± 0.08 (near). The mean patient satisfaction score was 9.08 ± 1.1, and no case required IOL

explantation because of visually disturbing phenomena or patient dissatisfaction. CONCLUSION: Excellent stereoacuity was observed after bilateral implantation of ERV IOLs, which correlated well with patient satisfaction and quality of vision.

167: Tiwari V, Rajeswari MR, Tiwari M. Proteomic analysis of iron-regulated membrane proteins identify FhuE receptor as a target to inhibit siderophore-mediated iron acquisition in Acinetobacter baumannii. Int J Biol Macromol. 2019 Mar 15;125:1156-1167. doi: 10.1016/j.ijbiomac.2018.12.173. Epub 2018 Dec 20. PubMed PMID: 30579900.

Survival of the Acinetobacter baumannii inside host requires different micronutrients such as iron, but their bioavailability is limited because of nutritional immunity created by host. A. baumannii has to develop mechanisms to acquire nutrient iron during infection. The present study is an attempt to identify membrane proteins involved in iron sequestration mechanism of A. baumannii using two-dimensional electrophoresis and LC-MS/MS analysis. The identified iron-regulated membrane protein (IRMP) of A. baumannii was used for its interaction studies with different siderophores, and designing of the inhibitor against A. baumannii targeting this IRMP. Membrane proteomic results identified over-expression of four membrane proteins (Fhu-E receptor, ferric-acinetobactin receptor, ferrienterochelin receptor, and ferric siderophore receptor) under iron-limited condition. A. baumannii produces siderophores that have good interaction with the FhuE receptor. Result also showed that FhuE receptor has interaction with siderophores produced by other bacteria. Interaction of FhuE receptor and siderophores helps in iron sequestration and survival of Acinetobacter under nutritional immunity imposed by the host. Hence it becomes essential to find a potential inhibitor for the FhuE receptor that can inhibit the survival of A. baumannii in the host. In-silico screening, and molecular mechanics studies identified ZINC03794794 and ZINC01530652 as a likely lead to design inhibitor against the FhuE receptor of A. baumannii. The designed inhibitor is experimentally validated for its antibacterial activity on the A. baumannii. Therefore, designed inhibitor interferes with the iron acquisition mechanism of Acinetobacter hence may prove useful for preventing infection caused by A. baumannii by limiting nutrient availability.

DOI: 10.1016/j.ijbiomac.2018.12.173
PMID: 30579900 [Indexed for MEDLINE]

168: Trikha V, Gaba S, Kumar A, Mittal S, Kumar A. Safe corridor for iliosacral and trans-sacral screw placement in Indian population: A preliminary CT based anatomical study. J Clin Orthop Trauma. 2019 Mar-Apr;10(2):427-431. doi: 10.1016/j.jcot.2018.01.007. Epub 2018 Jan 11. PubMed PMID: 30828220; PubMed Central PMCID: PMC6383070.

Objectives: Nonsurgical management of unstable pelvic ring injuries is associated with poor outcomes. Posterior pelvic ring injuries include sacroiliac joint disruption and sacral fractures or a combination of the two. Morbidity is high in non-operatively managed patients. Screw fixation is being increasingly used to manage unstable posterior pelvic injuries. Limitations include a steep learning curve and potential for neurovascular injury. This is the first study in Indian population to describe the safe corridor for screw placement and check the feasibility of screw in both upper and lower sacral segments.
Methods: This study involved retrospective analysis of 105 pelvic CT scans of patients admitted to the emergency department of a Level 1 trauma centre. Vertical height at the level of constriction (vestibule) of S1 and S2 was measured in coronal sections and anteroposterior width of constrictions was measured in axial sections. We created a trajectory for 7.3 mm cylinder keeping additional 2 mm free bony corridor around it and confirmed that bony limits were not breached in axial, coronal and sagittal sections. Whenever there was breach in bony limit we checked applicability of 6.5 mm screw.

Results: The vertical height and anteroposterior width of vestibule/constriction of S1 was significantly higher in males, whereas S2 vestibule height and width were similar in males and females. Both male and female pelves were amenable to S1 Trans-sacral and S1 Iliosacral screw fixation with a 7.3 mm screw when a safe corridor of 2 mm was kept on all sides. However, when S2 segment was analysed, only 42.9% of male pelves and 25.7% of female pelves were amenable to insertion of trans-sacral 7.3 mm screw.
Conclusion: An individualized approach is necessary and each patient's CT must be carefully studied before embarking on sacroiliac screw fixation in Indian population.

