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

1: Abhyankar YS, Dev S, Sarun OS, Saxena A, Joshi R, Darbari H, Sajish C,

Sonavane UB, Gavane V, Deshpande A, Dixit T, Harsh R, Badwe R, Rath GK, Laskar S, Faddegon B, Perl J, Paganetti H, Schuemann J, Srivastava A, Obcemea C, Nath AK, Sharma A, Buchsbaum J. Monte Carlo Processing on a Chip (MCoaC)-preliminary experiments toward the realization of optimal-hardware for TOPAS/Geant4 to drive discovery. Phys Med. 2019 Aug;64:166-173. doi: 10.1016/j.ejmp.2019.06.016. Epub 2019 Jul 16. PubMed PMID: 31515016.

Amongst the scientific frameworks powered by the Monte Carlo (MC) toolkit Geant4 (Agostinelli et al., 2003), the TOPAS (Tool for Particle Simulation) (Perl et al., 2012) is one. TOPAS focuses on providing ease of use, and has significant implementation in the radiation oncology space at present. TOPAS functionality extends across the full capacity of Geant4, is freely available to non-profit users, and is being extended into radiobiology via TOPAS-nBIO (Ramos-Mendez et al., 2018). A current "grand problem" in cancer therapy is to convert the dose of treatment from physical dose to biological dose, optimized ultimately to the individual context of administration of treatment. Biology MC calculations are some of the most complex and require significant computational resources. In order to enhance TOPAS's ability to become a critical tool to explore the definition and application of biological dose in radiation therapy, we chose to explore the use of Field Programmable Gate Array (FPGA) chips to speedup the Geant4 calculations at the heart of TOPAS, because this approach called "Reconfigurable Computing" (RC), has proven able to produce significant (around 90x) (Sajish et al., 2012) speed increases in scientific computing. Here, we describe initial steps to port Geant4 and TOPAS to be used on FPGA. We provide performance analysis of the current TOPAS/Geant4 code from an RC implementation perspective. Baseline benchmarks are presented. Achievable performance figures of the subsections of the code on optimal hardware are presented; Aspects of practical implementation of "Monte Carlo on a chip" are also discussed.

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DOI: 10.1016/j.ejmp.2019.06.016
PMID: 31515016

2: Agarwal M, Johnston MV, Stafstrom CE. SYNGAP1 mutations: Clinical, genetic, and pathophysiological features. Int J Dev Neurosci. 2019 Aug 24;78:65-76. doi: 10.1016/j.ijdevneu.2019.08.003. [Epub ahead of print] Review. PubMed PMID: 31454529.

SYNGAP1 is a gene that encodes the cytosolic protein SYNGAP1 (SYNaptic GTPase Activating Protein), an essential component of the postsynaptic density at excitatory glutamatergic neurons. SYNGAP1 plays critical roles in synaptic development, structure, function, and plasticity. Mutations in SYNGAP1 result in a neurodevelopmental disorder termed Mental retardation-type 5 (MRD5, OMIM #612621) with a phenotype consisting of intellectual disability, motor impairments, and epilepsy, attesting to the importance of this protein for normal brain development. Here we review the clinical and pathophysiological aspects of SYNGAP1 mutations with a focus on their effect on synaptogenesis, neural circuit function, and cellular plasticity. We conclude by comparing the molecular pathogenesis of SYNGAP1 mutations with those of another neurodevelopmental disorder that affects dendritic function and cellular plasticity, fragile X syndrome. Insights into the molecular similarities and differences underlying these disorders could lead to rationale therapy development.

DOI: 10.1016/j.ijdevneu.2019.08.003

PMID: 31454529

3: Agarwal N, Chandrappa H, Varshney G, Borkar SA. TO THE EDITOR. Spine (Phila Pa 1976). 2019 Aug 1;44(15):E927. doi: 10.1097/BRS.0000000000003105. PubMed PMID: 31335791.

4: Aggarwal A, Mittal A, Sasi A, Nischal N. Non-Hodgkin's Lymphoma in AIDS. QJM. 2019 Aug 20. pii: hcz216. doi: 10.1093/qjmed/hcz216. [Epub ahead of print] PubMed PMID: 31432084.

5: Agrawal S, Goyal A, Agarwal S, Khadgawat R. Hypercalcaemia, adrenal insufficiency and bilateral adrenal histoplasmosis in a middle-aged man: a diagnostic dilemma. BMJ Case Rep. 2019 Aug 28;12(8). pii: e231142. doi: 10.1136/bcr-2019-231142. PubMed PMID: 31466957.

A 45-year-old man presented with a 3-month history of involuntary weight loss, anorexia, postural dizziness and intermittent fever. On investigation, he was found to have parathyroid hormone (PTH)-independent hypercalcaemia, with negative workup for 25-hydroxyvitamin D or 1,25-dihydroxyvitamin D excess, thyrotoxicosis, multiple myeloma and bony metastases. On further evaluation, he was detected to have primary hypoadrenalism with bilateral adrenal enlargement, secondary to adrenal histoplasmosis. Hypercalcaemia improved with hydration and physiological steroid replacement even before initiation of antifungal therapy, confirming adrenal insufficiency as the cause for hypercalcaemia. Hypercalcaemia resulting from hypoadrenalism secondary to adrenal histoplasmosis is rare and should be suspected whenever evaluating a patient with PTH-independent hypercalcaemia.

DOI: 10.1136/bcr-2019-231142
PMID: 31466957

6: Alexanderson-Rosas E, Espinola-Zavaleta N, Garcia EV, Peix A, Massardo T, Pabon LM, Antonio-Villa NE, Carvajal-Juarez I, Mesquita CT, Jimenez-Heffernan A, Patel C, Karthikeyan G, Kumar A, Butt S, Kalaivani M, Marin V, Morozova O, Paez D. Diastolic dyssynchrony assessment by gated myocardial perfusion-SPECT in subjects who underwent cardiac resynchronization therapy. J Nucl Cardiol. 2019 Aug 13. doi: 10.1007/s12350-019-01845-2. [Epub ahead of print] PubMed PMID: 31410734.

BACKGROUND: Left ventricular diastolic dyssynchrony (LVDD) can be assessed by gated myocardial perfusion single-photon emission computed tomography (GMP-SPECT). LVDD is an area of interest in subjects who underwent cardiac resynchronization therapy (CRT). The aim of this post hoc analysis was to assess the role of LVDD in subjects with CRT who were followed up at 6-month period.
MATERIAL & METHODS: Left ventricular diastolic dyssynchrony was assessed by GMP-SPECT at baseline and after CRT procedure in 160 subjects from 10 different cardiological centers. CRT procedure was performed as per current guidelines. Outcomes were defined as improvement in ≥1 New York Heart Association (NYHA) class, left ventricular ejection fraction (LVEF) by 5%, and reduction in end-systolic volume (ESV) by 15% and 5% points in Minnesota Living with Heart Failure Questionnaire. LVDD was defined as diastolic phase standard deviation ≥40 ± 14°.
RESULTS: Improvement in NYHA functional class occurred in 105 (65.6%), LVEF in 74 (46.3%), decrease in ESV in 86 (53.8%), and Minnesota score in 85 (53.1%) cases. Baseline LV diastolic standard deviation was 53.53° ± 20.85 and at follow-up 40.44° ± 26.1283; ($P < 0.001$). LVDD was not associated with improvement in clinical outcomes at follow-up.

CONCLUSION: CRT improves both systolic and diastolic dyssynchrony values at 6-month follow-up. LVDD at baseline is correlated with cardiac functionality at follow-up, but not with overall favorable clinical outcomes.

DOI: 10.1007/s12350-019-01845-2
PMID: 31410734

7: Ambereen A, Lal B, Agarwal B, Yadav R, Roychoudhury A. Sandwich technique for the surgical management of oral submucous fibrosis. Br J Oral Maxillofac Surg. 2019 Aug 9. pii: S0266-4356(19)30307-9. doi: 10.1016/j.bjoms.2019.07.020. [Epub ahead of print] PubMed PMID: 31402194.

8: Anthwal D, Lavania S, Gupta RK, Verma A, Myneedu VP, Sharma PP, Verma H, Malhotra V, Gupta A, Gupta NK, Sarin R, Haldar S, Tyagi JS. Development and evaluation of novel bio-safe filter paper-based kits for sputum microscopy and transport to directly detect Mycobacterium tuberculosis and associated drug resistance. PLoS One. 2019 Aug 13;14(8):e0220967. doi: 10.1371/journal.pone.0220967. eCollection 2019. PubMed PMID: 31408508; PubMed Central PMCID: PMC6692035.

India has the highest burden of Tuberculosis (TB) and multidrug-resistant TB (MDR-TB) worldwide. Innovative technology is the need of the hour to identify these cases that remain either undiagnosed or inadequately diagnosed due to the unavailability of appropriate tools at primary healthcare settings. We developed and evaluated 3 kits, namely 'TB Detect' (containing BioFM-Filter device), 'TB Concentration and Transport' (containing Trans-Filter device) and 'TB DNA Extraction' kits. These kits enable bio-safe equipment-free concentration of sputum on filters and improved fluorescence microscopy at primary healthcare centres, ambient temperature transport of dried inactivated sputum filters to central laboratories and molecular detection of drug resistance by PCR and DNA sequencing (Mol-DST). In a 2-site evaluation (n = 1190 sputum specimens) on presumptive TB patients, BioFM-Filter smear exhibited a significant increase in positivity of 7% and 4% over ZN smear and LED-FM smear ($p<0.05$), respectively and an increment in smear grade status (1+ or 2+ to 3+) of 16% over ZN smear and 20% over LED-FM smear. The sensitivity of Mol-DST in presumptive MDR-TB and XDR-TB cases (n = 148) was 90% for Rifampicin (95% confidence interval [CI], 78-96%), 84% for Isoniazid (95% CI, 72-92%), 83% for Fluoroquinolones (95% CI, 66-93%) and 75% for Aminoglycosides (95% CI, 35-97%), using phenotypic DST as the reference standard. Test specificity was 88-93% and concordance was ~89-92% (κ value 0.8-0.9). The patient-friendly kits described here address several of the existing challenges and are designed to provide 'Universal Access' to rapid TB diagnosis, including drug-resistant disease. Their utility was demonstrated by application to sputum at 2 sites in India. Our findings pave the way for larger studies in different point-of-care settings, including high-density urban areas and remote geographical locations.

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PMCID: PMC6692035
PMID: 31408508

9: Babu BV, Viswanathan K, Ramesh A, Gupta A, Tiwari S, Palatty BU, Varghese S, Sharma Y. An Interventional Study on Comprehensive Emergency Care and Trauma Registry for Road Traffic Injuries in India: A Protocol. Adv J Emerg Med. 2019 Aug 5;3(4):e50. doi: 10.22114/ajem.v0i0.232. eCollection 2019 Fall. PubMed PMID: 31633105; PubMed Central PMCID: PMC6789063.

Road traffic injuries (RTIs) stands as one of the leading causes of mortality and morbidity across the globe. Effective injury surveillance systems and pre-hospital and in-hospital interventions set up in developing countries have

shown promising results in controlling the problem. This study aimed to standardise and evaluate an evidence-based intervention for safety, efficacy and quality of post-crash pre-hospital and in-hospital trauma care services to improve the outcome in RTI victims. In addition, it establishes the android-based trauma registry for effective RTI surveillance. This multi-centric, prospective, observational study is commissioned by the Indian Council of Medical Research (ICMR) as a National Task Force Project. This study is being conducted in five sites, viz., Anand, Bengaluru, Delhi, Lucknow and Thrissur located across India. Each centre will have a level I, two level II and three level III trauma hospitals. The study will be carried out in four phases namely: i) preparatory phase, ii) trauma registry establishment and pre-intervention data collection, iii) intervention and iv) impact evaluation. The preparatory phase, which lasts for four months includes the situational analysis pertaining to managing RTIs. Trauma registry will be initiated from the fifth month. Pre-intervention data will be collected for six months. The intervention will be conducted for six months in the form of prehospital notification, training for trauma care providers and trauma care quality improvement. Post-intervention data collection will continue for 12 months and the impact of the intervention will be assessed. The primary outcome measure will be early preventable mortality, defined as death at 24 hours after admission for patients with a calculated probability of survival >50% based on their injury severity score.

DOI: 10.22114/ajem.v0i0.232
PMCID: PMC6789063
PMID: 31633105

10: Baby B, Singh R, Suri A, Dhanakshirur RR, Chakraborty A, Kumar S, Kalra PK, Banerjee S. A review of virtual reality simulators for neuroendoscopy. Neurosurg Rev. 2019 Aug 23. doi: 10.1007/s10143-019-01164-7. [Epub ahead of print] Review. PubMed PMID: 31444716.

Neurosurgery is a challenging surgical specialty that demands many technical and cognitive skills. The traditional surgical training approach of having a trainee coached in the operating room by the faculty is time-consuming, costly, and involves patient risk factors. Simulation-based training methods are suitable to impart the surgical skills outside the operating room. Virtual simulators allow high-fidelity repeatable environment for surgical training. Neuroendoscopy, a minimally invasive neurosurgical technique, demands additional skills for limited maneuverability and eye-hand coordination. This study provides a review of the existing virtual reality simulators for training neuroendoscopic skills. Based on the screening, the virtual training methods developed for neuroendoscopy surgical skills were classified into endoscopic third ventriculostomy and endonasal transsphenoidal surgery trainers. The study revealed that a variety of virtual reality simulators have been developed by various institutions. Although virtual reality simulators are effective for procedure-based skills training, the simulators need to include anatomical variations and variety of cases for improved fidelity. The review reveals that there should be multi-centric prospective and retrospective cohort studies to establish concurrent and predictive validation for their incorporation in the surgical educational curriculum.

DOI: 10.1007/s10143-019-01164-7
PMID: 31444716

11: Bagga A, Khandelwal P, Mishra K, Thergaonkar R, Vasudevan A, Sharma J, Patnaik SK, Sinha A, Sethi S, Hari P, Dragon-Durey MA; Indian Society of Pediatric Nephrology. Hemolytic uremic syndrome in a developing country:

Consensus guidelines. Pediatr Nephrol. 2019 Aug;34(8):1465-1482. doi: 10.1007/s00467-019-04233-7. Epub 2019 Apr 15. PubMed PMID: 30989342.

BACKGROUND: Hemolytic uremic syndrome (HUS) is a leading cause of acute kidney injury in children. Although international guidelines emphasize comprehensive evaluation and treatment with eculizumab, access to diagnostic and therapeutic facilities is limited in most developing countries. The burden of Shiga toxin-associated HUS in India is unclear; school-going children show high prevalence of anti-factor H (FH) antibodies. The aim of the consensus meeting was to formulate guidelines for the diagnosis and management of HUS in children, specific to the needs of the country.
METHODS: Four workgroups performed literature review and graded research studies addressing (i) investigations, biopsy, genetics, and differential diagnosis; (ii) Shiga toxin, pneumococcal, and infection-associated HUS; (iii) atypical HUS; and (iv) complement blockade. Consensus statements developed by the workgroups were discussed during a consensus meeting in March 2017.
RESULTS: An algorithm for classification and evaluation was developed. The management of Shiga toxin-associated HUS is supportive; prompt plasma exchanges (PEX) is the chief therapy in patients with atypical HUS. Experts recommend that patients with anti-FH-associated HUS be managed with a combination of PEX and immunosuppressive medications. Indications for eculizumab include incomplete remission with plasma therapy, life-threatening features, complications of PEX or vascular access, inherited defects in complement regulation, and recurrence of HUS in allografts. Priorities for capacity building in regional and national laboratories are highlighted.
CONCLUSIONS: Limited diagnostic capabilities and lack of access to eculizumab prevent the implementation of international guidelines for HUS in most developing countries. We propose practice guidelines for India, which will perhaps be applicable to other developing countries.

DOI: 10.1007/s00467-019-04233-7
PMID: 30989342

12: Baidya Kayal E, Kandasamy D, Khare K, Bakhshi S, Sharma R, Mehndiratta A. Intravoxel incoherent motion (IVIM) for response assessment in patients with osteosarcoma undergoing neoadjuvant chemotherapy. Eur J Radiol. 2019 Oct;119:108635. doi: 10.1016/j.ejrad.2019.08.004. Epub 2019 Aug 10. PubMed PMID: 31445487.

PURPOSE: To explore the role of quantitative Intravoxel incoherent motion (IVIM) parameters and their histogram analysis in characterizing changes in Osteosarcoma receiving neoadjuvant chemotherapy (NACT) and evaluating therapeutic response.
METHODS: Forty patients (N = 40; Male:Female = 30:10; Age = 17.7 ± 5.9years; Metastatic:localized = 17:23) with histologically confirmed Osteosarcoma treated with 3-cycles of NACT were analyzed prospectively. All patients underwent Diffusion weighted imaging (DWI) with 11 b-values (0-800 s/mm2) using 1.5 T MRI scanner at pre-treatment (t0), after 1-cycle (t1) and after 3-cycles (t2) of NACT. Non-invasive response evaluation of NACT was performed using RECIST1.1 criteria. Apparent-diffusion-coefficient (ADC) and IVIM parameters - Diffusion-coefficient (D), Perfusion-coefficient (D*) & Perfusion-fraction (f) and their relative percentage changes from time-point t0-t1 (Δ2) and t0-t2 (Δ2) were evaluated and histogram analysis was performed at three time-points and compared with respect to RECIST1.1 scores.
RESULTS: Using RECIST1.1 criteria, 11 (27.5%), 21 (52.5%) and 8 (20%) patients were in Partial-responder (PR), Stable-disease (SD) and Progressive-disease (PD) groups respectively. Pre-NACT (t0), average ADC, D,D*&f in tumor volume were 1.36 ± 0.33 × 10-3 mm2/s, 1.3 ± 0.3 × 10-3 mm2/s, 28.44 ± 10.34 × 10-3 mm2/s & 13.95 ± 2.83% respectively. Using ANOVA test, during NACT (t1, t2), D*-variance (p = 0.038, 0.003) and f-skewness (p = 0.03, 0.03) and at t2, D*-entropy

(p=0.001) and f-entropy (p=0.002) and their Δ2 changes (p=0.001, 0.003) were statistically significant among response groups. At t1, D*-variance and f-skewness jointly showed AUC=0.77 & 0.74 in classifying PR (Sensitivity=73%; Specificity=70%) and SD (Sensitivity=74; Specificity=75%) groups respectively in patient cohort. Δ1 & Δ2 changes of D*-mean, D*-variance, D*-entropy and f-entropy correlated well (0.5-0.6) with tumor-diameter and tumor-volume changes.
CONCLUSIONS: Quantitative IVIM parameters, especially D* &f and their histogram analysis were informative and can be used as noninvasive surrogate markers for early response assessment during the course of NACT in Osteosarcoma.

DOI: 10.1016/j.ejrad.2019.08.004
PMID: 31445487

13: Banerjee A, Bala R, Aggarwal R. Atypical presentation of thyroid storm: a diagnostic dilemma. BMJ Case Rep. 2019 Aug 26;12(8). pii: e231090. doi: 10.1136/bcr-2019-231090. PubMed PMID: 31451477.

Thyroid storm (accelerated hyperthyroidism) is an uncommon life-threatening emergency. The diagnosis is difficult and at times delayed owing to atypical presentation. Early diagnosis is the key to its successful management. We came across a patient who had presentations of acute abdomen but later diagnosed in thyroid storm. Multiorgan involvement leads all resuscitative measures futile and prevented us to salvage the patient.

DOI: 10.1136/bcr-2019-231090
PMID: 31451477

14: Bansal D, Kumar S, Jain S, Dogra PN. 'Poles apart presentation': diagnosis and management of iatrogenic posterior urethral false tract in cases of pelvic fracture urethral injury. BMJ Case Rep. 2019 Aug 21;12(8). pii: e231166. doi: 10.1136/bcr-2019-231166. PubMed PMID: 31439562.

Iatrogenic creation of false tract in posterior urethra while managing a case of pelvic fracture urethral injury is a dreadful complication. The spectrum of presentation ranges from complete urinary incontinence to urinary retention. We describe three such cases created due to railroading or attempted repair. Case 1 presented with total urinary incontinence following open perineal urethroplasty for posterior urethral trauma while two cases presented with failure to void after endoscopic or open surgical management for the same. One patient was managed with endoscopic resection of the septum between the false passage and true posterior urethra; two cases required redo urethroplasty. All patients voided well postoperatively and were continent. Surgeon experience and meticulous endoscopic evaluation are the keys to success. Forceful attempt at per urethral catheter placement in the acute setting should be avoided. Blind railroading of the catheter and unnecessarily forceful passage of suprapubic metal bougie during urethroplasty should be condemned.

DOI: 10.1136/bcr-2019-231166
PMID: 31439562

15: Bansal S, Mittal S, Tiwari P, Jain D, Arava S, Hadda V, Mohan A, Malik P, Pandey RM, Khilnani GC, Guleria R, Madan K. Rigid Mini-Thoracoscopy Versus Semirigid Thoracoscopy in Undiagnosed Exudative Pleural Effusion: The MINT Randomized Controlled Trial. J Bronchology Interv Pulmonol. 2019 Aug 30. doi: 10.1097/LBR.0000000000000620. [Epub ahead of print] PubMed PMID: 31478939.

BACKGROUND: There is debate regarding the ideal instrument for medical thoracoscopy. The authors compared rigid mini-thoracoscopy with semirigid thoracoscopy for thoracoscopic pleural biopsy.
METHODS: Consecutive subjects with undiagnosed exudative pleural effusion were randomized (1:1 ratio) to mini-thoracoscopy or semirigid thoracoscopy groups. The primary objective was a comparison of the diagnostic yield of pleural biopsy. Key secondary outcomes were the comparison of sedative/analgesic dose, operator-rated and patient-rated pain on visual analog scale (VAS), operator-rated overall procedural satisfaction (VAS), pleural biopsy size, and complications between the groups.
RESULTS: Of the 88 screened subjects, 73 were randomized: 36 to mini-thoracoscopy and 37 to semirigid thoracoscopy. Diagnostic yield of pleural biopsy in the mini-thoracoscopy (69.4%) and semirigid thoracoscopy groups (81.1%) was similar on intention-to-treat analysis (P=0.25). Although the operator-rated overall procedure satisfaction scores were similar between groups (P=0.87), operator-rated pain [VAS (mean±SD), 43.5±16.7 vs. 31.7±15.8; P<0.001] and patient-rated pain (VAS, 41.9±17.3 vs. 32.1±16.5; P=0.02) scores were greater in the mini-thoracoscopy group. Mean dose of fentanyl and midazolam received was similar between the 2 groups (P=0.28 and 0.68, respectively). Biopsy size was larger in the mini-thoracoscopy group (16.1±4.5 vs. 8.3±2.9mm; P<0.001). Three minor complications occurred in the mini-thoracoscopy group and 6 in the semirigid thoracoscopy group (P=0.11). There were no serious adverse events or procedure-related mortality.
CONCLUSION: Diagnostic yield of rigid mini-thoracoscopy is not superior to semirigid thoracoscopy. Use of semirigid thoracoscope may provide greater patient comfort.

DOI: 10.1097/LBR.0000000000000620
PMID: 31478939

16: Benjafield AV, Ayas NT, Eastwood PR, Heinzer R, Ip MSM, Morrell MJ, Nunez CM, Patel SR, Penzel T, PÃ©pin JL, Peppard PE, Sinha S, Tufik S, Valentine K, Malhotra
A. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med. 2019 Aug;7(8):687-698. doi: 10.1016/S2213-2600(19)30198-5. Epub 2019 Jul 9. PubMed PMID: 31300334.

BACKGROUND: There is a scarcity of published data on the global prevalence of obstructive sleep apnoea, a disorder associated with major neurocognitive and cardiovascular sequelae. We used publicly available data and contacted key opinion leaders to estimate the global prevalence of obstructive sleep apnoea.
METHODS: We searched PubMed and Embase to identify published studies reporting the prevalence of obstructive sleep apnoea based on objective testing methods. A conversion algorithm was created for studies that did not use the American Academy of Sleep Medicine (AASM) 2012 scoring criteria to identify obstructive sleep apnoea, allowing determination of an equivalent apnoea-hypopnoea index (AHI) for publications that used different criteria. The presence of symptoms was not specifically analysed because of scarce information about symptoms in the reference studies and population data. Prevalence estimates for obstructive sleep apnoea across studies using different diagnostic criteria were standardised with a newly developed algorithm. Countries without obstructive sleep apnoea prevalence data were matched to a similar country with available prevalence data; population similarity was based on the population body-mass index, race, and

geographical proximity. The primary outcome was prevalence of obstructive sleep apnoea based on AASM 2012 diagnostic criteria in individuals aged 30-69 years (as this age group generally had available data in the published studies and related to information from the UN for all countries).
FINDINGS: Reliable prevalence data for obstructive sleep apnoea were available for 16 countries, from 17 studies. Using AASM 2012 diagnostic criteria and AHI threshold values of five or more events per h and 15 or more events per h, we estimated that 936 million (95% CI 903-970) adults aged 30-69 years (men and women) have mild to severe obstructive sleep apnoea and 425 million (399-450) adults aged 30-69 years have moderate to severe obstructive sleep apnoea globally. The number of affected individuals was highest in China, followed by the USA, Brazil, and India.
INTERPRETATION: To our knowledge, this is the first study to report global prevalence of obstructive sleep apnoea; with almost 1 billion people affected, and with prevalence exceeding 50% in some countries, effective diagnostic and treatment strategies are needed to minimise the negative health impacts and to maximise cost-effectiveness.
FUNDING: ResMed.

DOI: 10.1016/S2213-2600(19)30198-5
PMID: 31300334

17: Bhardwaj P, Kumar J, Yadav RK. Patients driving the clinical trial designs - Democracy in clinical research. Rev Recent Clin Trials. 2019 Aug 8. doi: 10.2174/1574887114666190808142339. [Epub ahead of print] PubMed PMID: 31393256.

BACKGROUND: Many of the clinical trials remain inefficient owing to low retention rate, and an impact on the power of the study. In addition, regulatory bodies are recommending including the patient experience, especially, patient-reported outcomes, while making the clinical decisions, and approvals.
INTRODUCTION: Patient centricity has reached the stage where patients are both willing and required to participate in clinical trial designs, regulatory review and experts on other panels. Efforts are being made in the right direction and there are multiple aspects that have been or are being addressed.
OBJECTIVE: The current article focuses on how to include patients in clinical trial designs, the benefits, challenges, and solutions. This means patients who were merely the participants until now, they will be the drivers of trials now, and hence the clinical trials will be more efficient and productive.
KEY FINDINGS: There is a drive to enhance patients' participation in clinical trial designs, especially, visits, efficacy outcomes and their expectations with the treatment. Patients want to remain informed, right from before participation to the completion of trial. Patients are now becoming an important part of regulatory review, as apparent from recent initiatives by the FDA and EMA. This will enhance patients' awareness, and bring ownership and transparency. Various patient organizations, advocacy groups have made some great suggestions and taken initiatives in this direction. Clinical Trials Transformation Initiative, European Patient's Academy on Therapeutic Innovation, and Patient-Centered Outcomes Research Institute are a few key initiatives. However, there is a set of challenges emanating from the complexity of trials, associated with unique mechanism of action of drugs, their efficacy and safety profiles, which has to be dealt with properly.
CONCLUSION: Overall, the pharma domain is at the verge of putting the patient in the spotlight, and achieve a near-real democracy, where clinical research is the by the patient, for the patient and of the patient.

DOI: 10.2174/1574887114666190808142339
PMID: 31393256

18: Bhartiya M, Hans B, Sundaray S, Sagar A. Amitraz Poisoning: The not so (Un)common Poisoning. Cureus. 2019 Aug 20;11(8):e5438. doi: 10.7759/cureus.5438. PubMed PMID: 31482050; PubMed Central PMCID: PMC6701898.

Amitraz is a widely used insecticide and antiparasitic drug. It can cause poisoning in humans via oral, inhalation, and dermal routes. Clinical features hence produced may mimic organophosphate (OP) poisoning because of several shared features (miosis, bradycardia, hypotension) along with a history of possible insecticide poisoning. But the presence of hyperglycemia, hypothermia, and reduced gastrointestinal motility along with normal serum cholinesterase levels and the absence of fasciculations and a hypersecretory state (salivation, lacrimation, perspiration, and diarrhea) point against OP poisoning. Analysis of the poison container also helps confirm the poison. Management is mostly supportive with a good prognosis.

DOI: 10.7759/cureus.5438
PMCID: PMC6701898
PMID: 31482050

19: Bhasin D, Roy A. Complete Heart Block. Circulation. 2019 Aug 6;140(6):516-519. doi: 10.1161/CIRCULATIONAHA.119.042001. Epub 2019 Aug 5. PubMed PMID: 31381419.

20: Bhasym A, Annarapu GK, Saha S, Shrimali N, Gupta S, Seth T, Guchhait P. Neutrophils develop rapid proinflammatory response after engulfing Hb-activated platelets under intravascular hemolysis. Clin Exp Immunol. 2019 Aug;197(2):131-140. doi: 10.1111/cei.13310. Epub 2019 May 27. PubMed PMID: 31099890; PubMed Central PMCID: PMC6642866.

Neutrophils maintain immune homeostasis by engulfing apoptotic cells and debris. We describe the rapid activation of neutrophils after engulfing hemoglobin (Hb)-activated platelets, which are abundant in the circulation of hemolytic patients. Neutrophils from healthy individuals after engulfing Hb-activated platelets express elevated CD11b and secrete significant amounts of tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6, myeloperoxidase (MPO) and elastase within 4-h platelets, but not with free-Hb only in vitro. These neutrophils exhibit early onset of apoptosis and cell death after engulfing Hb-activated platelets, but not with free-Hb only. Further, our data from mice with phenylhydrazine-induced intravascular hemolysis display a gradual decrease in total neutrophil count, but the number of activated neutrophils and neutrophil-platelet aggregates increases, along with the rise of TNF-α, IL-1β, IL-6 and MPO in circulation. Our data from paroxysmal nocturnal hemoglobinuria (PNH) patients confirmed the observation of decreased total neutrophil counts, but elevated numbers of activated neutrophils, including neutrophil-platelet aggregates, in parallel with elevated expression of TNFA, IL1B and IL6 genes in neutrophils, also increased levels of these cytokines along with MPO in circulation, and this correlated directly with elevated intravascular hemolysis (high free-Hb in plasma). The patients' neutrophils displayed significant localization of intracellular Hb and platelets, unlike the counterparts from healthy individuals. Together, therefore, our observations suggest that Hb-activated platelets, which are abundant in the circulation of patients with hemolytic disorders, including PNH, promotes early onset of neutrophil activation and increases their proinflammatory response and leads to early apoptosis and cell death.

DOI: 10.1111/cei.13310
PMCID: PMC6642866 [Available on 2020-08-01]
PMID: 31099890

21: Bhatwalkar SB, Shukla P, Srivastava RK, Mondal R, Anupam R. Validation of environmental disinfection efficiency of traditional Ayurvedic fumigation practices. J Ayurveda Integr Med. 2019 Jul - Sep;10(3):203-206. doi: 10.1016/j.jaim.2019.05.002. Epub 2019 Aug 16. PubMed PMID: 31427141.

Environmental disinfection greatly reduces the occurrence of nosocomial or healthcare associated infections (HCAIs) which are the major healthcare problems worldwide. In India, Ayurvedic traditional fumigation with natural plant products is used to disinfect environment. In the present study, environmental disinfection efficiency of traditional fumigation practice has been evaluated by using natural plant products such as garlic (Allium sativum) peel, turmeric (Curcuma longa) powder, Carom (Trachyspermum ammi) seeds (Ajwain) and Loban (resin of Styrax benzoin and Boswellia species). The efficiency of traditional fumigation using these natural products to disinfect air and surface was evaluated. The effect of traditional fumigation on the microbiological quality of air was revealed by active air sampling. In addition, the ability of the traditional fumigation using garlic peel to disinfect inanimate surface was evaluated using three strains of methicillin resistant Staphylococcus aureus (MRSA). Glass slide was artificially contaminated with the bacteria and fumigated whereas non-fumigated slide served as control. The control and fumigated slides were analyzed for surviving bacteria and subjected to scanning electron microscopy (SEM) analysis. Traditional fumigation performed separately with three grams of garlic peel, turmeric, carom seeds and loban powder reduced the average air borne bacterial colony forming units (cfu)/m3 compared to non-fumigated control. The SEM analysis showed reduced number of bacteria in garlic peel fumigated surface samples. The results of the study strongly suggested that the traditional Ayurvedic fumigation with natural plant products is effective in reducing air-borne bacteria and in disinfecting inanimate surfaces. The traditional fumigation with herbal products has huge potential to address the problem of nosocomial infections.

DOI: 10.1016/j.jaim.2019.05.002
PMID: 31427141

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23: Biswas A, Devnani B, Agarwal S, Sharma MC, Sharma A. Combined Modality Management of Sinonasal Anaplastic Lymphoma Kinase-Positive Anaplastic Large Cell Lymphoma in a Young Adult-Report of a Rare Case. J Adolesc Young Adult Oncol. 2019 Aug;8(4):469-476. doi: 10.1089/jayao.2018.0158. Epub 2019 Apr 17. PubMed PMID: 30994389.

Sinonasal anaplastic lymphoma kinase (ALK)-positive anaplastic large cell lymphoma (ALCL) without nodal involvement is extremely rare and the rarity of this tumor often leads to diagnostic dilemma. It has been predominantly reported in pediatric, adolescent and young adult patients, mostly of Asian origin. A 21-year-old female patient presented with history of epistaxis for 1 year. On clinical and radiological examination, there was a 5 cm mass in the right nasal cavity, ethmoid, and frontal sinus. Biopsy at a local center had shown moderately

differentiated squamous cell carcinoma. Rebiopsy at our center showed possibility of a hematolymphoid malignancy(pancytokeratin-, CD45+, CD3-, CD20-) and further immunohistochemistry studies(CD4+, CD43+, CD30+, ALK+) revealed ALK-positive ALCL. Rest of the lymphoma work-up was essentially normal and she had stage IE disease. She was treated with a combination of four cycles of cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone (CHOP) regimen followed by local radiotherapy (36 Gray/20 fractions/4 weeks) by three-dimensional conformal technique. She tolerated the treatment well without any severe toxicity and had complete clinical and radiological response. At last follow-up visit, 40 months from the initial diagnosis, she was alive and disease free. Sinonasal ALK-positive ALCL is a rare tumor, which can be effectively treated with a combination of multiagent CHOP/CHOP-like regimen and local conformal radiotherapy.

24: Biswas S, Kumar P, Tansir G, Biswas A. Case Report: Cardiac Tamponade in Dengue Hemorrhagic Fever: An Unusual Manifestation of a Common Disease. Am J Trop Med Hyg. 2019 Aug;101(2):448-450. doi: 10.4269/ajtmh.19-0153. PubMed PMID: 31162011; PubMed Central PMCID: PMC6685585.

Dengue hemorrhagic fever is one of the most commonly encountered mosquito-borne viral infections of humans worldwide with multiple reported outbreaks. Cardiac involvement is a known manifestation of the disease usually presenting as rhythm abnormalities, myocarditis, or pericardial effusion, which may be clinically asymptomatic. We describe a case of a 30-year-old woman who presented to us with high-grade fever, headache, retro-orbital pain, generalized maculopapular rash with bilateral pleural effusion, and hypotension. Dengue non-structural protein 1 (NS1) antigen and IgM antibodies were positive on admission, supporting a diagnosis of dengue hemorrhagic fever. Cardiac troponin-I was elevated on admission (65 ng/L) with diffuse convex ST segment elevations on electrocardiogram, suggestive of possible myopericarditis. Echocardiogram on admission revealed minimal pericardial effusion with preserved ejection fraction. Despite administration of fluids and inotrope use, the patient's hypotension progressively deteriorated over the next 6 hours, associated with decreased urine output and worsening sensorium. Clinical examination revealed muffled heart sounds and raised jugular venous pressure. A repeat echocardiogram confirmed an increase in the pericardial effusion manifesting as cardiac tamponade. Ultrasound-guided pigtail catheter insertion led to a prompt removal of the excessive pericardial fluid and correction of hypotension. Early identification of this uncommon but important complication of dengue hemorrhagic fever led to a good outcome in our case.

DOI: 10.4269/ajtmh.19-0153
PMCID: PMC6685585 [Available on 2020-08-01]
PMID: 31162011

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Guidelines recommend true whole-body 18F-FDG PET/CT scans from vertex to toes in pediatric lymphoma patients, although this suggestion has not been validated in large clinical trials. The objective of the study was to evaluate the incidence and clinical impact of lesions outside the "eyes to thighs" regular field of view (R-FOV) in 18F-FDG PET/CT staging (sPET) and interim (iPET) scans in pediatric lymphoma patients. Methods: True whole-body sPET and iPET scans were prospectively obtained in pediatric lymphoma patients (11 worldwide centers). Expert panel central review of sPET and iPET scans were evaluated for lymphoma

lesions outside the R-FOV and clinical relevance of these findings. Results: A total of 610 scans were obtained in 305 patients. The sPET scans did not show lesions outside the R-FOV in 91.8% of the patients, whereas in 8.2% patients the sPET scans demonstrated lesions also outside the R-FOV (soft tissue, bone, bone marrow, and skin); however, the presence of these lesions did not change the clinical stage of any patient and did not affect treatment decision. Among the 305 iPET scans, there were no new positive 18F-FDG-avid lesions outside the R-FOV, when compared with their paired sPET scans. A single lesion outside the R-FOV on iPET occurred in 1 patient (0.3%), with the primary lesion diagnosed in the femur on sPET that persisted on iPET. Conclusion: The identification of additional lesions outside the R-FOV (eyes to thighs) using 18F-FDG PET/CT has no impact in the definition of the clinical stage of disease and minimal impact in the treatment definition of patients with pediatric lymphoma. As so, R-FOV for both sPET and iPET scans could be performed.

DOI: 10.2967/jnumed.118.222299
PMID: 30683766

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27: Chatterjee P, Srivastava AK, Kumar DA, Chakrawarty A, Khan MA, Ambashtha AK, Kumar V, De Taboada L, Dey AB. Effect of deep tissue laser therapy treatment on peripheral neuropathic pain in older adults with type 2 diabetes: a pilot randomized clinical trial. BMC Geriatr. 2019 Aug 12;19(1):218. doi: 10.1186/s12877-019-1237-5. PubMed PMID: 31405365; PubMed Central PMCID: PMC6689877.

BACKGROUND: This study assessed the safety and efficacy of deep tissue laser therapy on the management of pain, functionality, systemic inflammation, and overall quality of life of older adults with painful diabetic peripheral neuropathy.
METHODS: The effects of deep tissue laser therapy (DTLT) were assessed in a randomized, double-masked, sham-controlled, interventional trial. Forty participants were randomized (1:1) to receive either DTLT or sham laser therapy (SLT). In addition to the standard-of-care treatment, participants received either DTLT or SLT twice weekly for 4 weeks and then once weekly for 8 weeks (a 12-week intervention period). The two treatments were identical, except that laser emission was disabled during SLT. Assessments for pain, functionality, serum levels of inflammatory biomarkers, and quality of life (QOL) were performed at baseline and after the 12-week intervention period. The results from the two treatments were compared using ANOVA in a pre-test-post-test design.
RESULTS: All participants randomized to the DTLT group and 85% (17 of 20) of participants randomized to the SLT group completed the trial. No significant differences in baseline characteristics between the groups were observed. After the 12-week intervention period, pain levels significantly decreased in both groups and were significantly lower in the DTLT group than in the SLT group. The Timed Up and Go test times (assessing functionality) were significantly improved in both groups and were 16% shorter in the DTLT group than in the SLT group. Serum levels of IL-6 decreased significantly in both groups. Additionally, serum levels of MCP-1 decreased significantly in the DTLT group but not in the SLT group. Patients' quality of life improved significantly in the DTLT group but not in the SLT group.
CONCLUSIONS: Deep tissue laser therapy significantly reduced pain and improved the quality of life of older patients with painful diabetic peripheral

neuropathy.
TRIAL REGISTRATION: Clinical Trial Registry-India CTRI/2017/06/008739 . [Registered on: 02/06/2017]. The trial was registered retrospectively.

DOI: 10.1186/s12877-019-1237-5
PMCID: PMC6689877
PMID: 31405365

28: Chhabra HS, Sarda K, Jotwani G, Gourie-Devi M, Kaptanoglu E, Charlifue S, Yadav SL, Mohapatra B, Srivastava A, Phadke K. Stem cell/cellular interventions in human spinal cord injury: Is it time to move from guidelines to regulations and legislations? Literature review and Spinal Cord Society position statement. Eur Spine J. 2019 Aug;28(8):1837-1845. doi: 10.1007/s00586-019-06003-3. Epub 2019 May 16. Review. PubMed PMID: 31098715.

PURPOSE: In preclinical studies, many stem cell/cellular interventions demonstrated robust regeneration and/or repair in case of SCI and were considered a promising therapeutic candidate. However, data from clinical studies are not robust. Despite lack of substantial evidence for the efficacy of these interventions in spinal cord injury (SCI), many clinics around the world offer them as "therapy." These "clinics" claim efficacy through patient testimonials and self-advertisement without any scientific evidence to validate their claims. Thus, SCS established a panel of experts to review published preclinical studies, clinical studies and current global guidelines/regulations on usage of cellular transplants and make recommendations for their clinical use.
METHODS: The literature review and draft position statement was compiled and circulated among the panel and relevant suggestions incorporated to reach consensus. This was discussed and finalized in an open forum during the SCS Annual Meeting, ISSICON.
RESULTS: Preclinical evidence suggests safety and clinical potency of cellular interventions after SCI. However, evidence from clinical studies consisted of mostly case reports or uncontrolled case series/studies. Data from animal studies cannot be generalized to human SCI with regard to toxicity prediction after auto/allograft transplantation.
CONCLUSIONS: Currently, cellular/stem cell transplantation for human SCI is experimental and needs to be tested through a valid clinical trial program. It is not ethical to provide unproven transplantation as therapy with commercial implications. To stop the malpractice of marketing such "unproven therapies" to a vulnerable population, it is crucial that all countries unite to form common, well-defined regulations/legislation on their use in SCI. These slides can be retrieved from Electronic Supplementary Material.

DOI: 10.1007/s00586-019-06003-3
PMID: 31098715

29: Chouhan DK, Dhillon MS, Patel S, Bansal T, Bhatia A, Kanwat H. Multiple Platelet-Rich Plasma Injections Versus Single Platelet-Rich Plasma Injection in Early Osteoarthritis of the Knee: An Experimental Study in a Guinea Pig Model of Early Knee Osteoarthritis. Am J Sports Med. 2019 Aug;47(10):2300-2307. doi: 10.1177/0363546519856605. Epub 2019 Jul 3. PubMed PMID: 31268737.

BACKGROUND: Platelet-rich plasma (PRP) has emerged as the forerunner among disease-modifying treatment options for early osteoarthritis (OA) of the knee. However, no consensus is available regarding optimum dosing schedules.
PURPOSE: To determine whether multiple injections of PRP (3 injections) provide better short-term and long-term results than a single injection of PRP in a guinea pig model of knee OA.
STUDY DESIGN: Controlled laboratory study.
METHODS: 36 Dunkin-Hartley guinea pigs (weighing ~600-800 g) were chosen for this

study. The animals were assigned to group DC (disease control group), group G1 (single-PRP group), and group G2 (multiple-PRP group) containing 10, 10, and 12 animals, respectively. Another 4 animals were used for preparation of allogenic PRP. Groups G1 and G2 received 1 and 3 injections of PRP, respectively, at weekly intervals in the intervention knee while the contralateral knee was injected with normal saline. Group DC received no intervention in either knee. Half of the animals from each group (subgroups DC.3, G1.3, and G2.3) were sacrificed at 3 months, and the remaining half (subgroups DC.6, G1.6, and G2.6) were sacrificed at 6 months after intervention. Both knee joints were harvested for histological assessment of articular cartilage and synovium.
RESULTS: The mean synovial scores for groups G1 and G2 were significantly better than those for group DC at 3 months. No difference was found between groups G1 and G2 at 3 months. At 6 months, group G2 had significantly better mean synovial scores than group G1 and group DC. The mean articular cartilage scores in group G2 were significantly better than those in group DC at 3 months. However, at 6 months, no significant difference was found among any of the groups in terms of mean articular scores.
CONCLUSION: Both single and multiple injections of PRP exert similar anti-inflammatory effects on the synovium in the short term. However, this effect is sustained in the long term only for multiple injections. Multiple injections of PRP exert a chondroprotective effect, but only in the short term. This effect is not seen with a single injection of PRP.
CLINICAL RELEVANCE: This study provides insight into the histological basis for the superiority of multiple injections of PRP.

DOI: 10.1177/0363546519856605
PMID: 31268737

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BACKGROUND: In an exploratory analysis of an inactivated quadrivalent influenza vaccine (IIV4) trial in children 6-35 months without risk factors for influenza, we evaluated clinical presentation of influenza illness and vaccine impact on health outcomes.
METHODS: This phase III trial was conducted in 13 geographically diverse countries across 5 influenza seasons (2011-2014). Children were randomized 1:1 to IIV4 or control. Active surveillance was performed for influenza-like episodes (ILE); influenza was confirmed by reverse transcription polymerase chain reaction (RT-PCR). The total vaccinated cohort was evaluated (N = 12,018).
RESULTS: 5702 children experienced ≥1 ILE; 356 (IIV4 group) and 693 (control group) children had RT-PCR-confirmed influenza. Prevalence of ILE was similar in RT-PCR-positive and RT-PCR-negative cases regardless of vaccination. Breakthrough influenza illness was attenuated in children vaccinated with IIV4;

moderate-to-severe illness was 41% less likely to be reported in the IIV4 group than the control group [crude odds ratio: 0.59 (95% confidence intervals: 0.44-0.77)]. Furthermore, fever >39°C was 46% less frequent following vaccination with IIV4 than with control [crude odds ratio: 0.54 (95% confidence intervals: 0.39-0.75)] in children with breakthrough illness. Health outcome analysis showed that, each year, IIV4 would prevent 54 influenza cases per 1000 children and 19 children would need to be vaccinated to prevent 1 new influenza case.
CONCLUSIONS: In addition to preventing influenza in 50% of participants, IIV4 attenuated illness severity and disease burden in children who had a breakthrough influenza episode despite vaccination.

DOI: 10.1097/INF.0000000000002387
PMID: 31306399

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Cost effective and miniaturized methods aiming for high throughput monitoring of bacterial growth are of great significance, especially for tracking disease progression in early stage as well as in screening antibiotic resistant species. Here, we demonstrate an electrochemical platform for noninvasive monitoring of bacterial growth by encapsulating bacterial cells and carbon nanodots in alginate microspheres. The synthesized carbon nanodots have been explored for electrochemical properties, and its redox properties have been utilized for developing bacterial growth monitoring platform. These synthesized CDs are sensitive to pH change and respond as change in redox potential over time as pH of the medium changes due to growth and metabolic activities of bacteria. We determined the bacterial growth kinetics by measuring the redox potential changes of the carbon nanodots over time. The developed platform has been demonstrated to detect the presence of bacteria, the difference in growth rates of bacteria and its susceptibility to the antibiotic with low bacterial counts (103 CFU) in 20 min; thus, redox properties of CDs has the potential to provide a sensitive detection platform.

DOI: 10.1016/j.bios.2019.111640
PMID: 31494506

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BACKGROUND: There is reservation about accepting the notion of widespread vitamin D deficiency (VDD) in sunny countries because information base is largely urban indoors, and the cut-off serum 25(OH)D > 75.0 nmol/L to define sufficiency is perceived as high.
OBJECTIVE: We assessed the vitamin D status of subjects engaged in six types of outdoor jobs with freedom to seek shade, when needed.
DESIGN: Descriptive observational study.
SUBJECTS AND METHODS: A total of 573 outdoors, (hawkers, n = 144; auto-rickshaw drivers, n = 113; manual rickshaw pullers, n = 49; fuel-station attendants,

n = 84; gardeners, n = 96; traffic police personnel, n = 87) were assessed for serum 25(OH)D, iPTH and total calcium during summer and winter. Bank employees were indoor controls (n = 72). Serum 25(OH)D was defined as sufficient if ≥50.0 nmol/L and deficient when <30.0 nmol/L, as per 'Institute of Medicine'.
RESULTS: Mean serum 25(OH)D of 573 outdoors was 44.8 ± 19.6 nmol/L and showed a physiological inverse relation with iPTH (P < 0.001). 77.5% of the outdoors did not have VDD. Hawkers, gardeners, fuel-station attendants and rickshaw pullers had sufficient or near sufficient serum 25(OH)D. The mean serum 25(OH)D (30.6 ± 23.2 nmol/L) of indoors though lower by 12.7 nmol/L than outdoors was above the cut-off of VDD. Proportions with supranormal iPTH were comparable between outdoors and indoors (14.0% vs 20.8%). Despite winter dip, the mean serum 25(OH)D (31.2 ± 14.3 nmol/l) of outdoors was not deficient.
CONCLUSIONS: Vitamin D deficiency is not universal. Most urban outdoor workers do not have VDD.