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PMCID: PMC6383070 [Available on 2020-03-01]
PMID: 30828220

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To evade the possible toxicity associated with the formation of quinone-imine metabolite in amodiaquine (AQ), the para-hydroxyl group was replaced with a -F atom, and the resulting 4'-fluoro-amodiaquine (FAQ) was hybridized with substituted pyrimidines. The synthesized FAQ-pyrimidines displayed better in vitro potency than chloroquine (CQ) against the resistant P. falciparum strain (Dd2), exhibiting up to 47.3-fold better activity (IC50: 4.69 nM) than CQ (IC50: 222 nM) and 2.8-fold better potency than artesunate (IC50: 13.0 nM). Twelve compounds exhibited better antiplasmodial activity than CQ against the CQ-sensitive (NF54) strain. Two compounds were evaluated in vivo against a P. berghei-mouse malaria model. Mechanistic heme-binding studies, computational docking studies against Pf-DHFR and in vitro microsomal stability studies were performed for the representative molecules of the series to assess their antimalarial efficacy.

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Multigram drug depot systems for extended drug release could transform our capacity to effectively treat patients across a myriad of diseases. For example, tuberculosis (TB) requires multimonth courses of daily multigram doses for treatment. To address the challenge of prolonged dosing for regimens requiring

multigram drug dosing, we developed a gastric resident system delivered through the nasogastric route that was capable of safely encapsulating and releasing grams of antibiotics over a period of weeks. Initial preclinical safety and drug release were demonstrated in a swine model with a panel of TB antibiotics. We anticipate multiple applications in the field of infectious diseases, as well as for other indications where multigram depots could impart meaningful benefits to patients, helping maximize adherence to their medication.

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Orbit is an unusual and rare site for metastases from cancer. The most frequent site of a primary malignancy to metastasise to the orbit is the breast, followed by the lung. The malignant mixed mullerian tumour is a rare uterine and cervical carcinoma and accounts for <5% of uterine cancers. It is the primary tumour of the uterus, and de novo involvement of the cervix itself is extremely rare. We report the first case of cervical carcinoma with mixed mullerian aetiology to be associated with orbital metastasis and eventually leading to blindness and death.

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A major impediment to developing effective antimicrobials against Gram-negative bacteria like Salmonella is the ability of the bacteria to develop resistance against existing antibiotics and the inability of the antimicrobials to clear the intracellular bacteria residing in the gastrointestinal tract. As the critical balance of charge and hydrophobicity is required for effective membrane-targeting antimicrobials without causing any toxicity to mammalian cells, herein we report the synthesis and antibacterial properties of cholic acid-derived amphiphiles conjugated with alkyl chains of varied hydrophobicity. Relative to other hydrophobic counterparts, a compound with hexyl chain (6) acted as an effective antimicrobial against different Gram-negative bacteria. Apart from its ability to permeate the outer and inner membranes of bacteria; compound 6 can cross the cellular and lysosomal barriers of epithelial cells and macrophages and kill the facultative intracellular bacteria without disrupting the mammalian cell membranes. Oral delivery of compound 6 was able to clear the Salmonella-mediated gut infection and inflammation, and was able to combat persistent, stationary,

and multi-drug-resistant clinical strains. Therefore, our study reveals the ability of cholic acid-derived amphiphiles to clear intracellular bacteria and Salmonella-mediated gut infection and inflammation.

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Cervical cancer is a leading cause of cancer-related deaths among women in developing countries. Therefore, development of new chemotherapeutic agents is required. Unlike normal cells, cancer cells contain elevated copper levels which play an integral role in angiogenesis. Thus, targeting copper via copper-specific chelators in cancer cells can serve as effective anticancer strategy. In this work, a copper chelator pregnenolone acetate nucleus-based tetrazole derivative (ligand-L) was synthesized and characterized by elemental analysis, ESI-MS, 1H NMR and 13C NMR. DNA binding ability of ligand-L was studied using UV-Vis and fluorescence spectroscopy. Fluorescence spectroscopy studies reveal that quenching constant of ligand-l-DNA and ligand-L-Cu(II) were found to be 7.4 × 103 M-1 and 8.8 × 103 M-1, respectively. In vitro toxicity of ligand-L was studied on human cervical cancer C33A cancer cells. Results showed that ligand-L exhibit significant cytotoxic activity against cervical cancer C33A cells with IC50 value 5.0 ± 1.8 μM. Further, it was found that ligand-L cytotoxicity is due to redox cycling of copper to generate ROS which leads to DNA damage and apoptosis. In conclusion, this is the report where we synthesized pregnenolone acetate-based tetrazole derivative against C33A cells that targets cellular copper to induce pro-oxidant death in cancer cells. These findings will provide significant insights into the development of new chemical molecules with better copper chelating and pro-oxidant properties against cancer cells.

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