DOI: 10.1111/cen.14012
PMID: 31087795

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BACKGROUND: Enzyme linked immunosorbent assay (ELISA) test is used for screening of transfusion transmitted infections (TTI) in blood donors. Consecutive reactive results in ELISA is due to sample/reagent carryover or donor related. In this study we tried to find out the possibilities of family history/close contacts with patients of hepatitis among these consecutive reactive donors.
AIM: To analyze the consecutive reactive results in ELISA tests for TTI testing on samples of healthy blood donors.
MATERIAL AND METHODS: A retrospective observational study was conducted from January 2016 to July 2018 in a tertiary care hospital, North India. Consecutive reactive results by fourth generation ELISA for TTIs screening were evaluated for possible reasons. Confirmation tests were not done. Reactive donors were contacted telephonically for relevant history of close contact with infected personnel.
RESULTS: Out of 53,740 donations 1,061 were reactive for TTIs during our study period. Prevalence of Hepatitis B (HBV), Human Immunodeficiency (HIV) and Hepatitis C (HCV) virus infection in blood donors were 1.27%, 0.20% and 0.50% respectively. Consecutive reactive results for HBV were 9.20% (63/685), for HCV 6.0% (16/266) and nil for HIV. There was no sample carryover in this. Out of 79 consecutive reactive donors 69 donated for same patients and 32 were related with infected patient which are statistically significant (p < 0.0001).
DISCUSSION: This study recommends that in analysis of consecutive positive results in ELISA along with looking for procedure/sample error, there is also a need to take retrospective history of donors for close contact with infected patients.

DOI: 10.1016/j.transci.2019.05.013
PMID: 31324573

37: Dhochak N, Jat KR, Sankar J, Lodha R, Kabra SK. Predictors of Malnutrition in Children with Cystic Fibrosis. Indian Pediatr. 2019 Aug 10. pii: S097475591600132. [Epub ahead of print] PubMed PMID: 31441435.

OBJECTIVE: To determine occurrence of malnutrition in children with cystic fibrosis and identify predictors of malnutrition at time of enrolment and after 2 years of follow up.
DESIGN: Retrospective chart review.
SETTING: Pediatric chest clinic at tertiary-care centre in North India.
PATIENTS: Cystic fibrosis patients enrolled between 2009-2015 with at least 3 years follow-up.
PROCEDURE: Weight and height were noted at enrolment, and after 1 and 2 years of follow-up. Clinical details, medications, and pulmonary exacerbations during second year were recorded.
MAIN OUTCOME MEASURE: Occurrence of malnutrition i.e. weight for age Z-score ≤2.
RESULTS: 61 medical records were reviewed. Occurrence of malnutrition at baseline, and 1- and 2-year follow-up was 65.5%, 54.1% and 57.3%, respectively. Weight for age Z-score at enrolment significantly correlated with time to diagnosis from onset (r2=0.015, P=0.029). Weight for age Z-score at 2-year follow-up was significantly associated with steatorrhea (P=0.03), increased frequency of stools (P<0.01) and pulmonary exacerbation (P=0.03) during second year. Linear regression showed significant association between weight for age Z-score at 2 years with steatorrhea and pulmonary exacerbations, [r=-0.795 (-1.527, -0.062)] and [r=-0.261(-0.493, -0.028)]. Pulmonary exacerbations during second and third year had significant correlation with weight for age Z-score at the beginning of respective years (r = -0.219, P=0.015).
CONCLUSION: Occurrence of malnutrition is high in northern Indian children with cystic fibrosis, with uncontrolled fat malabsorption and recurrent respiratory infections being significant risk factors.

PMID: 31441435

38: Duseja A, Acharya SK, Mehta M, Chhabra S; Shalimar, Rana S, Das A, Dattagupta S, Dhiman RK, Chawla YK. High potency multistrain probiotic improves liver histology in non-alcoholic fatty liver disease (NAFLD): a randomised, double-blind, proof of concept study. BMJ Open Gastroenterol. 2019 Aug 7;6(1):e000315. doi: 10.1136/bmjgast-2019-000315. eCollection 2019. PubMed PMID: 31423319; PubMed Central PMCID: PMC6688701.

Objective: Pharmacological treatment of non-alcoholic fatty liver disease (NAFLD) is still evolving. Probiotics could be a promising treatment option, but their effectiveness needs to be established. The present study aimed to evaluate the efficacy of a high potency multistrain probiotic in adult patients with NAFLD.
Methods: Thirty-nine liver biopsy-proven patients with NAFLD were randomised in a double-blind fashion to either lifestyle modifications plus an oral multistrain probiotic (675 billion bacteria daily, n=19) or identical placebo (n=20) for 1 year. Lifestyle modifications included regular exercise for all and control of overweight/obesity (with additional dietary restrictions), hypertension and hyperlipidaemia in those with these risk factors. Primary objective of the study was the histological improvement in NAFLD activity score (NAS) and its components and secondary objectives were improvement in alanine transaminase (ALT) and cytokine profile.
Results: Thirty (76.9%) out of 39 patients with NAFLD completed the study with 1 year of follow-up. A repeat liver biopsy at 1 year could be done in 10 patients (52.6%) in probiotic group and five patients (25%) in placebo group. In comparison to baseline, hepatocyte ballooning (p=0.036), lobular inflammation (p=0.003) and NAS score (p=0.007) improved significantly at 1 year in the probiotic group. When compared with placebo, the NAS score improved significantly

in the probiotic group (p=0.004), along with improvements in hepatocyte ballooning (p=0.05) and hepatic fibrosis (p=0.018). A significant improvement in levels of ALT (p=0.046), leptin (p=0.006), tumour necrosis factor-α (p=0.016) and endotoxins (p=0.017) was observed in probiotic group in comparison to placebo at 1 year. No significant adverse events were reported in the study.
Conclusion: Patients with NAFLD managed with lifestyle modifications and multistrain probiotic showed significant improvement in liver histology, ALT and cytokines.
Trial registration number: The clinical trial is registered with CLINICAL TRIAL REGISTRYINDIA (CTRI); http://ctri.nic.in, No. CTRI/2008/091/000074.

DOI: 10.1136/bmjgast-2019-000315
PMCID: PMC6688701
PMID: 31423319

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Neurosyphilis has become an uncommon diagnosis in the current era. Neurological manifestations of syphilis usually lie within the spectrum of meningovascular syphilis, tabes dorsalis or general paresis of the insane. Although sensory ataxia may occur as part of spinal cord involvement, cerebellar ataxia has been rarely described as a manifestation of neurosyphilis. In this report, we describe a rare case neurosyphilis presenting in the form of a pure pancerebellar syndrome of subacute progression.

DOI: 10.1136/bcr-2019-231058
PMID: 31473646

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Obsessive-compulsive symptoms and/or obsessive-compulsive disorders (OCD) are frequently comorbid with schizophrenia, though the exact clinical and etiological relationship between them is poorly understood. Here we describe a case that, to the best of our knowledge, is the first report of new-onset OCD in a patient who was receiving high-frequency repetitive transcranial magnetic stimulation over left dorsolateral pre-frontal cortex as an adjuvant therapy for negative symptoms of schizophrenia. Thisreport supports our understanding of OCD as a brain disorder involving hyperactivity of pre-frontal cortex and cortico-striatal-thalamo-cortical circuit dysfunction.

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PMCID: PMC6705105
PMID: 31352712

43: Gogia V, Venkatesh P, Garg SP, Takkar B, Sheemar A. Patterns of uveitis in patients with proven systemic (pulmonary and extrapulmonary) tuberculosis. Int Ophthalmol. 2019 Aug;39(8):1665-1667. doi: 10.1007/s10792-018-0989-9. Epub 2018 Jul 18. PubMed PMID: 30022332.

PURPOSE: To report patterns of uveitis in patients with systemic tuberculosis.
METHODS: Records of patients presenting at uvea clinic of a tertiary eye care centre were evaluated retrospectively, and 47 cases with proven systemic tuberculosis were analyzed for patterns of uveitis. Tuberculosis had been proven with a combination of radio imaging and detection of acid fast bacilli in body fluids. All patients had been reviewed by a specialist as applicable before diagnosing tuberculosis. These patients had undergone a thorough ocular workup. Pattern of uveitis was the primary outcome measure.
RESULTS: Mean age was 35.34±15.56 years. Lung was the commonest systemic focus, seen in nearly 75% of the cases. Anterior uveitis was the most common presentation (48.9%), followed by posterior (25.5%), panuveitis (10.6%) and intermediate uveitis (10.6%). Multifocal serpiginoid choroidopathy (MSC) was seen in only one patient, while granulomatous choroiditis was the commonest type of posterior uveitis.
CONCLUSIONS: Anterior uveitis is the most frequent type of uveitis seen in patients with proven systemic tuberculosis. Rarity of MSC in such patients indicates possibility of etiologies other than tuberculosis in causing MSC.

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PMID: 30022332 [Indexed for MEDLINE]

44: Goyal A, Gupta Y, Kalaivani M, Sankar MJ, Kachhawa G, Bhatla N, Gupta N, Tandon N. Concordance of glycaemic and cardiometabolic traits between Indian women with history of gestational diabetes mellitus and their spouses: an opportunity to target the household. Diabetologia. 2019 Aug;62(8):1357-1365. doi: 10.1007/s00125-019-4903-4. Epub 2019 May 18. PubMed PMID: 31104096.

AIMS/HYPOTHESIS: The aim of this study was to investigate the concordance of dysglycaemia (prediabetes or diabetes) and cardiometabolic traits between women with a history of gestational diabetes mellitus (GDM) and their spouses.
METHODS: Using hospital medical records, women with GDM (diagnosed between 2012 and 2016) and their spouses were invited to participate in the study and to attend a scheduled hospital visit in a fasting state. Sociodemographic, anthropometric and medical data were collected, and a 75 g OGTT with serum insulin estimation, HbA1c measurement and fasting lipid profile were performed at the visit. Prediabetes and diabetes were defined using ADA criteria and the metabolic syndrome was defined using IDF criteria.
RESULTS: A total of 214 couples participated in the study. Women were tested at a mean ± SD age of 32.4±4.6 years and median (quartile [q]25-q75) of 19.5 (11-44) months following the index delivery, while men were tested at a mean ± SD age of 36.4±5.4 years. A total of 72 (33.6%) couples showed concordance for dysglycaemia, while 99 (46.3%) and 51 (23.8%) couples were concordant for overweight/obesity and the metabolic syndrome, respectively. A total of 146 (68.2%) couples showed concordance for any of the above three factors. The presence of dysglycaemia in one partner was associated with an increased risk of dysglycaemia in the other partner (OR 1.80 [95% CI 1.04, 3.11]). Similarly, being overweight/obese (OR 2.19 [95% CI 1.22, 3.93]) and presence of the metabolic syndrome (OR 2.01 [95% CI 1.16, 3.50]) in one partner was associated with an increased risk of these conditions in the other partner. Both women and men were more likely to have dysglycaemia if they had a partner with dysglycaemia. Women

with a partner with dysglycaemia had a significantly higher BMI, waist circumference and diastolic BP, and a significantly higher probability of low HDL-cholesterol (<1.29 mmol/l) and the metabolic syndrome compared with women with a normoglycaemic partner. No such differences were observed for men with or without a partner with dysglycaemia.
CONCLUSIONS/INTERPRETATION: The high degree of spousal concordance found in this study suggests social clustering of glycaemic and cardiometabolic traits among biologically unrelated individuals. This provides us with an opportunity to target the behavioural interventions at the level of the 'married couple', which may be a novel and cost-effective method of combating the current diabetes epidemic.

DOI: 10.1007/s00125-019-4903-4
PMID: 31104096

45: Guleria P, Agarwal S, Iyer VK, Jain D, Mathur SR, Yadav D. Subcategorisation of AUS/FLUS thyroid lesions as per the 2017 Bethesda System for Reporting Thyroid Cytopathology: a retrospective study from a tertiary care centre analysing risk of malignancy (ROM) of the different subcategories. J Clin Pathol. 2019 Nov;72(11):771-777. doi: 10.1136/jclinpath-2019-205985. Epub 2019 Aug 2. PubMed PMID: 31375535.

AIMS: The 2017 Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) recommends subclassification of atypia of undetermined significance (AUS)/follicular lesion of undetermined significance (FLUS) into six subcategories. The present study evaluates the risk of malignancy (ROM) and risk of neoplasm (RON) among these.
METHODS: All thyroid aspirates reported as AUS/FLUS over a 4.5-year period, with available histology, were reviewed and subclassified as per TBSRTC. ROM and RON were calculated and compared.
RESULTS: Of 2554 thyroid aspirates, 281 (11.0%) were AUS/FLUS. Eighty-one with available histology were evaluated. ROM was 51.8%. Cytologic and architectural atypia (AUS-C&A) was the most prevalent (62.9%), followed by Hürthle cell type (19.6%), AUS-A (11.1%), AUS-not otherwise specified (NOS) (7.4%), cytologic atypia (AUS-C) (4.9%) and atypical lymphoid cells (1.2%). Papillary thyroid carcinoma (PTC) and adenomatous goitre (AG) were the most common histological diagnoses (27% each). On histology, AUS-C had 2/4 PTC and 2/4 AG on histology. AUS-A had 4/9 follicular neoplasm (FN) and 2/9 non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) while AUS C&A had 18/51 PTC, 13/51 AG, 11/51 NIFTP and 5/51 FN. ROM and RON were similar across subcategories, ROM was the highest for AUS-C&A (58.8%), AUS-C (50%) and AUS-NOS (50%). NIFTP reclassification as non-malignant reduced ROM to 35.8% (absolute reduction of 16% and a relative decrease of 31%) with the greatest relative decrease seen in AUS-A (50%), followed by AUS-C&A (37%), and none in others.
CONCLUSIONS: AUS/FLUS subcategorisation helped to indicate risk for the more likely neoplasm, whether PTC or FN. ROM was the highest for cases with cytological atypia but did not differ significantly across different subcategories. NIFTP changed the ROM of AUS-A and AUS-C&A, since both NIFTP and FN have microfollicles.

DOI: 10.1136/jclinpath-2019-205985
PMID: 31375535

46: Gupta A, Sazawal S, Mahapatra M, Pati HP, Saxena R. Calreticulin Mutation by Immunohistochemistry: Can It Replace PCR? Appl Immunohistochem Mol Morphol. 2019 Aug 30. doi: 10.1097/PAI.0000000000000804. [Epub ahead of print] PubMed PMID:

31478923.

Before 2013, the diagnosis of about 30% to 45% cases of primary myelofibrosis (PMF) and essential thrombocythemia (ET) posed a diagnostic difficulty because of the missing reliable clonal marker. Calreticulin (CALR) mutation was identified as a recurrent mutation in about 60% to 88% of JAK2/MPL-negative PMF and ET. Molecular methods like Sanger sequencing and polymerase chain reaction (PCR) are considered gold standard, but they have limited availability, complex techniques, and labor intensive. In contrast to molecular methods, immunohistochemistry (IHC) is a widely available, rapid, simple, and cost-effective option. There are only few studies evaluating the utility of IHC for CALR mutation detection. Hence, we studied the role of IHC in CALR mutation detection and compared it with PCR. Thirty-one JAK2V617F-negative PMF and ET were evaluated for CALR mutation status. PCR was done and interpreted by comparing bands with the expected product size. The bone marrow biopsy was simultaneously put up for IHC using antimutated CALR monoclonal antibody (CAL2). CALR mutation was detected in 64.5% (20/31) cases. Prevalence of CALR mutation in JAK2-negative PMF and ET was 60.9% (14/23) and 75% (6/8), respectively. Sensitivity, specificity, positive predictive value, and negative predictive value of IHC analyzed were 89.4%, 100%, 100%, and 84.6%, respectively. A very good level of agreement (κ=0.86) was observed between PCR and IHC. We suggest that IHC is the best screening test to detect CALR mutation in resource limited countries with limited availability and affordability of molecular methods.

DOI: 10.1097/PAI.0000000000000804
PMID: 31478923

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rats: molecular mechanism and ocular pharmacokinetics. Int Ophthalmol. 2019 Aug 27. doi: 10.1007/s10792-019-01165-x. [Epub ahead of print] PubMed PMID: 31456155.

PURPOSE: The current study was conducted to explore the potential of rutin in preventing sight-threatening diabetic retinopathy.
METHODS: Wistar albino rats (either sex) weighing 200-225 g were intraperitoneally injected with 45 mg/kg streptozotocin (pH 4.5). Rats having blood glucose≥300 mg/dL were divided into two groups (n=8; each group). Group I served as diabetic control and received normal saline p.o. Group II received rutin 50 mg/kg p.o. for 24 weeks. At the end of 24 weeks, retinal fundus and fluorescein imaging were done, rats were killed, and retinal biochemical assessments were conducted. Moreover, ocular pharmacokinetics of rutin was assessed in the normal rats after a single oral dose of 50 mg/kg.

RESULTS: Rutin treatment significantly ($p < 0.001$) lowered retinal vascular endothelial growth factor, tumor necrosis factor-α, and aldose reductase. Rutin treatment significantly ($p < 0.001$) elevated the levels of total antioxidant capacity of the retinas. Fundus examination of rutin-treated group showed significantly lower tortuosity index and normal fluorescein angiography. Rutin was detected in the retina as well as in aqueous humor of normal rats. CONCLUSION: Rutin treatment significantly arrested the biochemical disturbances of diabetic retinopathy. The distribution of orally ingested rutin in ocular tissues further substantiate its site-specific action.

DOI: 10.1007/s10792-019-01165-x
PMID: 31456155

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Autism spectrum disorder is a neurodevelopmental condition in which affected individuals have difficulties while interacting and communicating socially, and repetitive behaviors. It has a multifactorial etiology. Various risk factors, including genetic and environmental influences, have been explored while trying to understand its causation. As older evidence was suggestive of a high heritability, a majority of research focused on finding the underlying genetic causes of autism. Due to these efforts, there have been advances in the knowledge of some of the genetic factors associated with autism. But a recent trend also shows an increasing interest in exploration of various potential environmental triggers. These efforts have brought us closer to understanding the elusive disorder more so than ever before. The current review discusses the recent trends in research exploring the etiopathogenesis of autism spectrum disorder.

DOI: 10.1111/pcn.12860
PMID: 31077508

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55: Jangir H, Nambirajan A, Seth A, Sahoo RK, Dinda AK, Nayak B, Kaushal S. Prognostic stratification of muscle invasive urothelial carcinomas using limited immunohistochemical panel of Gata3 and cytokeratins 5/6, 14 and 20. Ann Diagn Pathol. 2019 Aug 3;43:151397. doi: 10.1016/j.anndiagpath.2019.08.001. [Epub ahead of print] PubMed PMID: 31494492.

BACKGROUND: Genomic studies have delineated distinct molecular subgroups of urothelial carcinomas whose prognostic impact extends beyond traditional stage and grade groupings. The 'basal' subgroup shows increased gene expression levels of KRT5, KRT6, and KRT14 and low expression levels of GATA binding protein 3, and is associated with an extremely poor outcome. Identification of this subset is necessary for improved patient management and research on targeted therapies. We aimed to assess the prognostic utility of immunohistochemistry (IHC) for basal markers: cytokeratin 5/6 (CK5/6) and 14 (CK14), and luminal markers: cytokeratin 20 (CK20) and Gata3 in muscle invasive urothelial carcinomas (MIBC).

MATERIALS AND METHODS: Study was of retrospective design (2014-2017). All chemotherapy naïve patients of MIBC undergoing radical cystectomy were included. IHC was performed on formalin fixed paraffin-embedded whole tumor sections.
RESULTS: Among 40 cases of MIBC included, 45% (18/40) were positive for one or both basal markers, 37.5% (15/40) were positive for one or both luminal markers, while 15% (6/40) were positive for both basal and luminal markers. One case did not express any of the four markers. MIBCs expressing only basal markers presented at an advanced stage with frequent squamous differentiation and showed a trend towards shorter overall survival. Gata3+ MIBCs showed the best outcome irrespective of expression of other markers, while CK14+/Gata3- MIBCs were associated with worst outcomes. Gata3-/CK14- MIBCs showed intermediate survival outcomes. CK5/6, CK20 and p53 expression did not significantly correlate with outcome.
CONCLUSION: IHC for Gata-3 and CK14 stratified MIBC into distinct prognostic subsets.

DOI: 10.1016/j.anndiagpath.2019.08.001
PMID: 31494492

56: Jha J, Singh MK, Singh L, Pushker N, Bajaj MS, Sen S, Kashyap S. Prognostic relevance of ATM protein in uveal melanoma and its association with clinicopathological factors. Int J Clin Oncol. 2019 Aug 3. doi: 10.1007/s10147-019-01519-6. [Epub ahead of print] PubMed PMID: 31377937.

PURPOSE: Uveal melanoma (UM) is an intraocular malignancy commonly arising from choroid which can cause visual loss or metastasis. Ataxia-telangiectasia mutated (ATM) protein is an activator of DNA damage response and its role in uveal melanoma (UM) is still unexplored. Therefore, the study aims to detect the expression and localization of ATM protein and its association with clinicopathological parameters METHODS: Expression of nuclear ATM (nATM) was investigated on 69 formalin fixed paraffin embedded choroidal melanoma samples by immunohistochemistry and validated by western blotting. Results were then correlated with clinical and histopathological parameters. Prognostic significance was determined by the Kaplan-Meier analysis and the multivariate analysis by Cox's hazard proportional method.
RESULTS: Loss of nATM was observed in 65% of cases, which was statistically significant with the reduced disease-free survival ($p=0.042$). This loss was more frequently found in cases with high-risk histopathological factors like epithelioid cell type, tumor infiltrating lymphocytes and high pigmentation which might help in the progression of melanoma. On multivariate analysis, extraocular spread and loss of nATM were found to be independent prognostic factors ($p<0.05$).
CONCLUSION: Our data suggest that loss of nATM protein might serve as a poor prognostic marker in the pathogenesis of uveal melanoma which may lead to increased risk of metastasis.

DOI: 10.1007/s10147-019-01519-6
PMID: 31377937

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Often a single blood pressure (BP) measurement is used to diagnose and manage hypertension in busy clinics. However, repeated BP measurements have been shown to be more representative of the true BP status of the individual. Improper

measurement of office BP can lead to inaccurate classification, overestimation of a patient's true BP, unnecessary treatment, and misinterpretation of the true prevalence of hypertension. There is no consensus among major guidelines on the number of recommended measurements at a single visit or the method of arriving at final clinic BP reading. The participants of the National Family Health Survey (NFHS-4), a nationwide survey conducted in India from 2015 to 2016, were used for the analysis. The prevalence and median difference in systolic blood pressure (SBP) and diastolic blood pressure (DBP) for single as well as combinations of two or more readings were calculated. Cross-tabulation was used to assess classification of individuals based on first BP reading compared with the mean of two or more BP measurements. There was a 63% higher prevalence of hypertension when only the first reading was considered for diagnosis in comparison to the mean of the second and third readings. A decrease of 3.6 mmHg and 2.4 mm Hg in mean SBP and DBP, respectively, was observed when the mean of the second and third readings was compared to the first reading. In those who are identified to have grade 1 or higher categories of hypertension, we recommend three BP measurements, with the mean of the second and third measurements being the clinic BP.

DOI: 10.1038/s41371-019-0200-4
PMID: 30979950

58: Kapoor M, Agrawal D, Ravi S, Roy A, Subramanian SV, Guleria R. Missing female patients: an observational analysis of sex ratio among outpatients in a referral tertiary care public hospital in India. BMJ Open. 2019 Aug 7;9(8):e026850. doi: 10.1136/bmjopen-2018-026850. PubMed PMID: 31391189; PubMed Central PMCID: PMC6687005.

OBJECTIVE: To investigate gender discrimination in access to healthcare and its relationship with the patient's age and distance from the healthcare facility.
DESIGN AND SETTING: An observational study based on outpatient data from a large referral public hospital in Delhi, India.
PARTICIPANTS: Confirmed clinical appointments.
PRIMARY AND SECONDARY OUTCOME MEASURES: Estimates from the logistic regression are used to compute sex ratios (male/female) of patient visits with respect to distance from the hospital and age. Missing female patients for each state-a measure of the extent of gender discrimination-is computed as the difference in the actual number of female patients who came from each state and the number of female patients that should have visited the hospital had male and female patients come in the same proportion as the sex ratio of the overall population from the 2011 census.
RESULTS: Of 2377028 outpatient visits, excluding obstetrics and gynaecology patients, the overall sex ratio was 1.69 male to one female visit. Sex ratios, adjusted for age and hospital department, increased with distance. The ratio was 1.41 for Delhi, where the facility is located; 1.70 for Haryana, an adjoining state; 1.98 for Uttar Pradesh, a state further away; and 2.37 for Bihar, the state furthest from Delhi. The sex ratios had a U-shaped relationship with age: 1.93 for 0-18 years, 2.01 for 19-30 years, and 1.75 for 60 years or over compared with 1.43 and 1.40 for the age groups 31-44 and 45-59 years, respectively. We estimate there were 402 722 missing female outpatient visits from these four states, which is 49% of the total female outpatient visits for these four states.
CONCLUSION: We found gender discrimination in access to healthcare, which was worse for female patients who were in the younger and older age groups, and for those who lived at increasing distances from the hospital.

DOI: 10.1136/bmjopen-2018-026850

PMCID: PMC6687005
PMID: 31391189

59: Karwasra R, Singh S, Sharma D, Sharma S, Sharma N, Khanna K. Pomegranate supplementation attenuates inflammation, joint dysfunction via inhibition of NF-Î°B signaling pathway in experimental models of rheumatoid arthritis. J Food Biochem. 2019 Aug;43(8):e12959. doi: 10.1111/jfbc.12959. Epub 2019 Jun 17. PubMed PMID: 31368549.

Incisive search of innovative compounds for regulating pain, inflammation, and bone damage, with nominal side effects has focused on nutritional supplements. The endeavor of this research work was to investigate, for first time, the inhibitory effect of pomegranate rind extract in established models of nociception and inflammation. Pomegranate (50, 100, and 200 mg/kg) and indomethacin (3 mg/kg) was assessed in eddy's hot plate-induced algesia, carrageenan, and Complete Freund's adjuvant-induced models in Wistar rats. Results of study conclude that pomegranate at a dose of 200 mg/kg showed significant ($p < 0.001$) reduction in paw swelling in both inflammatory experimental models. In addition, observations recorded a significant ($p < 0.05$) increase in nociceptive threshold. Henceforth, we might say that pomegranate (200 mg/kg) decline pain and inflammation by downregulating the activation of TNF-R1, TNF-α, IL-1β, IL-6, NF-κB, oxidative stress markers, and tissue histology. PRACTICAL APPLICATIONS: The research work represents the first report on inhibitory mechanism of NF-κB by pomegranate rind extract, enriched in tannins and flavanoids. The findings of the study provide satisfactory evidence of pomegranate rind in amelioration of adjuvant-induced arthritis. Pomegranate rind, being enrich in bioactive compounds like phenolics and flavanoids possess potent antioxidant activity that might contribute in attenuating rheumatoid arthritis.

DOI: 10.1111/jfbc.12959
PMID: 31368549

60: Kashyap N, Singhal M, Tiwari R, Chauhan S, Manas R. Scalp Avulsion Injuries and Replantation: Is Deep Temporal Artery an Alternate Option? Ann Plast Surg. 2019 Aug 7. doi: 10.1097/SAP.0000000000002005. [Epub ahead of print] PubMed PMID: 31397683.

Scalp avulsion injuries are usually attributed to entrapment of long hair or clothing in agricultural or industrial machinery or traffic accidents. Though rare, these injuries may be dangerous, and resulting cosmetic defect and alopecia lead to social stigma and poor self-esteem. Early intervention in the form of microvascular repair and replantation prevent morbidity and improve outcome. In this case series, we have discussed 3 cases of scalp replantation, 2 complete and 1 partial. Immediate microvascular reconstruction was planned in each case. Single surgical team approach was followed, vessels were identified and operated under an operative microscope. No vein grafts were used. Operative outcome was good, and scalp healed well. Cosmetic outcome was excellent, and there was no need for secondary revisions or use of tissue expanders. Immediate referral of such cases to institutes with facility for microvascular repair is recommended to reduce ischemia time. Superficial temporal artery is the first choice for microvascular repair in scalp replants, and a single artery anastomosis is sufficient to perfuse the entire scalp. Deep temporal artery is a viable alternative in cases where repair with superficial temporal vessels will require use of vein graft, cutting short operative time and associated complications.

DOI: 10.1097/SAP.0000000000002005
PMID: 31397683

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Spermatic cord malignancies are very rare tumours. Less than 100 cases of cord liposarcoma have been reported in the literature. Divergent differentiation into leiomyosarcoma and liposarcoma is a rare phenomenon but can occur. Lipoleiomyosarcoma usually represents the well-differentiated subtype of this entity. We report such a rare case in spermatic cord with an unusual presentation as a recurrent inguinal hernia in a 62-year-old man.

DOI: 10.1136/bcr-2018-228952
PMID: 31383673

63: Kim JD, Cho EJ, Ahn C, Park SK, Choi JY, Lee HC, Kim DY, Choi MS, Wang HJ, Kim IH, Yeon JE, Seo YS, Tak WY, Kim MY, Lee HJ, Kim YS, Jun DW, Sohn JH, Kwon SY, Park SH, Heo J, Jeong SH, Lee JH, Nakayama N, Mochida S, Ido A, Tsubouchi H, Takikawa H, Shalimar, Acharya SK, Bernal W, O'Grady J, Kim YJ. A Model to Predict 1-Month Risk of Transplant or Death in Hepatitis A-Related Acute Liver Failure. Hepatology. 2019 Aug;70(2):621-629. doi: 10.1002/hep.30262. Epub 2019 Feb 17. PubMed PMID: 30194739.

Acute liver failure (ALF) caused by hepatitis A is a rare but fatal disease. Here, we developed a model to predict outcome in patients with ALF caused by hepatitis A. The derivation set consisted of 294 patients diagnosed with hepatitis A-related ALF (ALFA) from Korea, and a validation set of 56 patients from Japan, India, and United Kingdom. Using a multivariate proportional hazard model, a risk-prediction model (ALFA score) consisting of age, international normalized ratio, bilirubin, ammonia, creatinine, and hemoglobin levels acquired on the day of ALF diagnosis was developed. The ALFA score showed the highest discrimination in the prediction of liver transplant or death at 1 month (c-statistic, 0.87; 95% confidence interval [CI], 0.84-0.92) versus King's College criteria (KCC; c-statistic, 0.56; 95% CI, 0.53-0.59), U.S. Acute Liver Failure Study Group index specific for hepatitis A virus (HAV-ALFSG; c-statistic, 0.70; 95% CI, 0.65-0.76), the new ALFSG index (c-statistic, 0.79; 95% CI, 0.74-0.84), Model for End-Stage Liver Disease (MELD; c-statistic, 0.79; 95% CI, 0.74-0.84), and MELD including sodium (MELD-Na; c-statistic, 0.78; 95% CI, 0.73-0.84) in the derivation set (all $P < 0.01$). In the validation set, the performance of the ALFA score (c-statistic, 0.84; 95% CI, 0.74-0.94) was significantly better than that of KCC (c-statistic, 0.65; 95% CI, 0.52-0.79), MELD (c-statistic, 0.74; 95% CI, 0.61-0.87), and MELD-Na (c-statistic, 0.72; 95% CI, 0.58-0.85) (all $P < 0.05$), and better, but not statistically significant, than that of the HAV-ALFSG (c-statistic, 0.76; 95% CI, 0.61-0.90; $P = 0.28$) and new ALFSG indices (c-statistic, 0.79; 95% CI, 0.65-0.93; $P = 0.41$). The model was well-calibrated in both sets. Conclusion: Our disease-specific score provides refined prediction of outcome in patients with ALF caused by hepatitis A.

DOI: 10.1002/hep.30262
PMID: 30194739

64: Krishna A, Bansal VK, Misra MC, Prajapati O, Kumar S. Totally Extraperitoneal Repair in Inguinal Hernia: More Than a Decade's Experience at a Tertiary Care Hospital. Surg Laparosc Endosc Percutan Tech. 2019 Aug;29(4):247-251. doi: 10.1097/SLE.0000000000000682. PubMed PMID: 31135709.

INTRODUCTION: There are 2 standard techniques of laparoscopic groin hernia repair, totally extraperitoneal repair (TEP) and transabdominal preperitoneal repair (TAPP). TEP has the advantage that the peritoneal cavity is not breached but is, however, considered to be more difficult to master when compared with TAPP. We describe herein our experience of TEP repair of inguinal hernia over the last 14 years.
MATERIALS AND METHODS: This study is a retrospective analysis of a prospectively maintained database of all patients with groin hernia who underwent TEP repair in a single surgical unit between January 2004 and January 2018. Patients' demographic profile and hernia characteristics (duration, side, extent, content, and reducibility) were noted in the prestructured proforma. Clinical outcomes included the operation time, intraoperative and postoperative complications, length of postoperative hospital stay, hernia recurrence, chronic pain, recurrence, seroma, and wound infections. Long-term follow-up was carried out in the outpatient department.
RESULTS: Over the last 14 years, TEP repair was performed in 841 patients and a total of 1249 hernias were repaired. The mean age of patients was 50.7 years. There were 748 primary and 345 unilateral hernias. The majority were direct (61%) inguinal hernias. Telescopic dissection was the commonest method of space creation. The average operating time was 54.8 and 77.9 minutes for unilateral and bilateral hernias, respectively. With 81 conversions, the success rate for TEP was 93.5%. Seroma was the most common postoperative complication seen in 81 patients. The incidence of chronic groin pain was 1.4%. The follow-up ranged from 3 months to 10 years, and there were only 3 recurrences (<1%).
CONCLUSION: In conclusion, TEP repair is an excellent technique of laparoscopic inguinal hernia repair with acceptable complications after long-term follow-up.

DOI: 10.1097/SLE.0000000000000682
PMID: 31135709

65: Kumar G, Sood M, Verma R, Mahapatra A, Chadda RK. Family caregivers' needs of young patients with first episode psychosis: A qualitative study. Int J Soc Psychiatry. 2019 Aug;65(5):435-442. doi: 10.1177/0020764019852650. Epub 2019 Jun 13. PubMed PMID: 31190603.

BACKGROUND: The caregivers of patients with first episode psychosis (FEP) experience significant distress. It is important to understand their needs to plan adequate interventions for them.
AIM: The aim of this study was to explore the needs of caregivers of young patients with FEP in India, using a qualitative approach.
METHODS: The study was conducted in two phases. In phase I, a script for conducting focus group discussions (FGDs) with caregivers was developed, based on literature search and expert opinion generated from FGD with mental health professionals. In phase II, five FGDs were conducted with 30 caregivers of young patients with FEP having minimal of 6 participants in each FGD. Data was analyzed using principles of grounded theory.
RESULTS: Seven broad themes and subthemes of the needs of caregivers emerged from the FGDs. The final themes, which highlighted the needs of caregivers of young patients with FEP, were (in order of ranking) as follows: information regarding treatment, information regarding illness, services provided by the government, optimum quality of care from treatment facility, management of psychosocial issues related to patient's illness, availability and accessibility of treatment, and identification and recognition of mental health and physical problems in

family members.
CONCLUSION: Qualitative method was useful to identify the needs of the caregivers of young patients with FEP in multiple domains.

DOI: 10.1177/0020764019852650
PMID: 31190603

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OBJECTIVE: The aim of this article is to describe the normal anatomy of the root of the small bowel mesentery (RSBM) as well as the multidetector computed tomography (MDCT) features of the various primary and secondary lesions that affect the RSBM.
RESULTS: The small bowel mesentery attaches the jejunum and ileum to the posterior abdominal wall, the line of attachment forming the RSBM. Several primary as well as secondary lesions involve the RSBM. The RSBM has anatomical contiguity with the mesocolon and other peritoneal ligaments, which forms a route for the spread of infection, neoplasms as well as several other abdominal pathologies. MDCT plays an important role in the evaluation of mesenteric root lesions.
CONCLUSION: Familiarity with the lesions involving the RSBM and their characteristic appearances on MDCT is important in giving thoughtful differential diagnosis and guiding the treating physician in further management.

DOI: 10.1007/s00261-019-02053-9
PMID: 31079195

Monoclonal antibodies (mAbs) and their derivatives have achieved remarkable success as medicine, targeting both diagnostic and therapeutic applications associated with communicable and non-communicable diseases. In the last 3 to 4 decades, tremendous success has been manifested in the field of cancer therapy, autoimmune diseases, cardiovascular and infectious diseases. MAbs are the fastest growing class of biopharmaceuticals, with more than 25 derivatives are in clinical use and 7 of these have been isolated through phage display technology. Phage display technology has gained impetus in the field of medical and health sciences, as a large repertoire of diverse recombinant antibodies, targeting various antigens have been generated in a short span of time. A prominent number of phage display derived antibodies are already approved for therapy and significant numbers are currently in clinical trials. In this review we have discussed the various strategies employed for generation of monoclonal antibodies; their advantages, limitations and potential therapeutic applications. We also discuss the potential of phage display antibody libraries in isolation of monoclonal antibodies.

DOI: 10.1016/j.ijbiomac.2019.06.006
PMID: 31170490

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Monoclonal antibodies (mAbs) and their derivatives have achieved remarkable success as medicine, targeting both diagnostic and therapeutic applications associated with communicable and non-communicable diseases. In the last 3 to 4 decades, tremendous success has been manifested in the field of cancer therapy, autoimmune diseases, cardiovascular and infectious diseases. MAbs are the fastest growing class of biopharmaceuticals, with more than 25 derivatives are in clinical use and 7 of these have been isolated through phage display technology. Phage display technology has gained impetus in the field of medical and health sciences, as a large repertoire of diverse recombinant antibodies, targeting various antigens have been generated in a short span of time. A prominent number of phage display derived antibodies are already approved for therapy and significant numbers are currently in clinical trials. In this review we have discussed the various strategies employed for generation of monoclonal antibodies; their advantages, limitations and potential therapeutic applications. We also discuss the potential of phage display antibody libraries in isolation of monoclonal antibodies.

DOI: 10.1016/j.ijbiomac.2019.06.006
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70: Kumar V, Surve A, Azad S, Venkatesh P, Bagri N, Prasad P, Gupta Y. Juvenile idiopathic arthritis-related uveitis mimicking endophthalmitis. J AAPOS. 2019 Aug;23(4):238-241. doi: 10.1016/j.jaapos.2019.03.001. Epub 2019 Apr 5. PubMed PMID: 30959168.

Juvenile idiopathic arthritis (JIA) is a group of disorders occurring in children with arthritis of more than 6 weeks' duration. JIA may have varied systemic and ocular presentations, which can pose a diagnostic challenge. Chronic uveitis with insidious onset is the most common type of ocular presentation. This report highlights a case of enthesitis-related arthritis, a type of JIA, in a 12-year-old boy who presented with severe intermediate uveitis that mimicked endophthalmitis.

DOI: 10.1016/j.jaapos.2019.03.001
PMID: 30959168

71: Kumar VL, Verma S, Das P. Artesunate suppresses inflammation and oxidative stress in a rat model of colorectal cancer. Drug Dev Res. 2019 Aug 30. doi: 10.1002/ddr.21590. [Epub ahead of print] PubMed PMID: 31471932.

Anti-inflammatory drugs are well known to reduce the risk of colon cancer and prophylactic use of such agents is gaining acceptance as a cancer prevention therapy. As artesunate, an antimalarial drug, has been shown to exhibit chemopreventive properties, the present study was carried out to evaluate its inhibitory effect on oxidative stress and inflammation in a rat model of colon carcinogenesis. A chemical carcinogen, 1,2-dimethylhydrazine was injected twice at an interval of 1 week to induce preneoplastic lesions in the colon and the parameters indicating oxidative stress and inflammation were evaluated after 8 weeks. Artesunate (50 and 150 mg/kg) and aspirin (60 mg/kg) were administered

orally throughout the study. Analysis of colon tissue revealed that both the drugs preserved histoarchitecture, inhibited cellular influx, decreased the levels of oxidative stress and inflammatory markers, downregulated cyclooxygenase-2, inducible nitric oxide synthase, nuclear factor κB, and interleukin 1β in comparison to the experimental control. Suppression of oxidative stress and pro-inflammatory signaling by both the drugs were found to contribute to inhibition of colon carcinogenesis. The protection afforded by these drugs was found to be comparable. Our study shows that like aspirin, use of artesunate could also reduce the risk of colon cancer and it has a potential for further evaluation for the treatment purpose.

DOI: 10.1002/ddr.21590
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OBJECTIVE: To assess the correlation between fetal blood vessel Doppler measurements and fetal anemia among Rhesus isoimmunized pregnancies after two intrauterine transfusions as a potential guide to therapy.
METHODS: A prospective observational study was conducted among 30 women who attended a single hospital in India between April 2, 2015 and October 30, 2016. The participants underwent a third intrauterine transfusion based on a middle cerebral artery (MCA) peak systolic velocity (PSV) of greater than 1.50 multiples of the median (MoM). Cordocentesis was performed before the third intrauterine transfusion and hematocrit values correlated with the blood vessel Doppler measurements.
RESULTS: The MCA PSV MoM and fetal hematocrit MoM had a correlation coefficient of -0.43 (95% confidence interval -0.68 to 0.08; P=0.017). The sensitivity, specificity, positive predictive value, and negative predictive value were 68%, 57%, 83%, and 33%, respectively. The descending aorta PSV δ and fetal hematocrit δ had a correlation coefficient of -0.54 (95% confidence interval -0.75 to -0.23; P=0.001). An area under the curve of 0.80 (standard error 0.085; P=0.017) had 87% sensitivity and 57% specificity for diagnosing fetal anemia.
CONCLUSION: The descending aorta PSV could offer a useful diagnostic adjunct to MCA PSV after two intrauterine transfusions.

DOI: 10.1002/ijgo.12825
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OBJECTIVES: This paper provides a discussion about the potential scope of applicability of Artificial Intelligence methods within the telehealth domain. These methods are focussed on clinical needs and provide some insight to current directions, based on reports of recent advances.
METHODS: Examples of telehealth innovations involving Artificial Intelligence to support or supplement remote health care delivery were identified from recent literature by the authors, on the basis of expert knowledge. Observations from

the examples were synthesized to yield an overview of contemporary directions for the perceived role of Artificial Intelligence in telehealth.
RESULTS: Two major focus areas for related contemporary directions were established. These were first, quality improvement for existing clinical practice and service delivery, and second, the development and support of new models of care. Case studies from each focus area have been chosen for illustration purposes.
CONCLUSION: Examples of the role of Artificial Intelligence in delivery of health care remotely include use of tele-assessment, tele-diagnosis, tele-interactions, and tele-monitoring. Further developments of underlying algorithms and validation of methods will be required for wider adoption. Certain key social and ethical considerations also need consideration more generally in the health system, as Artificial-Intelligence-enabled-telehealth becomes more commonplace.

Georg Thieme Verlag KG Stuttgart.

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74: Lele A, Kannan N, Vavilala MS, Sharma D, Mossa-Basha M, Agyem K, Mock C, Pandey RM, Dash HH, Mahapatra A, Gupta D. Patients Who Benefit from Intracranial Pressure Monitoring without Cerebrospinal Fluid Drainage After Severe Traumatic Brain Injury. Neurosurgery. 2019 Aug 1;85(2):231-239. doi: 10.1093/neuros/nyy247. PubMed PMID: 30053135.

BACKGROUND: India has a high traumatic brain injury (TBI) burden and intracranial pressure monitoring (ICP) remains controversial but some patients may benefit.
OBJECTIVE: To examine the association between ICP monitor placement and outcomes, and identify Indian patients with severe TBI who benefit from ICP monitoring.
METHODS: We conducted a secondary analysis of a prospective cohort study at a level 1 Indian trauma center. Patients over 18 yr with severe TBI (admission Glasgow coma scale score < 8) who received tracheal intubation for at-least 48 h were examined. Propensity-based analysis using inverse probability weighting approach was used to examine ICP monitor placement within 72 h of admission and outcomes. Outcomes were in-hospital mortality and Glasgow Outcome Scale (GOS) score at discharge, 3, 6, and 12 mo. Death, vegetative, or major impairment defined unfavorable outcome.
RESULTS: The 200 patients averaged 36 [18 to 85] yr of age and average injury severity score of 31.4 [2 to 73]. ICP monitors were placed in 126 (63%) patients. Patients with ICP monitor placement experienced lower in-hospital mortality (adjusted relative risk [aRR]; 0.50 [0.29, 0.87]) than patients without ICP monitoring. However, there was no benefit at 3, 6, and 12 mo. With ICP monitor placement, absence of cerebral edema (aRR 0.54, 95% confidence interval 0.35-0.84), and absence of intraventricular hemorrhage (aRR 0.52, 95% confidence interval 0.33-0.82) were associated with reduced unfavorable outcomes.
CONCLUSION: ICP monitor placement without cerebrospinal fluid drainage within 72 h of admission was associated with reduced in-patient mortality. Patients with severe TBI but without cerebral edema and without intraventricular hemorrhage may benefit from ICP monitoring.

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OBJECTIVE: To gain an understanding of the variation in available resources and clinical practices between neonatal units (NNUs) in the low-income and middle-income country (LMIC) setting to inform the design of an observational study on the burden of unit-level antimicrobial resistance (AMR).
DESIGN: A web-based survey using a REDCap database was circulated to NNUs participating in the Neonatal AMR research network. The survey included questions about NNU funding structure, size, admission rates, access to supportive therapies, empirical antimicrobial guidelines and period prevalence of neonatal blood culture isolates and their resistance patterns.
SETTING: 39 NNUs from 12 countries.
PATIENTS: Any neonate admitted to one of the participating NNUs.
INTERVENTIONS: This was an observational cohort study.
RESULTS: The number of live births per unit ranged from 513 to 27 700 over the 12-month study period, with the number of neonatal cots ranging from 12 to 110. The proportion of preterm admissions <32 weeks ranged from 0% to 19%, and the majority of units (26/39, 66%) use Essential Medicines List 'Access' antimicrobials as their first-line treatment in neonatal sepsis. Cephalosporin resistance rates in Gram-negative isolates ranged from 26% to 84%, and carbapenem resistance rates ranged from 0% to 81%. Glycopeptide resistance rates among Gram-positive isolates ranged from 0% to 45%.
CONCLUSION: AMR is already a significant issue in NNUs worldwide. The apparent burden of AMR in a given NNU in the LMIC setting can be influenced by a range of factors which will vary substantially between NNUs. These variations must be considered when designing interventions to improve neonatal mortality globally.

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BACKGROUND: Elevated blood pressure incurs a major health and economic burden, particularly in low-income and middle-income countries. The Triple Pill versus

Usual Care Management for Patients with Mild-to-Moderate Hypertension (TRIUMPH) trial showed a greater reduction in blood pressure in patients using fixed-combination, low-dose, triple-pill antihypertensive therapy (consisting of amlodipine, telmisartan, and chlorthalidone) than in those receiving usual care in Sri Lanka. We aimed to assess the cost-effectiveness of the triple-pill strategy.
METHODS: We did a within-trial (6-month) and modelled (10-year) economic evaluation of the TRIUMPH trial, using the health system perspective. Health-care costs, reported in 2017 US dollars, were determined from trial records and published literature. A discrete-time simulation model was developed, extrapolating trial findings of reduced systolic blood pressure to 10-year health-care costs, cardiovascular disease events, and mortality. The primary outcomes were the proportion of people reaching blood pressure targets (at 6 months from baseline) and disability-adjusted life-years (DALYs) averted (at 10 years from baseline). Incremental cost-effectiveness ratios were calculated to estimate the cost per additional participant achieving target blood pressure at 6 months and cost per DALY averted over 10 years.
FINDINGS: The triple-pill strategy, compared with usual care, cost an additional US$9·63 (95% CI 5·29 to 13·97) per person in the within-trial analysis and $347·75 (285·55 to 412·54) per person in the modelled analysis. Incremental cost-effectiveness ratios were estimated at $7·93 (95% CI 6·59 to 11·84) per participant reaching blood pressure targets at 6 months and $2842·79 (-28·67 to 5714·24) per DALY averted over a 10-year period.
INTERPRETATION: Compared with usual care, the triple-pill strategy is cost-effective for patients with mild-to-moderate hypertension. Scaled up investment in the triple pill for hypertension management in Sri Lanka should be supported to address the high population burden of cardiovascular disease.
FUNDING: Australian National Health and Medical Research Council.

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PMID: 31477545

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BACKGROUND: Comparative characteristics of the cricothyroid injection and spray-as-you-go methods for lidocaine administration during diagnostic flexible bronchoscopy are not clear.
OBJECTIVES: Co-primary outcomes were comparison of cough count from bronchoscope introduction until reaching carina and operator-rated overall procedure satisfaction on a Visual Analogue Scale (VAS) between groups. Secondary outcomes were cumulative lidocaine dose, procedure duration, assistant-rated cough, willingness to return for repeat procedure, and procedural complications between groups.
METHODS: Consecutive subjects were randomized (1:1) to either the cricothyroid or the spray-as-you-go method for topical anesthesia to the vocal cords and trachea. All received nasal 2% lidocaine gel and pharyngeal 10% lidocaine spray.
RESULTS: A total of 500 subjects were randomized, and 495 subjects were analyzed (248 cricothyroid and 247 spray-as-you-go). Cough count until reaching carina (median [range]) was significantly lower (cricothyroid, 1 [0-10], and spray-as-you-go, 4 [0-30], $p < 0.0001$) and operator-rated overall procedure satisfaction, VAS (mean ± standard deviation) (cricothyroid, 7.86 ± 1.39 and spray-as-you-go, 6.86 ± 1.59, $p < 0.0001$) significantly greater in the

cricothyroid group. Patient willingness to return for repeat procedure was greater (87.1 vs. 70.5%, p < 0.001)) and cumulative lidocaine dose significantly lower (305.08 ± 13.40 vs. 322.18 ± 10.67 mg, p < 0.001) in the cricothyroid group. Minor complications occurred in 6 patients in the cricothyroid group and 9 patients in the spray-as-you-go group.
CONCLUSION: Cricothyroid lidocaine administration is associated with less cough and superior operator-rated procedure satisfaction during bronchoscopy at a lower cumulative lidocaine dose.

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Brachytherapy (BT) for locally advanced cervical cancer is vital for optimal outcomes. There is heterogeneity in brachytherapy treatment practice for cervical cancer across India. In an attempt to standardize various processes involved in cervical cancer brachytherapy, the expert members of the Indian Brachytherapy Society (IBS) developed a document related to radiation therapy treatment of cervical cancer with special emphasis on brachytherapy. The guidelines are based on high quality clinical evidence, expert opinion and consensus wherever evidence was lacking. The document provides a guide for external beam radiation and details of all the processes involved in high-dose-rate (HDR) brachytherapy including patient selection, preparation, principles and technique of BT applications, target and normal tissue definition, dose prescriptions, BT planning, reporting parameters, common complications of BT and their management, scope for research, etc. In summary, we present here practical tips and tricks, recording and reporting of cervical cancer brachytherapy, which can be implemented in various clinical environments and forms the basis of this report.

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10.1177/1129729819868927. [Epub ahead of print] PubMed PMID: 31423893.

BACKGROUND: Comparison between various approaches of ultrasound (USG)-guided internal jugular vein cannulation, that is, short-axis out-of-plane approach, long-axis in-plane approach, and oblique-axis approach, is sparse. In this network meta-analysis of randomized controlled trials, all three approaches were evaluated to identify the best technique for USG-guided internal jugular vein cannulation.
METHODS: Randomized controlled trials comparing short-axis out-of-plane approach, long-axis in-plane approach, and oblique-axis approach in any combination (i.e. comparison of any two or all three) for USG-guided internal jugular vein cannulation were included in this meta-analysis. Bayesian network meta-analysis was conducted with a non-informative prior effect size and heterogeneity, and all results were reported as posterior median odds ratio with 95% credible interval.
RESULTS: Data of 658 patients from five randomized controlled trials were included in this meta-analysis. No difference was obtained in first attempt success rate of cannulation in three approaches (posterior median odds ratio between long-axis and short-axis view, oblique-axis and short-axis view, and long-axis and oblique-axis view were 0.67 (0.20, 2.08), 0.92 (0.09, 4.790), and 1.3420 (0.1680, 6.7820), respectively). No difference was seen in the incidence of carotid artery puncture and overall success rate of cannulation.
CONCLUSION: All three commonly used approaches for USG-guided internal jugular vein cannulation, that is, short axis, long axis, and oblique axis, are comparable in terms of clinical utility and safety. There is insufficient evidence to recommend one approach over another for this purpose.

DOI: 10.1177/1129729819868927
PMID: 31423893

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We report results on unsupervised organization of cervical cells using microscopy of Pap-smear samples in brightfield (3-channel color) as well as high-resolution quantitative phase imaging modalities. A number of morphological parameters are measured for each of the 1450 cell nuclei (from 10 woman subjects) imaged in this study. The principal component analysis (PCA) methodology applied to this data shows that the cell image clustering performance improves significantly when brightfield as well as phase information is utilized for PCA as compared to when brightfield-only information is used. The results point to the feasibility of an image-based tool that will be able to mark suspicious cells for further examination by the pathologist. More importantly, our results suggest that the information in quantitative phase images of cells that is typically not used in clinical practice is valuable for automated cell classification applications in general.

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Objective: To study photoreceptor changes after a successful macular hole surgery using adaptive optics.
Materials and Methods: Three patients who underwent a successful macular hole surgery were studied. Cone density, spacing, and number of nearest neighbors were analyzed at 2° and 4° of eccentricity in all four quadrants using adaptive optics.
Results: All three patients gained a visual acuity better than logMAR 0.477 (Snellen equivalent 6/18) at 6 months following successful macular hole surgery. Following successful closure of the macular hole, photoreceptors were appreciated at 2° and 4° of eccentricity from the center. However, as compared with the fellow normal eye, cell density was reduced significantly in the inferior (12,929.33±2047.50 versus 23,839.67±3711.16 cells/mm2 at 2°) and temporal quadrant (13,890±3424.26 versus 22,578.67±5651.34 cells/mm2 at 2°), and intercell spacing was increased significantly in inferior (9.6±0.92 versus 7.14±0.545 μm) and nasal quadrant (8.83±0.39 versus 7.49±0.42 μm). Number of nearest neighbors was unaffected after the hole closure.
Conclusion: Postoperative recovery of vision after successful closure of the hole occurs because of the migration or shifting of cells from parafoveal retina toward the center. Cells nearest to the hole margin (at 2° eccentricity) appear to shift more as compared with cells which are further away.

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Nurse informatics specialist is the new concept in India moreover it's a kind of challenge in the highly populated All India Institute of medical sciences, a quaternary care premium medical institute in India to digitalise all the medical / administrative paper work. The paper emphasizes on nature of duties for nursing Informatics practicner, desirable skills, challenges and finally implementing nursing Informatics concept in India, in All india Institute of Medical sciences. For the first time the nursing informatics concept is used and implemented in India, and I am the part of this concept. I will be further sharing my experiences of Nursing informatics practice in India.

DOI: 10.3233/SHTI190731
PMID: 31438425 [Indexed for MEDLINE]

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Copper oxide nanomaterials were synthesized by a facile sustainable biological method using two plant species (Zanthoxylum armatum DC. and Berberis lycium Royle). The formation of materials was confirmed by FT-IR, ATR, UV-visible, XRD, TEM, SEM, EDX, TGA and PL. The antibacterial activity was evaluated by agar well diffusion method to ascertain the efficacy of plant species extract and extract derived copper oxide nanomaterials against six Gram-positive bacteria namely

Staphylococcus aureus, Streptococcus mutans, Streptococcus pyogenes, Corynebacterium diphtheriae, Corynebacterium xerosis, Bacillus cereus and four Gram-negative bacteria such as Klebsiella pneumonia, Escherichia coli, Pseudomonas aeruginosa and Proteus vulgaris against the standard drug, Ciprofloxacin for Gram-positive and Gentamicin for Gram-negative bacteria, respectively. In both cases, copper oxide nanomaterials were found to be sensitive in all the bacterial species. Sensitivity of copper oxide nanomaterials shows an be higher as compared to plant species extract against different bacteria. Scavenging activity of plant extracts along with nanomaterials have been accessed using previously reported protocols employing ascorbic acid as standard. Scavenging activity of copper oxide nanomaterials shows an increase with increase in concentration. The biological activity (bactericidal and scavenging efficiency) of plant derived copper oxide nanomaterials revealed that these materials can be used as potent antimicrobial agent and DPPH scavengers in industrial as well as pharmacological fields.

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PMID: 31207044 [Indexed for MEDLINE]

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Broad and potent neutralizing antibodies (bnAbs) with multiple epitope specificities evolve in HIV-1-infected children. Herein, we studied two antiretroviral-naive chronically HIV-1 clade C-infected monozygotic pediatric twins, AIIMS_329 and AIIMS_330, with potent plasma bnAbs. Elite plasma neutralizing activity was observed since the initial sampling at 78 months of age in AIIMS_330 and persisted throughout, while in AIIMS_329 it was seen at 90 months of age, after which the potency decreased over time. We evaluated potential viral characteristics associated with the varied immune profiles by generating single genome-amplified pseudoviruses. The AIIMS_329 viruses generated from the 90-month time point were neutralization sensitive to bnAbs and contemporaneous plasma antibodies, while viruses from the 112-month and 117-month time points were resistant to most bnAbs and contemporaneous plasma. AIIMS_329 viruses developed resistance to plasma neutralizing antibodies (nAbs) plausibly by N160 glycan loss and V1 and V4 loop lengthening. The viruses generated from AIIMS_330 (at 90 and 117 months) showed varied susceptibility to bnAbs and autologous contemporaneous plasma antibodies, while the viruses of the 112-month time point, at which the plasma nAb specificities mapped to the V2 glycan, V3 glycan, and CD4 binding site (CD4bs), were resistant to contemporaneous plasma antibodies as well as to most bnAbs. Chimeric viruses were constructed from 90-month-time-point PG9-sensitive AIIMS_329 and AIIMS_330 viruses with swapped V1V2 regions of their respective evolved viruses (at 112 and 117 months), which led to higher resistance to neutralization by PG9 and autologous plasma antibodies. We observed the evolution of a viral pool in the AIIMS_330 donor comprising plasma antibody neutralization-sensitive or -resistant diverse autologous viruses that may have contributed to the development and maintenance of elite neutralizing activity.IMPORTANCE Herein, we report the longitudinal development of bnAbs in a pair of chronically HIV-1 clade C-infected monozygotic pediatric twins, AIIMS_329 and AIIMS_330, who acquired the infection by vertical transmission. The plasma from both donors, sharing a similar genetic makeup and infecting virus, showed the evolvement of bnAbs targeting common epitopes in the V2 and V3 regions of the envelope, suggesting that bnAb development in these

twins may perhaps be determined by specific sequences in the shared virus that can guide the development of immunogens aimed at eliciting V2 and V3 bNAbs. Characterization of the neutralization-sensitive and -resistant viruses coevolving with bNAbs in the contemporaneous AIIMS_330 plasma provides information toward understanding the viral alterations that may have contributed to the development of resistance to bnAbs. Further longitudinal studies in more monozygotic and dizygotic twin pairs will help in delineating the role of host and viral factors that may contribute to the development of bnAbs.

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PMCID: PMC6694815 [Available on 2020-02-13]
PMID: 31217240

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Studies conducted in animal models have suggested that membrane complement regulatory proteins play an important role in the pathophysiology of coronary artery disease (CAD). In this study, a total of 100 individuals, with stable CAD and 100 healthy controls, both groups predominantly male, were recruited. We evaluated the plasma levels of complement regulatory proteins (Cregs) CD35, CD46, CD55, and CD59 and their surface expression on granulocytes, lymphocytes, and monocytes by flow cytometry. The mRNA expression of these Cregs in total leukocytes was determined by quantitative PCR. The soluble forms of Cregs, C3c, Mannose binding protein-associated serine protease 2 (MASP-2), Platelet activating factor-acetyl hydrolase (PAF-AH), and inflammatory cytokines were quantified by ELISA. High plasma levels of C3c, indicative of complement activation, in addition to significantly low levels of Cregs, were observed in CAD patients. A significantly lower expression of CD46 and CD55 on the surface of lymphocytes, monocytes, and granulocytes and higher surface expression of CD35 and CD59 on granulocytes ($p < 0.0001$) was seen in CAD patients as compared to healthy donors. The high expression of CD59 on granulocytes positively correlated with the severity of disease and may serve as a potential marker of disease progression in CAD.

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Tay-Sachs disease (TSD) (OMIM) is a neurodegenerative lysosomal storage disorder caused due to mutations in the HEXA gene. To date, nearly 190 mutations have been reported in HEXA gene. Here, we have characterized 34 enzymatically confirmed TSD families to investigate the presence of novel as well as known variants in HEXA gene. Overall study detected 25 variants belonging to 31 affected TSD patients and 3 carrier couples confirmed by enzyme study. Of these 17 patients harbors 15 novel variants, including seven missense variants [p.V206L, p.Y213H, p.R252C, p.F257S, p.C328G, p.G454R, and p.P475R], four nonsense variant [p.S9X, p.E91X,

p.W420X, and p.W482X], two splice site variants [c.347-1G>A and c.460-1G>A], and two small deletion [c.1349delC (p.A450VfsX3) and c.52delG (p.G18Dfs*82)]. While remaining 17 patients harbors 10 previously reported variants that includes six missense variants [p.M1T, p.R170Q, p.D322Y, p.D322N, p.E462V, and p.R499C], one nonsense variant [p.Q106X], two splice site variants [c.1073+1G>A and c.459+4A>G] and one 4bp insertion [c.1278insTATC (p.Y427IfsX5)]. In conclusion, Indian infantile TSD patients provide newer insight into the molecular heterogeneity of the TSD. Combining present study and our earlier studies, we have observed that 67% genotypes found in Indian TSD patients are novel, which are associated with severe infantile phenotypes, while rest 33% genotypes found in our cohort were previously reported in various populations. In addition, higher frequency of the p.E462V and c.1278insTATC mutations in the present study further support and suggest the prevalence of p.E462V mutation in the Indian population.

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Giant cell tumor (GCT) of bone is a common benign lesion that causes significant morbidity due to the failure of modern medical and surgical treatment. Surface ultra-structures of giant cells (GCs) may help in distinguishing aggressive tumors from indolent GC lesions. This study aimed to standardize scanning electron microscopic (SEM) imaging of GC from GCT of bone. Fresh GCT collected in Dulbecco's Modified Eagle Medium was washed to remove blood, homogenized, or treated with collagenase to isolate the GCs. Mechanically homogenized and collagenase-digested GCs were imaged on SEM after commonly used drying methodologies such as air-drying, tetramethylsilane (TMS)-drying, freeze-drying, and critical point-drying (CPD) for the optimization of sample processing. The collagenase-treated samples yielded a greater number of isolated GC and showed better surface morphology in comparison to mechanical homogenization. Air-drying was associated with marked cell shrinkage, and freeze-dried samples showed severe cell damage. TMS methodology partially preserved the cell contour and surface structures, although the cell shape was distorted. GC images with optimum surface morphology including membrane folding and microvesicular structures on the surface were observed only in collagenase-treated and critical point-dried samples. Collagenase digestion and critical point/TMS-drying should be performed for optimal SEM imaging of individual GCs.

DOI: 10.1017/S1431927619014855
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OBJECTIVE: To compare development/cognition, adaptive function and maladaptive behavior of HIV-infected and HIV-exposed uninfected children between 2 to 9 years with HIV-uninfected controls.
METHODS: This hospital-based cross-sectional study was conducted from November, 2013 to March, 2015. 50 seropositive HIV-infected, 25 HIV-exposed uninfected and 25 HIV-uninfected children between 2 to 9 years were administered Developmental Profile 3, Vineland Adaptive Behavior Scale 2, and Child Behavior Checklist for assessing development, adaptive function and maladaptive behaviour, respectively. Additional data was obtained by history, examination and review of records.
RESULTS: Significant developmental/cognitive impairment was observed in 38 (76%), 16 (64%) and 6 (24%) HIV-infected, HIV-exposed uninfected, and HIV-uninfected children, respectively. Significant impairment in adaptive function was found in 12 (24%) and 2 (8%) HIV-infected and HIV-exposed uninfected children, respectively. Maladaptive behavior was not seen in any group.
CONCLUSIONS: High magnitude of impaired development/cognition and adaptive function in HIV-exposed and HIV-infected children warrants assessment of these domains during follow-up of these children, and incorporation of interventions for these deficits in standard care for this group.

PMID: 31441434

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PURPOSE: To evaluate tear neuropeptides (NPs) (vasoactive intestinal peptide (VIP), neuropeptide Y (NPY), calcitonin gene-related peptide (CGRP), substance P (SP), nerve growth factor (NGF)) in chronic ocular topical hypotensive therapy with and without benzalkonium chloride (BAK) preservative.
METHODS: A comparative, open label, cross-sectional study of patients using antiglaucoma medications for >6 months with BAK (group I), without BAK (group II) and controls was done. Tear NPs (ELISA), ocular surface evaluation tests (tear breakup time (TBUT), Schirmer's test, corneal and conjunctival staining score) and confocal central corneal subbasal nerve fibre layer (SBNFL) imaging was done.
RESULTS: Of 153 eyes evaluated, group 1 (82 eyes (41 patients; mean age 48±14.5 years)) and group 2 (71 eyes (36 patients; mean age 43.11±15 years)) were on therapy for a mean duration of 10.05±2.0 and 9.67±2.3 months, respectively. Tear analysis showed elevated SP and NGF ($p<0.01$); decreased CGRP ($p=0.03$), VIP and NPY ($p<0.01$) compared with controls (n=30, mean age 29.33±5.7 years). Tear NP levels (SP ($p=0.1$), NGF ($p=0.33$), CGRP ($p=1$), VIP ($p=0.87$), NPY ($p=0.83$)) and SBNFL ($p=0.09$) were comparable in both groups. There was no correlation seen between tear NP levels and clinical tests and SBNFL.
CONCLUSION: Our study analysis points towards altered tear NP levels in eyes on chronic topical hypotensive therapy in comparison with controls with no significant difference in tear NP levels and central corneal SBNFL density between the BAK preservative and BAK-free antiglaucoma therapy.

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PMID: 31383648

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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.

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PMID: 30922197

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BACKGROUND: The aim of the present study was to systematically review and analyze the available evidence on the role of surgery in improving outcomes in patients with migraine headaches.
METHODS: An electronic search of PubMed, Scopus, CENTRAL (Cochrane Central Register of Controlled Trials), and Google Scholar databases was performed for English-language articles reporting results of peripheral nerve surgery for migraine headaches.
RESULTS: The search strategy revealed a total of 1528 records, of which 23 studies were included in the review. A total of 1151 headache patients were treated in the included studies. The trigger site of migraine addressed varied across studies. Meta-analysis of data of 616 patients revealed that migraine surgery significantly reduces migraine headache frequency (random: mean, 9.52; 95% confidence interval, 7.14-11.9; P < 0.00001; I = 94%). Similarly, when data of 797 patients were analyzed, there was statistically significant reduction in migraine headache intensity in patients undergoing migraine headache surgery (random: mean, 3.97; 95% confidence interval, 3.31-4.62; P < 0.00001; I = 94%). On pooling of data of all 23 studies, 8.3% to 76.4% of patients reported complete elimination of headache after surgery, whereas 3.9% to 33.3% had no relief.
CONCLUSIONS: Peripheral nerve decompression surgery is highly effective in reducing migraine headache frequency and migraine headache intensity. However, not all patients benefit from the surgical procedure, with a small subset showing no improvement. Further clinical and anatomical studies are needed to define the exact mechanism of nerve compression in migraine patients and as to why a subset of patients does not respond to surgical treatment.

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BACKGROUND: In a significant percentage of patients with small cell lung carcinoma (SCLC), cytology samples represent the only source of tumor tissue. Ancillary immunocytochemistry (ICC) for neuroendocrine markers is an important adjunct for the diagnosis of SCLC. Insulinoma-associated protein 1 (INSM1) is a novel neuroendocrine marker proposed as an economical single-marker alternative to the traditional 3-marker panel of chromogranin, synaptophysin, and CD56. To the authors' knowledge, limited studies have evaluated INSM1 immunohistochemistry (IHC) for the diagnosis of SCLC and reported high sensitivities and specificities. The objective of the current study was to evaluate the sensitivity and specificity of INSM1 ICC on direct smears (DS) from patients with SCLC in comparison with IHC on small biopsies (SBs).
METHODS: All available DS and SBs from patients with SCLC who were diagnosed over the previous year were retrieved. Immunostaining for INSM1 was performed on alcohol-fixed DS and formalin-fixed SBs wherever available. A total of 10 DS and SBs from patients with non-small cell lung carcinoma were included for comparison. Nuclear staining for INSM1 in ≥1% tumor cells was interpreted as positive.
RESULTS: Among a total of 60 patients with SCLC who were included in the current study, a total of 37 underwent INSM1 IHC on SBs and 36 underwent INSM1 ICC on DS. ICC was noninterpretable in 3 DS due to necrosis. The sensitivity of INSM1 IHC was 97% (36 of 37 cases) whereas the sensitivity of INSM1 ICC was 91% (30 of 33 cases) for the diagnosis of SCLC. Among matched IHC and ICC results available for 11 patients, 91% of cases (10 of 11 patients) demonstrated concordant IHC-ICC staining. All cases of non-small cell lung carcinoma were negative for INSM1 (100% specificity).
CONCLUSIONS: INSM1 appears to be a robust and reliable ICC marker for the confirmation of SCLC diagnosis on cytology smears.

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Immune check-point blockade (ICB) targeting programmed cell death ligand-1 (PD-L1)/programmed death-1 (PD-1) axis has created paradigm shift in cancer treatment. 'ST-RELA' and 'PF-A' molecular subgroups of ependymomas (EPN) show poor outcomes. We aimed to understand the potential candidature of EPNs for ICB. Supratentorial (ST) Grade II/III EPNs were classified into ST-RELA, ST-YAP, and ST-not otherwise specified (NOS), based on RELA/YAP1 fusion transcripts and/or L1CAM and p65 protein expression. Posterior fossa (PF) EPNs were classified into PF-A and PF-B based on H3K27me3 expression. Immunohistochemistry for PD-L1 and CD8 was performed. RelA protein enrichment at PDL1 promoter site was analysed by chromatin immunoprecipitation-qPCR (ChIP-qPCR). Eighty-three intracranial EPNs were studied. Median tumor infiltrating CD8+cytotoxic T-lymphocyte (CTL) density was 6/mm2, and was higher in ST-EPNs (median 10/mm2) as compared to PF-EPNs (median 3/mm2). PD-L1 expression was noted in 17/83 (20%) EPNs, including

12/31 ST-RELA and rare ST-NOS (2/12), PF-A (2/25) and PF-B (1/13) EPNs. Twelve EPNs (14%) showed high CTL density and concurrent PD-L1 positivity, of which majority (10/12) were ST-RELA EPNs. Enrichment of RelA protein was seen at PDL1 promoter. Increased CTL densities and upregulation of PD-L1 in ST-RELA ependymomas suggests potential candidature for immunotherapy.

DOI: 10.1007/s10014-019-00350-1
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BACKGROUND: IgG4-related disease is an autoimmune process that presents with tumefactive lesions characterized by storiform fibrosis, a dense lymphoplasmacytic infiltrate rich in IgG4+ plasma cells, obliterative phlebitis, and often elevated serum IgG4 levels. Central nervous system IgG4-related disease is very rare and usually occurs in the form of hypertrophic pachymeningitis or hypophysitis. Presentation as a large solitary meningioma-like mass with overlying hyperostosis in a young adult has not been reported before.
CASE SUMMARY: A 16-year-old male presented with focal seizures for 5 months. Imaging showed a large, extra-axial, and contrast-enhancing mass lesion in the left frontoparietal region with focal calvarial thickening. Histopathology revealed a fibrosclerotic lesion involving dura with a polymorphic infiltrate of plasma cells, mature lymphocytes, histiocytes, and occasional eosinophils. Immunohistochemical workup excluded the possibilities of meningioma, lymphoproliferative neoplasms, and histiocytic lesions. Majority of plasma cells were IgG4+ rendering a diagnosis of IgG4-related disease. Further serological and imaging workup did not reveal any evidence of systemic involvement. His serum IgG4 levels were normal. Considering a gross total resection of the lesion, no further treatment was given and the patient has been asymptomatic since.
CONCLUSION: IgG4-related lesions of the CNS are under-recognized and accurate diagnosis, especially in those with isolated CNS disease and normal serum IgG4 levels, necessitates robust histopathological and laboratory workup to exclude mimics. They may occur as large dural masses with hyperostosis and differentiation from lymphoplasmacyte-rich meningiomas, in particular, can be challenging. While steroids are the mainstay of treatment in IgG4-related disease, surgical resection may be curative in solitary lesions presenting with compressive symptoms.

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PMID: 31073682

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Rare missense variants play a crucial role in amyotrophic lateral sclerosis (ALS) pathophysiology. We report rare/novel missense variants from 154 Indian ALS patients, identified through targeted sequencing of 25 ALS-associated genes. As pathogenic variants could explain only a small percentage of ALS pathophysiology in our cohort, we investigated the frequency of tolerated and benign novel/rare variants, which could be potentially ALS susceptible. These variants were identified in 5.36% (8/149) of sporadic ALS (sALS) cases; with one novel variant each in ERBB4, SETX, DCTN1, and MATR3; four rare variants, one each in PON2 and

ANG and two different rare variants in SETX. Identified variants were either absent or present at extremely rare frequencies (MAF < 0.01) in large population databases and were absent in 50 healthy controls sequenced through Sanger method. Furthermore, an oligogenic basis of ALS was observed in three sALS, with co-occurrence of intermediate-length repeat expansions in ATXN2 and a rare/novel variant in DCTN1 and SETX genes. Additionally, molecular dynamics and biochemical functional analysis of an angiogenin variant (R21G) identified from our cohort demonstrated loss of ribonucleolytic and nuclear translocation activities. Our findings suggest that rare variants could be potentially pathogenic and functional studies are warranted to decisively establish the pathogenic mechanisms associated with them.

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PURPOSE: High mortality rate due to liver cirrhosis has been reported over the globe in the previous years. Early detection of cirrhosis may help in controlling the disease progression toward hepatocellular carcinoma (HCC). The lack of trained CT radiologists and increased patient population delays the diagnosis and further management. This study proposes a computer-aided diagnosis system for detecting cirrhosis and HCC in a very efficient and less time-consuming approach.
METHODS: Contrast-enhanced CT dataset of 40 patients (n = 40; M:F = 5:3; age = 25-55 years) with three groups of subjects: healthy (n = 14), cirrhosis (n = 12) and cirrhosis with HCC (n = 14), were retrospectively analyzed in this study. A novel method for the automatic 3D segmentation of liver using modified region-growing segmentation technique was developed and compared with the state-of-the-art deep learning-based technique. Further, histogram parameters were calculated from segmented CT liver volume for classification between healthy and diseased (cirrhosis and HCC) liver using logistic regression. Multi-phase analysis of CT images was performed to extract 24 temporal features for detecting cirrhosis and HCC liver using support vector machine (SVM).
RESULTS: The proposed method produced improved 3D segmentation with Dice coefficient 90% for healthy liver, 86% for cirrhosis and 81% for HCC subjects compared to the deep learning algorithm (healthy: 82%; cirrhosis: 78%; HCC: 70%). Standard deviation and kurtosis were found to be statistically different ($p < 0.05$) among healthy and diseased liver, and using logistic regression, classification accuracy obtained was 92.5%. For detecting cirrhosis and HCC liver, SVM with RBF kernel obtained highest slice-wise and patient-wise prediction accuracy of 86.9% (precision = 0.93, recall = 0.7) and 80% (precision = 0.86, recall = 0.75), respectively, than that of linear kernel (slice-wise: accuracy = 85.4%, precision = 0.92, recall = 0.67; patient-wise: accuracy = 73.33%, precision = 0.75, recall = 0.75).
CONCLUSIONS: The proposed computer-aided diagnosis system for detecting cirrhosis and hepatocellular carcinoma (HCC) showed promising results and can be used as effective screening tool in medical image analysis.

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Ets-1 is one of the crucial member of transcription factor family which share a unique DNA binding domain. It is predominantly expressed in various tumor subtypes and has shown its association in the regulation of various important genes which include ECM-degrading proteases. Our study aimed to understand the mechanism(s) in the pathogenesis of breast carcinogenesis by Ets-1 transcription factor and its downstream target gene MMP-9. Role of Ets-1 in MCF-7 and MDA-MB-231 breast cancer cells was studied by RNA-interference in combination with pull down and ChIP assays to identify the regulation of MMP-9 in these cell lines. Our results showed that transfection of Ets-1 siRNA in breast cancer cell lines resulted in downregulation of Ets-1 and MMP-9. Ets-1 knock down also showed reduced cell invasion and altered expression of EMT markers. Moreover, we could also predict that MMP-9 gene promoter harbors a binding site for Ets-1 transcription factor may be responsible in direct transactivation of Ets-1 along with EMT markers. Phenotypic changes and molecular alterations that may result in increased aggressiveness/invasiveness and metastatic nature of cancerous cells may lead to changes in EMT markers. Therefore, these findings may suggest a plausible role of Ets-1 dependent regulation of MMP-9 gene and may have a significant impact on breast carcinogenesis.

DOI: 10.1016/j.gene.2019.143952
PMID: 31265880 [Indexed for MEDLINE]

110: Nyamathi AM, Shin SS, Sinha S, Carpenter CL, Garfin DR, Ramakrishnan P, Yadav K, Ekstrand ML. Sustained Effect of a Community-based Behavioral and Nutrition Intervention on HIV-related Outcomes Among Women Living With HIV in Rural India: A Quasi-experimental Trial. J Acquir Immune Defic Syndr. 2019 Aug 1;81(4):429-438. doi: 10.1097/QAI.0000000000002044. PubMed PMID: 30973547; PubMed Central PMCID: PMC6594881.

BACKGROUND: Women living with HIV (WLH) in rural communities face challenges to obtaining treatment and accurate disease-related information. Nutritional deficits exacerbate disease progression.
SETTING: WLH were recruited from primary health centers in rural India.
METHOD: A quasi-experimental trial of a comprehensive Accredited Social Health Activist (Asha)-supported intervention compared 4 distinct Asha-based programs [(1) standard education (SE) alone; (2) nutrition education (+NE); (3) nutrition supplements (+NS); or (4) nutrition education and nutrition supplements (+NENS)] on key disease and nutrition-related outcomes [CD4 count, body mass index (BMI),

serum albumin, and hemoglobin]. Assessments occurred at baseline, and months 6 (immediately after intervention), 12, and 18. Multilevel modeling examined effects of program (group) over time.
FINDINGS: Among 600 WLH enrolled (n = 150 per arm), mean age, CD4 count, and BMI (kg/m) were 34.31, 447.42, and 20.09, respectively, at baseline. At 18-month follow-up, program 4 (+NENS) experienced greatest improvements in CD4 counts compared with program 1 (+SE) [adjusted difference = 223.81, 95% confidence interval (CI): 170.29 to 277.32]. For BMI, programs 3 (+NS; adjusted difference = 2.33, 95% CI: 1.39 to 3.26) and 4 (+NENS; adjusted difference = 2.14, 95% CI: 1.17 to 3.12) exhibited greater gains compared with program 1 (+SE). Programs 3 and 4 were not significantly different from each other (adjusted difference = -0.18, 95% CI: -1.12 to 0.76). Hemoglobin and serum albumin also improved over time; program 4 (+NENS) exhibited the greatest gains.
CONCLUSIONS: A low-cost Asha-supported behavioral and nutritional intervention improved outcomes for WLH. Gains were sustained at 18-month follow-up. Similar approaches may help improve HIV and other infectious disease-related outcomes in vulnerable populations.

DOI: 10.1097/QAI.0000000000002044
PMCID: PMC6594881 [Available on 2020-08-01]
PMID: 30973547

111: Ojha V, Ganga K, Sinha M, Sharma A. Right coronary artery pseudoaneurysm after drug eluting stent: Dilemma solved on dual source CT. Ann Thorac Surg. 2019 Aug 31. pii: S0003-4975(19)31263-9. doi: 10.1016/j.athoracsur.2019.07.038. [Epub ahead of print] PubMed PMID: 31479644.

112: Ojha V, Pandey NN, Ganga KP, Kumar S. Origin of bilateral subclavian arteries from the site of coarctation: A hitherto undescribed configuration. Ann Thorac Surg. 2019 Aug 14. pii: S0003-4975(19)31170-1. doi: 10.1016/j.athoracsur.2019.06.070. [Epub ahead of print] PubMed PMID: 31421106.

113: 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 Aug;34(8):1296-1315. doi: 10.1111/jgh.14648. Epub 2019 Jul 1. 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

114: Panda S, Thakar A, Sikka K, Sharma SC. Role of sternomastoid muscle interposition in concomitant transoral oncologic resection and neck dissection. Head Neck. 2019 Aug;41(8):2724-2731. doi: 10.1002/hed.25753. Epub 2019 Apr 4. PubMed PMID: 30945800.

BACKGROUND: To report the experience with sternomastoid (SM) myofascial flap for reconstruction/buttressing of lateral pharyngeal wall and floor of mouth defects following transoral onco-surgery.
METHODS: Prospectively collected data from February 2012-January 2018. SM flap harvested as a superiorly based flap supplied by the occipital artery and consisting of only the anterior SM head.
RESULTS: A total of 42 patients were included (TORS, n = 40; TOUSS, n = 2). Three of 42 patients developed transient pharyngo-cervical communications with subsequent spontaneous healing. Flap loss was not noted in any patient. Forty-one of 42 patients resumed normal swallowing and one patient was PEG dependent. Fifteen of 42 patients had pretreatment metastatic neck nodes. No patient however developed nodal recurrence over a median follow-up of 30 months.
CONCLUSION: The modified SM flap as reported here is a simple locally available reconstructive option when undertaking transoral surgery. Oncological concerns may however limit its use in situations with large nodal metastasis or extracapsular spread.

DOI: 10.1002/hed.25753
PMID: 30945800

115: Pandey NN, Sinha M, Rajagopal R, Raju SN, Sharma A, Kumar S. Unique association of Hemitruncus with Proximal Interruption of the Anomalous Pulmonary Artery. Ann Thorac Surg. 2019 Aug 19. pii: S0003-4975(19)31191-9. doi: 10.1016/j.athoracsur.2019.06.081. [Epub ahead of print] PubMed PMID: 31437435.

116: Pandey NN, Bhambri K, Kumar S. Rare and Anomalous Retro-Oesophageal Course of the Left Brachiocephalic Vein in Tetralogy of Fallot: Evaluation on CT Angiography With Relevant Embryology. Heart Lung Circ. 2019 Aug 16. pii: S1443-9506(19)31402-7. doi: 10.1016/j.hlc.2019.07.014. [Epub ahead of print] PubMed PMID: 31501047.

117: Philip NM, Naranje P, Bagchi S, Das CJ, Agarwal SK. Multiple abscesses in a renal transplant recipient. Kidney Int. 2019 Aug;96(2):526. doi: 10.1016/j.kint.2019.02.005. PubMed PMID: 31331482.

118: Porwal K, Pal S, Tewari D, Pal China S, Singh P, Tewari M, Prajapati G, Singh P, Cheruvu S, Khan YA, Sanyal S, Gayen JR, Ampapathi R, Mridha AR, Chattopadhyay N. Increased bone marrow-specific adipogenesis by clofazimine causes impaired fracture healing, osteopenia and osteonecrosis without extra-skeletal effects in rats. Toxicol Sci. 2019 Aug 8. pii: kfz172. doi: 10.1093/toxsci/kfz172. [Epub ahead of print] PubMed PMID: 31393584.

Mycobacterium leprae infection causes bone lesions and osteoporosis, however, the effect of anti-leprosy drugs on the bone is unknown. We, therefore, set out to

address it by investigating osteogenic differentiation from bone marrow (BM)-derived mesenchyme stem cells (MSCs). Out of seven anti-leprosy drugs, only clofazimine (CFZ) reduced MSCs viability (IC50 ~1μM) and their osteogenic differentiation but increased adipogenic differentiation on a par with rosiglitazone, and this effect was blocked by a peroxisome proliferator-activated receptor gamma (PPARγ) antagonist, GW9662. CFZ also decreased osteoblast viability and resulted in impaired bone regeneration in a rat femur osteotomy model at 1/3rd human drug dose owing to increased callus adipogenesis as GW9662 prevented this effect. CFZ treatment decreased BM-MSCs population and homing of MSCs to osteotomy site despite drug levels in BM being much less than it's in vitro IC50 value. In adult rats, CFZ caused osteopenia in long bones marked by suppressed osteoblast function due to enhanced adipogenesis and increased osteoclast functions. A robust increase in marrow adipose tissue (MAT) by CFZ did not alter hematologic parameters but likely reduced BM vascular bed leading to osteonecrosis (ON) characterized by empty osteocyte lacunae. However, CFZ had no effect on visceral fat content and was not associated with any metabolic and hematologic changes. Levels of unsaturated fatty acids in MAT were higher than saturated fatty acids and CFZ further increased the former. From these data, we conclude that CFZ has skeletal toxicity and could be used for creating a rodent ON model devoid of extra-skeletal effects.

DOI: 10.1093/toxsci/kfz172
PMID: 31393584

119: Pujari A, Kumar S, Markan A, Chawla R, Damodaran S, Kumar A. Buckling surgery on a goat's eye: A simple technique to enhance residents' surgical skill. Indian J Ophthalmol. 2019 Aug;67(8):1327-1328. doi: 10.4103/ijo.IJO_1779_18. PubMed PMID: 31332123; PubMed Central PMCID: PMC6677078.

Buckling surgery is one of the common procedures performed by the retinal surgeons for visual rehabilitation at the earliest in cases of retinal detachment. The optimal surgical skill in this section can only be achieved with repeated practices and clinical experiences. Here, we describe an easy and inexpensive way to perform, practice, and refine surgical skills by demonstrating this complicated surgery in a simple manner on goat's eyes. The advantages of this technique are real-tissue handling experiences and repeatability of the procedure with almost similar practical implications. Thus, whenever feasible, every attempt should be made to refine the residents or budding ophthalmologists surgical skills by undertaking this technique in their routine curriculum.

DOI: 10.4103/ijo.IJO_1779_18
PMCID: PMC6677078
PMID: 31332123

120: Pujari A, Selvan H, Goel S, Dada T. Direct Smartphone Disc Video Documentation for Pediatric Glaucomas During Evaluation Under Anesthesia. J Glaucoma. 2019 Aug;28(8):e143-e144. doi: 10.1097/IJG.0000000000001294. PubMed PMID: 31162176.

The newer version of iPhone, that is iPhone Xs max camera application is opened and a video mode is selected with a with continuous light source on. This device is now slowly advanced towards the patient's eye (pharmacologically dilated while evaluating under anesthesia) and the optic disc and peripapillary area findings can be documented with great ease. This video graphic and/or standstill images obtained from the video can be stored in the smartphones or on the cloud memory

for future assessment/comparison.

DOI: 10.1097/IJG.0000000000001294
PMID: 31162176

121: Qureshi SS, Gupta JK, Goyal A, Narayan Yadav H. A novel approach in the management of hyperhomocysteinemia. Med Hypotheses. 2019 Aug;129:109245. doi: 10.1016/j.mehy.2019.109245. Epub 2019 May 23. PubMed PMID: 31371071.

Hyperhomocysteinemia (Hhcy) is a biochemical alteration with plasma levels of homocysteine higher than 15 μmol/L, associated with atherosclerosis, and with vascular thrombosis by disrupting endothelial cells. Homocysteine is a sulfur-containing amino acid derived from methionine which is an essential amino acid. Excess homocysteine produced in the body is expelled out by liver and kidney from the systemic circulation. Hhcy is caused by the excess deficiencies of the vitamins like pyridoxine (B6), folic acid (B9), or cyanocobalamin (B12). High protein consumers are usually at risk for hyperhomocysteinemia because of low plasma B12 levels. It is approximated that mild Hhcy occurs in 5-7% of the general population and 40% in patients with vascular disease. Patients with heart failure, impaired renal function, and diabetes should be screened since the prevalence of Hhcy in these patients appears to be quite high. In this article, we hypothesise that citicoline is a novel drug for the management of Hhcy. Furthermore, the side effects of citicoline are also minimal and self-limiting. If this strategy is validated, citicoline will be the cost-effective way to be administered for Hhcy. Many evidences are available which suggest that ignoring homocysteine levels in patients with the vascular disease would be unwise. Thus, there is an urgent need for health care providers to develop effective preventions and interventions program (folic acid, Vitamin B6 and Vitamin B12 supplementation as well as lifestyle change) to reduce this disorder.

DOI: 10.1016/j.mehy.2019.109245
PMID: 31371071

122: Rai S, Siddiqui OM, Meher SK, Shariff A, Banga S. Role of Nursing Informatics in Implementation of SNOMED-CT in India. Stud Health Technol Inform. 2019 Aug 21;264:1718-1719. doi: 10.3233/SHTI190613. PubMed PMID: 31438309.

SNOMED-CT project under the Ministry of Health and Family Welfare is operational at AIIMS since July 2016. A team of nurses were recruited under SNOMED project who actively works for integrating existing EHR with SNOMED-CT, monitoring, training of users auditing the data, resets creation and development of National Drug Database. This paper emphasizes role of Nursing Informatics in implementation of SNOMED-CT project in India as well as in any other country.

DOI: 10.3233/SHTI190613
PMID: 31438309 [Indexed for MEDLINE]

123: Raina R, Grewal MK, Blackford M, Symons JM, Somers MJG, Licht C, Basu RK, Sethi SK, Chand D, Kapur G, McCulloch M, Bagga A, Krishnappa V, Yap HK, de Sousa Tavares M, Bunchman TE, Bestic M, Warady BA, de Ferris MD. Renal replacement therapy in the management of intoxications in children: recommendations from the Pediatric Continuous Renal Replacement Therapy (PCRRT) workgroup. Pediatr Nephrol. 2019 Nov;34(11):2427-2448. doi: 10.1007/s00467-019-04319-2. Epub 2019 Aug 24. PubMed PMID: 31446483.

BACKGROUND: Intentional or unintentional ingestions among children and

adolescents are common. There are a number of ingestions amenable to renal replacement therapy (RRT).
METHODS: We systematically searched PubMed/Medline, Embase, and Cochrane databases for literature regarding drugs/intoxicants and treatment with RRT in pediatric populations. Two experts from the PCRRT (Pediatric Continuous Renal Replacement Therapy) workgroup assessed titles, abstracts, and full-text articles for extraction of data. The data from the literature search was shared with the PCRRT workgroup and two expert toxicologists, and expert panel recommendations were developed.
RESULTS AND CONCLUSIONS: We have presented the recommendations concerning the use of RRTs for treatment of intoxications with toxic alcohols, lithium, vancomycin, theophylline, barbiturates, metformin, carbamazepine, methotrexate, phenytoin, acetaminophen, salicylates, valproic acid, and aminoglycosides.

DOI: 10.1007/s00467-019-04319-2
PMID: 31446483

124: Raj N, Padhy SK, Kumar V. Choroidal metastasis as the presenting feature of metastatic lung carcinoma. Clin Exp Optom. 2019 Aug 16. doi: 10.1111/cxo.12950. [Epub ahead of print] PubMed PMID: 31418922.

125: Ramam M. The Continuing Relevance of Leprosy. JAMA Dermatol. 2019 Aug 7. doi: 10.1001/jamadermatol.2019.1730. [Epub ahead of print] PubMed PMID: 31389975.

126: Rawal I, Ghosh S, Hameed SS, Shivashankar R, Ajay VS, Patel SA, Goodman M, Ali MK, Narayan KMV, Tandon N, Prabhakaran D. Association between poor oral health and diabetes among Indian adult population: potential for integration with NCDs. BMC Oral Health. 2019 Aug 20;19(1):191. doi: 10.1186/s12903-019-0884-4. PubMed PMID: 31429749; PubMed Central PMCID: PMC6701092.

BACKGROUND: Studies in high-income countries have reported associations between oral health and diabetes. There is however a lack of evidence on this association from low and middle-income countries, especially India. The current study aimed to assess the prevalence of common oral diseases and their association with diabetes.
METHODS: This cross-sectional study was nested within the second Cardiometabolic Risk Reduction in South Asia Surveillance Study. A subset of study participants residing in Delhi were administered the World Health Organization's Oral Health Assessment Questionnaire and underwent oral examination for caries experience and periodontal health assessment using standard indices. Diabetes status was ascertained by fasting blood glucose, glycosylated hemoglobin values or self-reported medication use. Information was captured on co-variates of interest. The association between oral health and diabetes was investigated using Multivariable Zero-Inflated Poisson (ZIP) regression analysis.
RESULTS: Out of 2045 participants, 47% were women and the mean age of study participants was 42.17 (12.8) years. The age-standardised prevalence (95% confidence interval) estimates were 78.9% (75.6-81.7) for dental caries, 35.9% (32.3-39.6) for periodontitis. Nearly 85% participants suffered from at least one oral disease. Compared to diabetes-free counterparts, participants with diabetes had more severe caries experience [Mean Count Ratio (MCR) = 1.07 (1.03-1.12)] and attachment loss [MCR = 1.10 (1.04-1.17)]. Also, the adjusted prevalence of periodontitis was significantly higher among participants with diabetes [42.3%(40.0-45.0)] compared to those without diabetes [31.3%(30.3-32.2)].
CONCLUSION: We found that eight out of ten participants in urban Delhi suffered from some form of oral disease and participants with diabetes had worse oral health. This highlights the need for public health strategies to integrate oral health within the existing Non-Communicable Disease control programs.

DOI: 10.1186/s12903-019-0884-4

PMCID: PMC6701092
PMID: 31429749

127: Razik A, Das CJ, Gupta A, Wanamacher D, Verma S. Urinary diversions: a primer of the surgical techniques and imaging findings. Abdom Radiol (NY). 2019 Aug 22. doi: 10.1007/s00261-019-02179-w. [Epub ahead of print] PubMed PMID: 31440802.

OBJECTIVE: The article attempts to describe the indications, classification, and surgical anatomy of the commonly performed urinary diversion procedures, followed by the imaging protocol and radiological appearances of the normal postoperative anatomy and complications related to these procedures.
CONTENTS: Diversion procedures are used to reroute urine after cystectomy and in patients with refractory neurogenic or outlet obstruction of the urinary bladder. Broadly, these can be classified as continent and incontinent diversions. Patients with urinary diversions frequently undergo radiological investigations for the detection of complications. Commonly, a loopogram or pouchogram is performed few weeks after the surgery to look for leak, whereas CT or MRI is used for long-term follow-up. Postoperative complications can be early (within 30 days of the surgery) or delayed and include leaks, collections, strictures, calculi, parastomal hernia, small bowel obstruction, and oncologic recurrence.
CONCLUSION: A variety of urinary diversion procedures are commonly performed and interpretation of the postsurgical anatomy can be overwhelming for the general radiologist. This article provides a basic understanding of the normal anatomy as well as a thorough discussion on the imaging protocol and radiological appearances of the potential complications associated with these procedures.

DOI: 10.1007/s00261-019-02179-w
PMID: 31440802

128: Real SAS, Parveen F, Rehman AU, Shaik R, Deo SVS, Husain SA. Mutation, methylation and expression analysis of LIFR gene in Indian breast cancer patients. Mutat Res. 2019 Aug 12;816-818:111677. doi: 10.1016/j.mrfmmm.2019.111677. [Epub ahead of print] PubMed PMID: 31557600.

LIFR functions as a tumor suppressor and metastatic suppressor of breast cancer. The present study investigates the status of LIFR gene in Indian breast cancer patients. A total of 137 breast cancer tissue and 137 adjacent normal tissue which served as controls were analyzed for mutation by automated DNA sequencing, methylation through methylation-specific polymerase chain reaction and its corresponding expression at mRNA and protein level using real-time quantitative polymerase chain reaction and immunohistochemistry respectively in Indian breast cancer patients. All the molecular findings were statistically correlated with clinopathological parameters of the patients to identify its association. LIFR mRNA expression was found to be 2.534 ± 3.52 fold downregulated with subsequent absence of protein in 67.15% cases (92/137). The absence of LIFR protein coincided with 80.95% (85/105) methylated cases thereby showing a very strong correlation among the LIFR promoter methylation and LIFR protein expression ($p = 0.0001$). We also observed G2968C nucleotide change in 6/137 cases of exon 20 of LIFR gene resulting in Glu990Gln mutation. Correlation of LIFR promoter methylation with geographic location and age at menopause and LIFR mutation with age at menarche, age at first live birth, molecular subtypes of breast cancer, and lymph node status remained significant even after bonferroni correction ($p \leq 0.0027$). All these data suggests the relevance of these associations in relation to Indian breast cancer patients. The loss of LIFR protein was frequently found in Indian breast cancer patients, and aberrant promoter methylation showed a significant correlation with its downregulation.

DOI: 10.1016/j.mrfmmm.2019.111677
PMID: 31557600

129: 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 Aug;64(8):2327-2337. doi: 10.1007/s10620-019-05557-y. Epub 2019 Mar 4. 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

130: Sahoo T, Gulla KM. Early transpyloric feeding: an old wine in a new bottle. J Perinatol. 2019 Aug;39(8):1153-1154. doi: 10.1038/s41372-019-0417-7. Epub 2019 Jun 20. PubMed PMID: 31222154.

131: Sahu MK, C B, Arora Y, Singh SP, Devagouru V, Rajshekar P, Chaudhary SK. Peritoneal Dialysis in Pediatric Postoperative Cardiac Surgical Patients. Indian J Crit Care Med. 2019 Aug;23(8):371-375. doi: 10.5005/jp-journals-10071-23221. PubMed PMID: 31485107; PubMed Central PMCID: PMC6709843.

Background: We determined the prevalence of acute kidney injury requiring peritoneal dialysis (PD), the factors associated with early PD initiation, prolonged PD and mortality among pediatric postoperative cardiac surgical patients.
Materials and Methods: The hospital records of 23 children, aged 12 years or younger, who had undergone cardiac surgery and required PD subsequently, during a 1-year period were reviewed. Demographic data, intraoperative variables, and postoperative complications were compared between survivors and nonsurvivors of PD, between the short and long duration PD groups, and between the early and late PD initiation groups.

Results: Six hundred and eight pediatric patients who underwent open heart surgery were enrolled in this study. 23 (3.78%) of them required PD. When compared with survivors (n = 11), non survivors (n =12) were more likely to have a higher serum procalcitonin (p = 0.01), higher serum potassium on day 2 (p = 0.001), day 3 (p = 0.04), day of termination of PD (p = 0.001) and a lower urine output on day 3 of PD (p = 0.03). Prolonged PD was associated with time of PD initiation (p = 0.01), a higher postoperative serum creatinine on day 3 (p = 0.01) of PD initiation as well on the day of PD termination (p = 0.01) and the final outcome in terms of survival (p = 0.02). Factors significantly associated with an early PD initiation were CPB time (p = 0.04), sepsis (p = 0.02) and shorter PD duration (p = 0.003).
Conclusion: PD is very useful mode of renal replacement therapy among pediatric postoperative cardiac surgical patients. The intraoperative and postoperative variables have important association with the time of PD initiation, PD duration and patient survival.
How to cite this article: Sahu MK, Bipin C, Arora Y, Singh SP, Devagouru V, Rajshekar P, et al. Peritoneal Dialysis in Pediatric Postoperative Cardiac Surgical Patients. Indian J Crit Care Med 2019;23(8):371-375.

DOI: 10.5005/jp-journals-10071-23221
PMCID: PMC6709843
PMID: 31485107

132: Saini S, Kaur C, Pal I, Kumar P, Jacob TG, Thakar A, Roy KK, Roy TS. Morphological development of the human cochlear nucleus. Hear Res. 2019 Oct;382:107784. doi: 10.1016/j.heares.2019.107784. Epub 2019 Aug 20. PubMed PMID: 31522073.

Morphological studies in developing brain determine critical periods of proliferation, neurogenesis, gliogenesis, and apoptosis. During these periods both intrinsic and extrinsic pathological factors can hamper development. These time points are not available for the human cochlear nucleus (CN). We have used design-based stereology and determined that 18-22 weeks of gestation (WG) are critical in the development of the human CN. Twenty-three fetuses and seven postnatal brainstems were processed for cresyl violet (CV) staining and immunoexpression of NeuN (neurons), GFAP (astrocytes), Ki-67 (proliferation) and TUNEL (apoptosis) and 3-D reconstruction. The volume of CN, total number of neurons selected profiles and the volume of neurons and their nuclei were estimated. Data were grouped (G) into: G1:18-20 WG, G2: 21-24 WG, G3: 25-28 WG and G4 >29 WG. The dimensions of morphologically identified neurons were also measured. The CN primordium was first identifiable at 10WG. Definitive DCN (Dorsal cochlear nucleus) and VCN (ventral cochlear nucleus) were identifiable at 16 WG. There was a sudden growth spurt in total volume of CN, number of neurons and astrocytes from 18 WG. We also observed an increase in proliferation and apoptosis after 22 WG. The number of neurons identifiable by CV was significantly lower than that by NeuN-immunostaining till 25 WG (p=0.020), after which, both methods were equivalent. Eight morphological types of neurons were identifiable by 26 WG and could be resolved into four clusters by volume and diameter. The CN changed orientation from small, flat and horizontal at 10-16 WG to larger and oblique from 18WG onwards. Prevention of exposure to noxious factors at 18-22 WG may be important in preventing congenital deafness.

DOI: 10.1016/j.heares.2019.107784
PMID: 31522073

133: Sakthivel P, Kumar Irugu DV, Kakkar A, Kaur K, Jain S, Pramanik R, Biswas A. Squamous cell carcinoma as a somatic-type malignancy in an extragonadal immature

teratoma of the sinonasal region. Int J Pediatr Otorhinolaryngol. 2019 Aug 12;126:109639. doi: 10.1016/j.ijporl.2019.109639. [Epub ahead of print] PubMed PMID: 31442873.

Somatic-type malignancy arising in a teratoma of the sinonasal region is extremely unusual, creating a diagnostic dilemma. There are no definite guidelines for management of such cases. A 15-year-old male with a maxillary mass was misdiagnosed as angiomyolipoma, maxillary carcinoma, mucoepidermoid carcinoma, and teratocarcinosarcoma, followed by the final diagnosis of squamous cell carcinoma arising in an immature teratoma. He received neoadjuvant chemotherapy, followed by surgery and chemo-radiotherapy, and is disease-free at 21 months. This case highlights the difficulty faced when diagnosing neoplasms unusual to the head and neck region, particularly on small biopsies, and good outcome following appropriate multimodality management.

DOI: 10.1016/j.ijporl.2019.109639
PMID: 31442873

134: Sarangi J, Kakkar A, Roy D, Thakur R, Singh CA, Sharma MC. Ocular non-teratoid medulloepithelioma with teratoid metastases in ipsilateral intraparotid lymph nodes. Eur J Ophthalmol. 2019 Aug 14:1120672119870079. doi: 10.1177/1120672119870079. [Epub ahead of print] PubMed PMID: 31411051.

PURPOSE: To describe a rare presentation of a case of intraocular non-teratoid medulloepithelioma with teratoid metastases in ipsilateral intraparotid lymph nodes.
CASE DESCRIPTION: A 9-year-old male child with previous history of ciliary body non-teratoid medulloepithelioma presented with a swelling in the right pre-auricular region for 1 month. Magnetic resonance imaging and positron emission tomography-computed tomography showed a right intraparotid mass with enlarged ipsilateral cervical lymph nodes. A core biopsy was taken from the lesion, which on microscopy showed a tumor composed of small round cells arranged in cords, tubules lined by multilayered cells, and in cribriform pattern. These cells were embedded in a hypocellular, loose myxoid matrix. Based on the histopathological characteristics and previous history, a diagnosis of medulloepithelioma metastastic to ipsilateral parotid gland was made. The patient underwent right total conservative parotidectomy and bilateral neck dissection. Histopathological examination revealed metastatic medulloepithelioma in five out of eight intraparotid lymph nodes, with extranodal extension into the adjacent parotid parenchyma. Foci of hyaline cartilage were identified within the tumor, leading to a diagnosis of metastatic teratoid medulloepithelioma.
CONCLUSION: Intraparotid lymph node metastases from intraocular medulloepithelioma is a rare possibility and we recommend that the parotid should be evaluated in cases of intraocular medulloepithelioma at initial presentation as well as during the follow-up period. Also, metastasis should be considered in all pediatric patients with solitary mass lesions showing unconventional histology for a primary parotid neoplasm.

DOI: 10.1177/1120672119870079
PMID: 31411051

135: Saxena A, Relan J, Agarwal R, Awasthy N, Azad S, Chakrabarty M, Dagar KS, Devagourou V, Dharan BS, Gupta SK, Iyer KS, Jayranganath M, Joshi R, Kannan BRJ, Katewa A, Kohli V, Kothari SS, Krishnamoorthy KM, Kulkarni S, Kumar RM, Kumar RK, Maheshwari S, Manohar K, Marwah A, Mishra S, Mohanty SR, Murthy KS, Koneti NR, Suresh PV, Radhakrishnan S, Rajashekar P, Ramakrishnan S, Rao N, Rao SG, Reddy CHM, Sharma R, Shivaprakasha K, Subramanyan R, Suresh Kumar R, Talwar S, Tomar M,

Verma S, Raju V. Guidelines for the management of common congenital heart diseases in India: A consensus statement on indications and timing of intervention. Indian Heart J. 2019 May - Jun;71(3):207-223. doi: 10.1016/j.ihj.2019.07.006. Epub 2019 Aug 12. PubMed PMID: 31543193.

INTRODUCTION: A number of guidelines are available for management of congenital heart diseases from infancy to adult life. However, these guidelines are for patients living in high-income countries. Separate guidelines, applicable to Indian children, are required when recommending an intervention for congenital heart diseases, as often these patients present late in the course of the disease and may have co-existing morbidities and malnutrition.
PROCESS: Guidelines emerged following expert deliberations at the National Consensus Meeting on Management of Congenital Heart Diseases in India, held on the 10th and 11th of August, 2018 at the All India Institute of Medical Sciences.
OBJECTIVES: The aim of the study was to frame evidence-based guidelines for (i) indications and optimal timing of intervention in common congenital heart diseases and (ii) follow-up protocols for patients who have undergone cardiac surgery/catheter interventions for congenital heart diseases.
RECOMMENDATIONS: Evidence-based recommendations are provided for indications and timing of intervention in common congenital heart diseases, including left-to-right shunts, obstructive lesions, and cyanotic congenital heart diseases. In addition, protocols for follow-up of postsurgical patients are also described.

DOI: 10.1016/j.ihj.2019.07.006
PMID: 31543193

136: Saxena R, Dhiman R. Commentary: Abnormal pupillary light reflexes - A sign of diabetic autonomic neuropathy. Indian J Ophthalmol. 2019 Aug;67(8):1319. doi: 10.4103/ijo.IJO_770_19. PubMed PMID: 31332118; PubMed Central PMCID: PMC6677037.

137: Selokar NL, Sharma P, Saini M, Sheoran S, Rajendran R, Kumar D, Sharma RK, Motiani RK, Kumar P, Jerome A, Khanna S, Yadav PS. Successful cloning of a superior buffalo bull. Sci Rep. 2019 Aug 6;9(1):11366. doi: 10.1038/s41598-019-47909-8. PubMed PMID: 31388074; PubMed Central PMCID: PMC6684639.

Somatic cell nuclear transfer (SCNT) technology provides an opportunity to multiply superior animals that could speed up dissemination of favorable genes into the population. In the present study, we attempted to reproduce a superior breeding bull of Murrah buffalo, the best dairy breed of buffalo, using donor cells that were established from tail-skin biopsy and seminal plasma. We studied several parameters such as cell cycle stages, histone modifications (H3K9ac and H3K27me3) and expression of developmental genes in donor cells to determine their SCNT reprogramming potentials. We successfully produced the cloned bull from an embryo that was produced from the skin-derived cell. Growth, blood hematology, plasma biochemistries, and reproductive organs of the produced cloned bull were found normal. Subsequently, the bull was employed for semen production. Semen parameters such as CASA (Computer Assisted Semen Analysis) variables and in vitro fertilizing ability of sperms of the cloned bull were found similar to non-cloned bulls, including the donor bull. At present, we have 12 live healthy progenies that were produced using artificial insemination of frozen semen of the cloned bull, which indicate that the cloned bull is fertile and can be utilized in the buffalo breeding schemes. Taken together, we demonstrate that SCNT can be used to reproduce superior buffalo bulls.

DOI: 10.1038/s41598-019-47909-8
PMCID: PMC6684639
PMID: 31388074

138: Selvan H, Gupta V, Gupta S. Cyclodialysis: an updated approach to surgical strategies. Acta Ophthalmol. 2019 Aug 6. doi: 10.1111/aos.14210. [Epub ahead of print] Review. PubMed PMID: 31386805.

Cyclodialysis is a rare occurrence and is difficult to treat, it being concealed behind the iris. In view of the varied success outcomes of the different available surgical repair techniques, there is at present no clear consensus regarding their management strategies. Through this article, we intend to appraise the established surgical methods, update the novel techniques in vogue, discuss their outcomes and propose a uniform system to codify these corrective techniques. They have been reclassified under the terms 'exocyclopexy', 'endocyclopexy', 'exocyclotamponade' and 'endocyclotamponade' based on the approach used and their mode of action. The ab-interno techniques (endocyclopexy and endocyclotamponade) are easier to perform, offer good success rates and better safety profiles such that they may be considered as a viable alternative to the standard exocyclopexy in either cataractous or pseudophakic and aphakic eyes.

DOI: 10.1111/aos.14210
PMID: 31386805

139: Selvan H, Gupta S, Gupta V. Retained Intraocular Surgical Needle. Ophthalmology. 2019 Aug;126(8):1083. doi: 10.1016/j.ophtha.2019.04.023. PubMed PMID: 31327373.

140: Selvan H, Brar AS, Angmo D. Cogan-Reese syndrome with Iris cyst: A novel presentation. Cont Lens Anterior Eye. 2019 Aug;42(4):467-469. doi: 10.1016/j.clae.2019.04.014. Epub 2019 May 17. PubMed PMID: 31104851.

PURPOSE: To report an atypical case of Cogan-Reese syndrome associated with iris cyst in a young adult male.
METHODS: Slit-lamp biomicroscopic examination, swept-source anterior segment optical coherence tomography (ASOCT) and ultrasound bio-microscopy (UBM) were done to evaluate and characterize the nature of the iris cyst. Gonioscopy, specular microscopy and confocal microscopy were attempted, but unsuccessful due to the large corneal opacity.
RESULTS: On slit-lamp biomicroscopy, a large nasal corneal opacity with overlying band-shaped keratopathy was noted, with history suggestive of a trivial non-penetrating trauma and likely healed corneal ulcer. Through the temporal clear cornea, the iris displayed altered pattern with overlying shiny membrane and multiple, small, discrete, hyperpigmented, irregular nodules suggestive of Cogan-Reese syndrome. On the nasal side, an iris cyst with typical 'stuck-on appearance' onto the endothelium was visible. ASOCT and UBM failed to show any evidence of epithelial downgrowth or Descemet membrane disintegrity, ruling out the possibility of a post-traumatic implantation iris cyst.
CONCLUSION: The occurrence of iris cyst in this case of Cogan-Reese syndrome is unique, and could be related to the disease pathogenesis, or a rare co-incidental finding.

DOI: 10.1016/j.clae.2019.04.014
PMID: 31104851

141: Shah AA, Jain D, Ababneh E, Agaimy A, Hoschar AP, Griffith CC, Magliocca KR, Wenig BM, Rooper LM, Bishop JA. SMARCB1 (INI-1)-Deficient Adenocarcinoma of the Sinonasal Tract: A Potentially Under-Recognized form of Sinonasal Adenocarcinoma with Occasional Yolk Sac Tumor-Like Features. Head Neck Pathol. 2019 Aug 29. doi: 10.1007/s12105-019-01065-7. [Epub ahead of print] PubMed PMID: 31468350.

The classification of sinonasal adenocarcinoma (SNAC) is complex. The high-grade, non-intestinal SNAC group is particularly heterogeneous, with tumors showing widely variable morphology. SMARCB1 (INI-1)-deficient sinonasal carcinoma is a newly described, aggressive tumor that usually resembles sinonasal undifferentiated carcinoma (SNUC) or non-keratinizing squamous cell carcinoma; however, glandular differentiation has been rarely reported and this feature may be under-recognized. We present a dedicated series of 12 SMARCB1-deficient SNACs. All tumors had an oncocytoid/plasmacytoid cytomorphology with variable degrees of glandular differentiation consisting of tubules and cribriform structures with foci of intracellular or intraluminal mucin. Three of 12 tumors exhibited foci of yolk sac tumor-like histologic features. The tumors were uniformly high-grade, with nuclear pleomorphism, elevated mitotic rates and frequent necrosis. By immunohistochemistry, all tumors were entirely SMARCB1-deficient, and 10 of 12 were CK7-positive. Occasional expression of CDX2 (4 of 12), CK20 (3 of 12), and p40 (3 of 10) was seen. Expression of yolk sac markers was variably present in tumors that harbored yolk sac-like areas but also tumors that did not: glypican-3 (10 of 11), SALL4 (6 of 11), HepPar-1 (4 of 11), PLAP (1 of 10), and AFP (1 of 11). SMARCB1-deficient sinonasal carcinoma, particularly the oncocytoid/plasmacytoid form, can demonstrate variable degrees of glandular differentiation. This unexpected morphology combined with variable immunohistochemical results may lead to misdiagnoses of high-grade intestinal or non-intestinal SNAC, myoepithelial carcinoma, or even yolk sac tumor or metastatic hepatocellular carcinoma.

DOI: 10.1007/s12105-019-01065-7
PMID: 31468350

142: Shah VD, Uddaraju M, Singh A, Das RR. Clinical Profile, Etiology, and Outcome of Infantile Ocular Trauma: A Developing Country Perspective. Pediatr Emerg Care. 2019 Aug;35(8):558-560. doi: 10.1097/PEC.0000000000001209. PubMed PMID: 28632575.

OBJECTIVE: The aim of this article was to study the clinical profile, etiology, and outcome of infantile ocular trauma in a developing country setting.
METHODS: A retrospective study on corneal trauma in infants (≤12 months old) was undertaken in a tertiary care hospital during a 2-year period. An analysis of clinical profile, etiology, microbiological profile, clinical course, and outcome was studied.
RESULTS: Seventy-six infants were included. Approximately 69% presented within 24 hours of injury. The common presentations were inability to open the eyelids, redness of eyes, and watering. Self-infliction by child's hand (49%) was found to be the main cause of corneal trauma. Corneal abrasion was seen in 34 cases (45%), isolated epithelial defects were seen in 30%, and infective keratitis was seen in 25%. Infection was found in 14 cases (fungal filaments in 7 and gram-positive cocci in 7). Only 36 infants followed up regularly in the hospital. All the infants following up in the hospital recovered in due course.
CONCLUSIONS: Infantile ocular trauma is a common morbidity that is underreported. Self-infliction by child's hand was found to be the main cause of corneal trauma. Cases presenting early and following up regularly till recovery have a favorable

clinical course with good outcome. A high loss to follow-up indicates that awareness needs to be created among the caregivers.

DOI: 10.1097/PEC.0000000000001209
PMID: 28632575

143: Shaikh N, Kumar V, Venkatesh P. Iris nodules in Fuchs heterochromic iridocyclitis. Indian J Ophthalmol. 2019 Aug;67(8):1339. doi: 10.4103/ijo.IJO_2105_18. PubMed PMID: 31332130; PubMed Central PMCID: PMC6677052.

144: Shakya S, Kumari R, Suroliya V, Tyagi N, Joshi A, Garg A, Singh I, Kalikavil Puthanveedu D, Cherian A, Mukerji M, Srivastava AK, Faruq M. Whole exome and targeted gene sequencing to detect pathogenic recessive variants in early onset cerebellar ataxia. Clin Genet. 2019 Aug 20. doi: 10.1111/cge.13625. [Epub ahead of print] PubMed PMID: 31429931.

Over 100 genetically distinct causal known loci for hereditary ataxia phenotype poses a challenge for diagnostic work-up for ataxia patients in a clinically relevant time and precision. In the present study using next-generation sequencing, we have investigated pathogenic variants in early-onset cerebellar ataxia cases using whole exome sequencing in singleton/family-designed and targeted gene-panel sequencing. A total of 98 index patients were clinically and genetically (whole exome sequencing (WES) in 16 patients and targeted gene panel of 41 ataxia causing genes in 82 patients) evaluated. Four families underwent WES in family based design. Overall, we have identified 24 variants comprising 20 pathogenic and four likely-pathogenic both rare/novel, variations in 21 early onset cerebellar ataxia patients. Among the identified variations, SACS (n = 7) and SETX (n = 6) were frequent, while ATM (n = 2), TTPA (n = 2) and other rare loci were observed. We have prioritized novel pathogenic variants in RARS2 and FA2H loci through family based design in two out of four families.

DOI: 10.1111/cge.13625
PMID: 31429931

145: Sharma A, Jose AP, Pandey N, Vats S, Bagre V, Kumar H, Nair SC, Kumar P, Bhalla S, Padmanabhan S, Poulter N, Prabhakaran D, Roy A. A collaborative model for capacity building of primary care physicians in the management of Hypertension in India. J Hum Hypertens. 2019 Aug;33(8):562-565. doi: 10.1038/s41371-019-0213-z. Epub 2019 Jul 1. PubMed PMID: 31263179.

146: Sharma A, Sharma U, Jagannathan NR, Ray R, Rajeswari MR. Effect of Doxorubicin on Squamous Cell Carcinoma of Skin: Assessment by MRI Relaxometry at 4.7T. Cancer Invest. 2019;37(8):339-354. doi: 10.1080/07357907.2019.1651327. Epub 2019 Aug 14. PubMed PMID: 31412717.

Squamous cell carcinoma (SCC) of skin has no standard treatment regimen, resulting in recurrences/metastasis. Although, doxorubicin (Dox), an anthracycline antibiotic has demonstrated some degree of efficacy. Molecular imaging can help in assessment of treatment response and prognosis of SCCs. MRI data showed that spin-spin relaxation (T2) time was longer (138 ± 2 msec) in Dox treated Test-II and there is no significant difference in spin-lattice relaxation (T1) time with respective controls. These findings further corroborated with the histology, proliferation index, apoptotic index, and HMGA1 protein expression. Thus, MRI may be a useful tool for monitoring treatment response noninvasively for skin tumor prognosis.

DOI: 10.1080/07357907.2019.1651327

PMID: 31412717 [Indexed for MEDLINE]

147: Sharma K, Dhua A, Thomas D, Sankar MJ. Congenital sigmoid mesocolic defect as a cause of neonatal intestinal obstruction. BMJ Case Rep. 2019 Aug 28;12(8). pii: e230253. doi: 10.1136/bcr-2019-230253. PubMed PMID: 31466984.

Internal herniation through congenital sigmoid mesocolic defect as a cause of neonatal intestinal obstruction is rarely reported. Clinical judgement combined with judicious use of investigations and prompt exploration is essential to provide immediate relief of the obstruction and salvage the herniated loop of bowel, which otherwise might lead to morbidity and even death. We present a neonate with internal herniation of the ileum through a congenital mesocolic defect which was diagnosed by a prompt abdominal exploration in view of persistent clinical signs of intestinal obstruction. The relevant literature is also discussed highlighting the rarity of neonatal presentation of sigmoid mesocolic defect.

DOI: 10.1136/bcr-2019-230253
PMID: 31466984

148: Sharma N, Hussain AY, Nagpal R, Rathi A, Maharana PK, Sinha R, Agarwal T, Titiyal JS. Microkeratome-assisted ultrathin Descemet's stripping automated endothelial keratoplasty: A randomized trial comparing single-pass versus double-pass technique. Indian J Ophthalmol. 2019 Aug;67(8):1289-1294. doi: 10.4103/ijo.IJO_1660_18. PubMed PMID: 31332110; PubMed Central PMCID: PMC6677045.

Purpose: To compare the outcomes of two techniques, for preparation of microkeratome-assisted ultrathin grafts for Descemet's stripping automated endothelial keratoplasty (DSAEK).
Methods: The study involved 20 eyes of 20 patients with pseudophakic bullous keratopathy, randomized into two groups. Group 1 eyes underwent microkeratome-assisted DSAEK using the single-pass technique for lenticule preparation, whereas group 2 eyes underwent microkeratome-assisted DSAEK using the double-pass technique. Patients were followed up till 6 months, postoperatively. Best-corrected visual acuity (BCVA) at final follow-up was considered as the primary outcome measure, whereas graft thickness (GT) contrast sensitivity and endothelial cell loss were considered as the secondary outcome measures. A P value of <0.05 was considered as statistically significant.
Results: Baseline characteristics of two groups were comparable. The mean central GT was comparable in both groups at 6 months follow-up [group 1: 98 ± 24.46 μm, group 2: 129 ± 31.46 μm (P = 0.18)]. Both groups fared equally in terms of BCVA (P = 0.33). Contrast sensitivity was significantly better in group 1 eyes (P = 0.045). A statistically significant negative correlation was found between postoperative BCVA and postoperative GT (R = -0.728, P = 0.016). The percentage endothelial cell loss was slightly higher in group 2 eyes, although not statistically significant. Two eyes in group 2 experienced complications during lenticule preparation. None of the eye experienced any complication in the postoperative period.
Conclusion: Both techniques provided grafts with comparable thickness and endothelial cell loss and were associated with comparable BCVA, at final follow-up visit. The contrast sensitivity was, however, better in eyes receiving grafts prepared with the single-pass technique.

DOI: 10.4103/ijo.IJO_1660_18
PMCID: PMC6677045
PMID: 31332110

149: Sharma N, Singhal D, Maharana PK, Vajpayee RB. Tuck-In Tenon Patch Graft in Corneal Perforation. Cornea. 2019 Aug;38(8):951-954. doi: 10.1097/ICO.0000000000001955. PubMed PMID: 31276458.

PURPOSE: To describe the outcomes of tuck-in tenon patch graft (TPG) in the management of corneal perforation up to 5-mm size.
METHODS: Thirty-one cases of sterile corneal perforation (3-5 mm) underwent autologous TPG. The technique included, freshening of the edges, measuring the size of defect, creating a 360-degree stromal pocket around the perforation margin, harvesting the tenon graft followed by tucking into the stromal pocket, and application of cyanoacrylate glue or suturing the graft using 10-0 monofilament nylon suture. The main outcome measure was rate of healing (percentage of cases healed).
RESULTS: The mean age was 52.3 ± 8.9 years with 22 male and 9 female patients. The various etiologies of corneal perforation included trauma (n = 10), neurotrophic keratitis (n = 11), and peripheral ulcerative keratitis (n = 10). The mean size of corneal perforation was 4.2 ± 0.6 mm (range 3-5 mm). The mean duration of epithelial healing was 25.7 ± 6.7 days. Best-corrected visual acuity improved from 1.8 ± 0.4 to 1.2 ± 0.4 logarithm of the minimum angle of resolution units at 4 weeks after surgery ($P \leq 0.01$). Twenty-seven (87.1%) cases healed with formation of a leucomatous scar at 16.9 ± 2.7 weeks, whereas 4 cases had a flat anterior chamber. In three-fourths of the cases, a corneal graft was performed. In one case, graft resuturing was performed for post-op aqueous leak, which healed with the formation of a corneo-iridic scar.
CONCLUSIONS: TPG is a safe, simple, inexpensive, and an effective technique for the management of corneal perforations. The advantages include the autologous nature of the graft, cost effectiveness, and easy availability.

DOI: 10.1097/ICO.0000000000001955
PMID: 31276458 [Indexed for MEDLINE]

150: Sharma N, Venugopal R, Singhal D, Maharana PK, Sangwan S, Satpathy G. Microbial Keratitis in Stevens-Johnson Syndrome: A Prospective Study. Cornea. 2019 Aug;38(8):938-942. doi: 10.1097/ICO.0000000000001960. PubMed PMID: 30998617.

PURPOSE: To evaluate the microbiological profile and outcome in cases with infective keratitis in Stevens-Johnson syndrome (SJS).
METHODS: Eighty-three eyes of 68 patients with SJS presenting with microbial keratitis were recruited and managed with standard antimicrobial therapy.
RESULTS: Microbial keratitis developed in 34% of patients with SJS (83 eyes, 68 patients) over a period of 5 years. Four eyes (4.8%) had a history of concurrent topical steroid use at the onset of keratitis. Mean baseline best-corrected visual acuity was 1.8 ± 0.9 logMAR units. The site of corneal ulceration was central in 52 eyes (62.6%), paracentral in 17 eyes (20.5%), and peripheral in 14 eyes (16.8%). The mean ulcer area was 3.9 ± 2.7 mm. Approximately 15 of 24 (62.5%) culture-positive eyes had bacterial infection, most of which (80%) were caused by Gram-positive bacteria. Polymicrobial infection was noted in 7 of 24 eyes (29.1%). Although 57 of 83 (68.6%) eyes healed with medical therapy, 26 of 83 (31.3%) eyes had corneal perforation and were managed with cyanoacrylate glue application (30.7%) or therapeutic keratoplasty (69.3%). Systemic infection as an inciting factor of SJS and an early presentation for keratitis were the major risk factors associated with corneal perforation. Large mean ulcer size, paracentral ulcers, and punctal involvement were associated with a good visual outcome.
CONCLUSIONS: Infective keratitis in SJS is common, and unlike routine cases, surgical intervention is often required. However, the antibiotic sensitivity pattern suggests that resistance is not that high.

DOI: 10.1097/ICO.0000000000001960
PMID: 30998617 [Indexed for MEDLINE]

151: Sharma R. Continuous Metabolic Syndrome Score in Children: How Useful is it? Indian J Pediatr. 2019 Oct;86(10):881-882. doi: 10.1007/s12098-019-03047-7. Epub 2019 Aug 3. PubMed PMID: 31378001.

152: Sharma R, Goda R, Borkar SA, Katiyar V, Agarwal S, Kumar A, Mohapatra S, Kapil A, Suri A, Kale SS. Outcome following postneurosurgical Acinetobacter meningitis: an institutional experience of 72 cases. Neurosurg Focus. 2019 Aug 1;47(2):E8. doi: 10.3171/2019.5.FOCUS19278. PubMed PMID: 31370029.

OBJECTIVE: The authors aimed to evaluate the antimicrobial susceptibility pattern of Acinetobacter isolates responsible for nosocomial meningitis/ventriculitis in the neurosurgical ICU. The authors also sought to identify the risk factors for mortality following Acinetobacter meningitis/ventriculitis.
METHODS: This was a retrospective study of 72 patients admitted to the neurosurgical ICU between January 2014 and December 2018 with clinical and microbiological diagnosis of nosocomial postneurosurgical Acinetobacter baumanii meningitis/ventriculitis. Electronic medical data on clinical characteristics, underlying pathology, CSF cytology, antibiotic susceptibilities, and mortality were recorded. To evaluate the outcome following nosocomial postneurosurgical Acinetobacter meningitis/ventriculitis, patients were followed up until discharge or death in the hospital. Kaplan-Meier survival analysis and multivariable Cox proportional hazards models were used to compute factors affecting survival.
RESULTS: The study population was divided into two groups depending on the final outcome of whether the patient died or survived. Forty-three patients (59.7%) were included in the survivor group and 29 patients (40.3%) were included in the nonsurvivor group. Total in-hospital mortality due to Acinetobacter meningitis/ventriculitis was 40.3% (29 cases), with a 14-day mortality of 15.3% and a 30-day mortality of 25%. The 43 (59.7%) patients who survived had a mean length of hospital stay of 44 ± 4 days with a median Glasgow Outcome Scale-Extended score at discharge of 6. On univariate analysis, age > 40 years ($p = 0.078$), admission Glasgow Coma Scale (GCS) score ≤ 8 ($p = 0.003$), presence of septic shock ($p = 0.011$), presence of external ventricular drain (EVD) ($p = 0.03$), CSF white blood cell (WBC) count > 200 cells/mm3 ($p = 0.084$), and comorbidities (diabetes, $p = 0.036$; hypertension, $p = 0.01$) were associated with poor outcome. Carbapenem resistance was not a risk factor for mortality. According to a multivariable Cox proportional hazards model, age cutoff of 40 years ($p = 0.016$, HR 3.21), GCS score cutoff of 8 ($p = 0.006$, HR 0.29), CSF WBC count > 200 cells/mm3 ($p = 0.01$, HR 2.76), presence of EVD ($p = 0.001$, HR 5.42), and comorbidities ($p = 0.017$, HR 2.8) were found to be significant risk factors for mortality.
CONCLUSIONS: This study is the largest case series reported to date of postneurosurgical Acinetobacter meningitis/ventriculitis. In-hospital mortality due to Acinetobacter meningitis/ventriculitis was high. Age older than 40 years, GCS score less than 8, presence of EVD, raised CSF WBC count, and presence of comorbidities were risk factors for mortality.

DOI: 10.3171/2019.5.FOCUS19278
PMID: 31370029

153: Sharma R, Borkar SA, Phalak M, Joseph SL, Kale SS. Cervical alignment following laminoplasty for cervical spondylotic myelopathy. Surg Neurol Int. 2019 Aug 2;10:156. doi: 10.25259/SNI_346_2019. eCollection 2019. PubMed PMID: 31528491; PubMed Central PMCID: PMC6744730.

Background: Laminoplasty can result in the loss of cervical lordosis (LOCL) or the development of kyphosis after surgery. Here, we evaluated the clinical and

radiological parameters involved in predicting the postoperative LOCL following laminoplasty in patients with cervical spondylotic myelopathy (CSM) and ossification of the posterior longitudinal ligament (OPLL).
Methods: For 50 patients with CSM and 35 with OPLL undergoing laminoplasty, preoperative and 1-year postoperative X-rays were obtained to determine the incidence and risk factors contributing to postoperative LOCL. The patients were divided into two groups depending on whether the preoperative T1 slope was above or below the median preoperative T1S (26°); Group A - high T1 slope group (n = 40) and Group B - low T1 slope group (n = 45).
Results: Following laminoplasty, Group A patients had significantly higher preoperative lordosis (C2-C7 Cobb's angle) (P = 0.001) and significantly higher LOCL (P = 0.02) versus Group B patients with low T1 slopes. The preoperative T1 slope was also found to be significantly correlated with the preoperative C2-C7 Cobb's angles (R = 0.619, P = 0.001), LOCL (R = 0.487, P = 0.001), and preoperative C2-C7 sagittal vertical axis (R = 0.480, P = 0.001). Utilizing multivariate analysis and a generalized linear model, the preoperative T1 slope significantly impacted the Oswestry disability index (ODI) index (P = 0.002) and frequency of LOCL (P = 0.001) following laminoplasty.
Conclusion: The preoperative T1 slope is a significant predictor of the LOCL and change in ODI following laminoplasty for CSM/OPLL utilizing a cutoff value of 29.5°.

DOI: 10.25259/SNI_346_2019
PMCID: PMC6744730
PMID: 31528491

154: Sharma S, Ganga K. Reply to: "Re: Establishing IR in Emerging Countries-A Skill Development Initiative". J Vasc Interv Radiol. 2019 Aug;30(8):1314. doi: 10.1016/j.jvir.2019.05.025. PubMed PMID: 31349983.

155: Sharma V, Rani K, Roychoudhury A, Chawla A, Nikolajeff F, Kumar S. Novel Insights into Regulation of Human Teeth Biomineralization: Deciphering the Role of Post-Translational Modifications in a Tooth Protein Extract. Int J Mol Sci. 2019 Aug 19;20(16). pii: E4035. doi: 10.3390/ijms20164035. PubMed PMID: 31430851; PubMed Central PMCID: PMC6720696.

The importance of whole protein extracts from different types of human teeth in modulating the process of teeth biomineralization is reported. There are two crucial features in protein molecules that result in efficient teeth biomineralization. Firstly, the unique secondary structure characteristics within these proteins i.e. the exclusive presence of a large amount of intrinsic disorder and secondly, the presence of post-translational modifications (PTM) like phosphorylation and glycosylation within these protein molecules. The present study accesses the structural implications of PTMs in the tooth proteins through scanning electron microscopy and transmission electron microscopy. The deglycosylated/dephosphorylated protein extracts failed to form higher-order mineralization assemblies. Furthermore, through nanoparticle tracking analysis (NTA) we have shown that dephosphorylation and deglycosylation significantly impact the biomineralization abilities of the protein extract and resulted in smaller sized clusters. Hence, we propose these post-translational modifications are indispensable for the process of teeth biomineralization. In addition to basic science, this study would be worth consideration while designing of biomimetics architecture for an efficient peptide-based teeth remineralization strategy.

DOI: 10.3390/ijms20164035
PMCID: PMC6720696
PMID: 31430851

156: Shaw M, Sharma A, Rajagopal R, Kumar S. Isolated right subclavian artery with atrioventricular septal defect: a rare association. BMJ Case Rep. 2019 Aug 30;12(8). pii: e231790. doi: 10.1136/bcr-2019-231790. PubMed PMID: 31471369.

157: 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;13(4):615-620. doi: 10.31616/asj.2018.0217. Print 2019 Aug. PubMed PMID: 30909676; PubMed Central PMCID: PMC6680043.

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
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PMID: 30909676

158: Singh P, Arora A, Strand TA, Leffler DA, MÃ¤ki M, Kelly CP, Ahuja V, Makharia
GK. Diagnostic Accuracy of Point of Care Tests for Diagnosing Celiac Disease: A Systematic Review and Meta-Analysis. J Clin Gastroenterol. 2019 Aug;53(7):535-542. doi: 10.1097/MCG.0000000000001081. PubMed PMID: 29912751.

GOALS: To perform a systematic review and meta-analysis to estimate the overall diagnostic accuracy of point of care tests (POCTs) for diagnosing celiac disease (CD).
BACKGROUND: Recently, POCTs for CD have been developed and are commercially available. Studies have reported significant variability in their sensitivity (70% to 100%) and specificity (85% to 100%).
STUDY: We searched MEDLINE, EMBASE databases, and the Cochrane library through June 2017. Positive reference test was defined as villous atrophy along with positive celiac-specific serology and/or clinical improvement after gluten-free diet. Normal duodenal biopsy was defined as negative reference test. Bivariate random-effect model was used to present the summary estimates of sensitivities and specificities along with 95% confidence regions We assessed methodologic quality using the quality assessment of diagnostic accuracy studies-2 tool.

RESULTS: The pooled sensitivity and specificity of all POCTs (based on tTG or DGP or tTG+Anti-gliadin antibodies) for diagnosing CD were 94.0% [95% confidence interval (CI), 89.9-96.5] and 94.4% (95% CI, 90.9-96.5), respectively. The pooled positive and negative likelihood ratios for POCTs were 16.7 and 0.06, respectively. The pooled sensitivity and specificity for IgA-tTG-based POCTs were 90.5% (95% CI, 82.3-95.1) and 94.8% (95% CI, 92.5-96.4), respectively. CONCLUSIONS: The pooled sensitivity and specificity of POCTs in diagnosing CD are high. POCTs may be used to screen for CD, especially in areas with limited access to laboratory-based testing. Further research assessing the diagnostic accuracy of individual POCTs and comparing it with other available POCTs is needed.

DOI: 10.1097/MCG.0000000000001081
PMID: 29912751

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Pseudomonas aeruginosa is an opportunistic pathogen that utilizes the quorum-sensing (QS) process to regulate the production of different virulence factors and biofilm. N-3-oxo-dodecanoyl-L-homoserine lactone (C12) is a key QS molecule of P. aeruginosa which interacts with the mammalian immune cells and modulates their function. Here, we investigated the molecular mechanism of C12-induced apoptosis in neutrophils. Our data show that C12 causes apoptosis in neutrophils through an elevation in cytosolic and mitochondrial Ca2+ levels. Besides, C12 induces phosphatidylserine (PS) exposure, mitochondrial membrane potential (MMP) depolarization, mitochondrial permeability transition pore (MPTP) formation and mitochondrial reactive oxygen species (mROS) generation. C12-induced rise in intracellular Ca2+ level is majorly contributed by endoplasmic reticulum store through the activation of inositol 1, 4, 5-triphosphate receptor. Intracellular calcium chelation inhibited C12-induced mitochondrial dysfunction and apoptosis. Further, inhibition of mitochondrial Ca2+ uniporter by ruthenium red or Ru360 abrogated C12-induced mitochondrial Ca2+ uptake, MMP loss, MPTP opening, mROS production, and PS exposure. These mechanistic insights are expected to provide a better understanding of the role of C12 in P. aeruginosa pathogenesis.

DOI: 10.1007/s00430-019-00631-8
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PURPOSE: New strategies to restore sodium iodide symporter (NIS) expression and function in radioiodine therapy-refractive anaplastic thyroid cancers (ATCs) are urgently required. Recently, we reported the regulatory role of estrogen-related receptor gamma (ERRγ) in ATC cell NIS function. Herein, we identified DN200434 as a highly potent (functional IC50 = 0.006 μmol/L), selective, and orally available

ERRγ inverse agonist for NIS enhancement in ATC.
EXPERIMENTAL DESIGN: We sought to identify better ERRγ-targeting ligands and explored the crystal structure of ERRγ in complex with DN200434. After treating ATC cells with DN200434, the change in iodide-handling gene expression, as well as radioiodine avidity was examined. ATC tumor-bearing mice were orally administered with DN200434, followed by 124I-positron emission tomography/CT (PET/CT). For radioiodine therapy, ATC tumor-bearing mice treated with DN200434 were administered 131I (beta ray-emitting therapeutic radioiodine) and then bioluminescent imaging was performed to monitor the therapeutic effects. Histologic analysis was performed to evaluate ERRγ expression status in normal tissue and ATC tissue, respectively.
RESULTS: DN200434-ERRγ complex crystallographic studies revealed that DN200434 binds to key ERRγ binding pocket residues through four-way interactions. DN200434 effectively upregulated iodide-handling genes and restored radioiodine avidity in ATC tumor lesions, as confirmed by 124I-PET/CT. DN200434 enhanced ATC tumor radioiodine therapy susceptibility, markedly inhibiting tumor growth. Histologic findings of patients with ATC showed higher ERRγ expression in tumors than in normal tissue, supporting ERRγ as a therapeutic target for ATC.
CONCLUSIONS: DN200434 shows potential clinical applicability for diagnosis and treatment of ATC or other poorly differentiated thyroid cancers.

DOI: 10.1158/1078-0432.CCR-18-3007
PMID: 31010838

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Aedes albopictus (Skuse 1894) is prevalent in the urban/peri-urban Port Blair, posing a public health threat, during past outbreaks of chikungunya (2006) and dengue (2010). Despite its vector potential, information on the biology is scanty. Therefore, impact of temperature on survival of immature stages, under laboratory conditions, was studied on F1 population of Andamans. Ae. albopictus larvae were exposed to static temperatures viz. 37°C, 39°C, 41°C, 43°C and 45°C, and the lethal time to cause 50% (LT50) and 90% mortality (LT90) was computed. To assess adaptive thermotolerance, larvae exposed (37°C and 39°C) were re-exposed to higher temperatures (43°C and 45°C). All larvae survived at 37°C and 39°C for

the entire exposure period of 420 min, while variable mortality was observed at 41°C, 43°C and 45°C. Larvae re-exposed to 43°C and 45°C showed an increase in thermotolerance with respect to non-adapted larvae. The results are discussed in the context of survival, development and distribution.

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PMID: 30977000

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Traumatic dental injuries (TDI) have emerged as a significant global public health concern. One major problem which is developing and yet unreported is the incidence of traumatic dental injuries and soft tissue facial trauma due to the inadvertent falling of smart phones on to the face during their use in rest time. This is related to the weight of the smart phones and their excessive use in all parts of the world. This paper aims to highlight this phenomenon as an emerging etiological factor for dental and facial injuries in children. This article is protected by copyright. All rights reserved.

DOI: 10.1111/edt.12507
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Esthesioneuroblastoma is a rare neoplasm arising from the neural crest cells of olfactory epithelium mostly in the nasal vault. We describe the Ga DOTANOC PET/CT findings of a 44-year-old woman who was operated for right nasal mass diagnosed as paraganglioma in the past and then develop a mass in the right nasal cavity after 2 years which upon surgery diagnosed to be esthesioneuroblastoma on histopathology.

DOI: 10.1097/RLU.0000000000002644
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Deregulated mitochondrial metabolism and biogenesis have been studied in acute myeloid leukemia (AML); yet, the relevance of mitochondrial-encoded gene expression on AML outcomes is unknown. This study was conducted to assess clinical significance of expression of mitochondrial-encoded genes, namely ND3, SDHB, Cytochrome b, Cytochrome C, and ATP6, in pediatric AML. Pediatric AML patients from July 2013 to June 2016 were enrolled in this prospective study. Relative genes expression was determined using real-time PCR, and expressed as fold change. 123 AML patients were enrolled, median age 10 (range 0.7-18 years). ND3 gene expression was significantly increased in poor-risk cytogenetics (P=0.03). In univariate analysis, high ND3 and ATP6 gene expression was significantly associated with inferior EFS (P=0.01 and P=0.04, respectively) and OS (P=0.02 and P=0.01, respectively), whereas, in multivariate analysis, ND3 gene expression emerged as the only independent prognostic factor for EFS and OS (P=0.04 and P=0.03). ND3 gene expression is a significant predictor of EFS and OS in pediatric AML, and should be evaluated as a potential biomarker.

DOI: 10.1007/s12185-019-02666-2
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OBJECTIVE: Prognostic scores help in predicting mortality and functional outcome post intracerebral hemorrhage (ICH). We aimed to validate the ICH and ICH-GS scores in a cohort of Indian patients with ICH and observe the impact of any surgical intervention on prognostication.
METHODS: This was an ambispective observational study of primary ICH cases enrolled between January 2014 and April 2018. Observed mortality on ICH and ICH GS scores for the entire cohort and individually for the medically and surgically managed patients was compared to the published mortality in the original derivation cohorts.
RESULTS: 617 patients, (464 retrospective and 153 prospective) of ICH were included. In hospital mortality and 30-day mortality was 28.7% and 28.5% respectively. There was a significant association of increasing mortality with increasing ICH and ICH-GS scores. Area under receiver operating characteristic curve for 30-day mortality was 75.9% and 74.1% for ICH and ICH-GS scores respectively. However, mortality observed at individual scores was significantly less than previously reported. Among the surgically intervened patients (n=265), both the expected mortality at baseline and discriminative ability of ICH and ICH-GS scores for 30-day mortality was significantly reduced following

surgical intervention (ROC in surgically intervened groups: 59.9 (52.6-67.2) and 63(56-70) for ICH and ICH-GS scores respectively).
CONCLUSIONS: Although ICH and ICH-GS scores are valid in Indian population, mortality at individual scores is lower than previously reported. Mortality prediction using ICH and ICH GS scores is significantly modified by surgical interventions. Thus, newer prognostic tools which incorporate surgical intervention need to be developed and validated in future.

DOI: 10.1016/j.jstrokecerebrovasdis.2019.05.003
PMID: 31151837 [Indexed for MEDLINE]

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There are limited treatment options for successful management of tinnitus, which is highly prevalent worldwide. The pathogenetic role of auditory cortex activation changes in tinnitus has been reported by various functional studies that suggest that the emerging neuromodulation techniques may pave way toward better treatment response. The current case report depicts the use of functional near-infrared spectroscopy (fNIRS) based on the assessment of improvement in auditory cortex functioning in chronic tinnitus by transcranial direct current stimulation (tDCS).

DOI: 10.5152/iao.2019.6022
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PMID: 31347512

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OBJECTIVE. Several clinical studies have shown the efficacy of 177Lu-labeled prostate-specific membrane antigen (PSMA) radioligand therapy (RLT) for metastatic castration-resistant prostate cancer (mCRPC). The purpose of this article is to present results of a systematic review and meta-analysis aimed at compiling and outlining efficacy and safety data on 177Lu-PSMA RLT for mCRPC across all studies published to date. CONCLUSION. The results of the systematic review and meta-analysis suggest that 177Lu-PSMA RLT is an effective treatment of advanced-stage mCRPC that is refractory to standard therapeutic options and that it has a low toxicity profile. High-level evidence from randomized control trials is crucial for confirming the effectiveness of 177Lu-PSMA RLT and for instituting this therapy in the routine clinical care of patients with mCRPC.

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PREDICT/Sunnybrook CTA Study Group. New and expanding ventricular hemorrhage predicts poor outcome in acute intracerebral hemorrhage. Neurology. 2019 Aug 27;93(9):e879-e888. doi: 10.1212/WNL.0000000000008007. Epub 2019 Aug 1. PubMed PMID: 31371565.

OBJECTIVE: To describe the relationship between intraventricular hemorrhage (IVH) expansion and long-term outcome and to use this relationship to select and validate clinically relevant thresholds of IVH expansion in 2 separate intracerebral hemorrhage (ICH) populations.
METHODS: We used fractional polynomial analysis to test linear and nonlinear models of 24-hour IVH volume change and clinical outcome with data from the Predicting Hematoma Growth and Outcome in Intracerebral Hemorrhage Using Contrast Bolus CT (PREDICT)-ICH study. The primary outcome was poor clinical outcome (modified Rankin Scale [mRS] score 4-6) at 90 days. We derived dichotomous thresholds from the selected model and calculated diagnostic accuracy measures. We validated all thresholds in an independent single-center ICH cohort (Massachusetts General Hospital).
RESULTS: Of the 256 patients from PREDICT, 127 (49.6%) had an mRS score of 4 to 6. Twenty-four-hour IVH volume change and poor outcome fit a nonlinear relationship, in which minimal increases in IVH were associated with a high probability of an mRS score of 4 to 6. IVH expansion ≥1 mL (n = 53, sensitivity 33%, specificity 92%, adjusted odds ratio [aOR] 2.68, 95% confidence interval [CI] 1.11-6.46) and development of any new IVH (n = 74, sensitivity 43%, specificity 85%, aOR 2.53, 95% CI 1.22-5.26) strongly predicted poor outcome at 90 days. The dichotomous thresholds reproduced well in a validation cohort of 169 patients.
CONCLUSION: IVH expansion as small as 1 mL or any new IVH is strongly predictive of poor outcome. These findings may assist clinicians with bedside prognostication and could be incorporated into definitions of hematoma expansion to inform future ICH treatment trials.

DOI: 10.1212/WNL.0000000000008007
PMID: 31371565

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BACKGROUND AND PURPOSE: The computed tomography angiography (CTA) spot sign is widely used to assess the risk of hematoma expansion following acute intracerebral hemorrhage (ICH). However, not all patients can receive intravenous contrast nor are all hospital systems equipped with this technology. We aimed to independently validate the Hematoma Expansion Prediction (HEP) Score, an 18-point non-contrast prediction scale, in an external cohort and compare its diagnostic capability to the CTA spot sign.
METHODS: We performed a retrospective analysis of the predicting hematoma growth and outcome in intracerebral hemorrhage using contrast bolus CT (PREDICT) Cohort Study. Primary outcome was significant hematoma expansion (≥6 mL or ≥33%). We generated a receiver operating characteristic (ROC) curve comparing the HEP score to significant expansion. We calculated sensitivity, specificity, positive and negative predictive values (PPV/NPV) for each score point. We determined independent predictors of significant hematoma expansion via logistic regression.
RESULTS: A total of 292 patients were included in primary analysis. Hematoma

growth of ≥6 mL or ≥33% occurred in 94 patients (32%). The HEP score was associated with significant expansion (adjusted odds ratio [aOR] 1.14, 95% confidence interval [CI] 1.01-1.30). ROC curves comparing HEP score to significant expansion had an area under the curve of 0.64 (95% CI 0.57-0.71). Youden's method showed an optimum score of 4. HEP Scores≥4 (n=100, sensitivity 49%, specificity 73%, PPV 46%, NPV 75%, aOR 1.99, 95% CI 1.09-3.64) accurately predicted significant expansion. PPV increased with higher HEP scores, but at the cost of lower sensitivity. The diagnostic characteristics of the spot sign (n=82, Sensitivity 49%, Specificity 81%, PPV 55%, NPV 76%, aOR 2.95, 95% CI 1.61-5.42) were similar to HEP scores≥4.
CONCLUSION: The HEP score is predictive of significant expansion (≥6 mL or ≥33%) and is comparable to the spot sign in diagnostic accuracy. Non-contrast prediction tools may have a potential role in the recruitment of patients in future intracerebral hemorrhage trials.

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PMID: 31123995