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AIIMS
New Delhi

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

1: Abraham G, Agarwal SK, Gowrishankar S, Vijayan M. Chronic Kidney Disease of Unknown Etiology: Hotspots in India and Other Asian Countries. *Semin Nephrol.* 2019 May;39(3):272-277. doi: 10.1016/j.semnephrol.2019.02.005. Review. PubMed PMID: 31054626.

There has been increased reporting of chronic kidney disease of unknown etiology (CKDu) in certain agricultural communities in the world. In India, an increased prevalence of CKDu has been observed in the states of Andhra Pradesh, Odisha, Goa, and Maharashtra. Although no single causative factor has been proved, several have been proposed: water-borne agrochemicals, silica, chemical flavors in betel nuts, and pesticides. The renal biopsy findings have been similar to those seen in Sri Lanka and Mesoamerican nephropathy in that the predominant findings have been tubular atrophy and interstitial fibrosis with little or no involvement of the glomerular and vascular compartments. Because most of the affected communities belong to the lower socioeconomic group including farmers, a multipronged approach is required for addressing this CKDu epidemic with an emphasis on awareness, prevention, screening, surveillance, provision of renal replacement therapy, increased government spending on health care, and systematic research.

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DOI: 10.1016/j.semnephrol.2019.02.005
PMID: 31054626

2: Acharya AM, Ravikiran N, Jayakrishnan KN, Bhat AK. The role of pedicled abdominal flaps in hand and forearm composite tissue injuries: Results of technical refinements for safe harvest. *J Orthop.* 2019 May 3;16(4):369-376. doi: 10.1016/j.jor.2019.04.008. eCollection 2019 Jul-Aug. PubMed PMID: 31193279; PubMed Central PMCID: PMC6525282.

We evaluated the outcome of new technical refinements in abdominal flap coverage of major defects in upper limb for its reliability and safety. 68 patients were assessed for indications, additional procedures, complications and DASH questionnaire evaluation at the end of a year. The mean size of flap was 56 cm² (range 6-250 cm²). Median DASH score was 11.5 (range: 0-63). Hand stiffness was observed in 39% of patients. However, this was absent in whom prophylactic pinning of metacarpophalangeal joints were done in James position. Abdominal flaps give satisfactory results in hand injuries. Competent hand therapy program is essential to get best results.

DOI: 10.1016/j.jor.2019.04.008
PMCID: PMC6525282 [Available on 2020-07-01]
PMID: 31193279

3: Agarwal A, Parekh N, Panner Selvam MK, Henkel R, Shah R, Homa ST, Ramasamy R, Ko E, Tremellen K, Esteves S, Majzoub A, Alvarez JG, Gardner DK, Jayasena CN, Ramsay JW, Cho CL, Saleh R, Sakkas D, Hotaling JM, Lundy SD, Vij S, Marmar J, Gosalvez J, Sabanegh E, Park HJ, Zini A, Kavoussi P, Micic S, Smith R, Busetto GM, Bakircioğlu ME, Haidl G, Balercia G, Puchalt NG, Ben-Khalifa M, Tadros N, Kirkman-Browne J, Moskovtsev S, Huang X, Borges E, Franken D, Bar-Chama N, Morimoto Y, Tomita K, Srini VS, Ombelet W, Baldi E, Muratori M, Yumura Y, La Vignera S, Kosgi R, Martinez MP, Evenson DP, Zylbersztejn DS, Roque M, Cocuzza M, Vieira M, Ben-Meir A, Orvieto R, Levitas E, Wisner A, Arafa M, Malhotra V, Parekattil SJ, Elbardisi H, Carvalho L, Dada R, Sifer C, Talwar P, Gudeloglu A, Mahmoud AMA, Terras K, Yazbeck C, Nebojsa B, Durairajanayagam D, Mounir A, Kahn LG, Baskaran S, Pai RD, Paoli D, Leisegang K, Moein MR, Malik S, Yaman O, Samanta L, Bayane F, Jindal SK, Kendirci M, Altay B, Perovic D, Harlev A. Male Oxidative Stress Infertility (MOSI): Proposed Terminology and Clinical Practice Guidelines for Management of Idiopathic Male Infertility. *World J Mens Health.* 2019 May 8. doi: 10.5534/wjmh.190055. [Epub ahead of print] Review. PubMed PMID: 31081299.

Despite advances in the field of male reproductive health, idiopathic male infertility, in which a man has altered semen characteristics without an identifiable cause and there is no female factor infertility, remains a challenging condition to diagnose and manage. Increasing evidence suggests that oxidative stress (OS) plays an independent role in the etiology of male infertility, with 30% to 80% of infertile men having elevated seminal reactive oxygen species levels. OS can negatively affect fertility via a number of pathways, including interference with capacitation and possible damage to sperm membrane and DNA, which may impair the sperm's potential to fertilize an egg and develop into a healthy embryo. Adequate evaluation of male reproductive potential should therefore include an assessment of sperm OS. We propose the term Male Oxidative Stress Infertility, or MOSI, as a novel descriptor for infertile men with abnormal semen characteristics and OS, including many patients who were previously classified as having idiopathic male infertility. Oxidation-reduction potential (ORP) can be a useful clinical biomarker for the classification of MOSI, as it takes into account the levels of both oxidants and reductants (antioxidants). Current treatment protocols for OS, including the use of antioxidants, are not evidence-based and have the potential for complications and increased healthcare-related expenditures. Utilizing an easy, reproducible, and cost-effective test to measure ORP may provide a more targeted, reliable approach for administering antioxidant therapy while minimizing the risk of antioxidant overdose. With the increasing awareness and understanding of MOSI as a distinct male infertility diagnosis, future research endeavors can facilitate the development of evidence-based treatments that target its underlying cause.

Copyright © 2019 Korean Society for Sexual Medicine and Andrology.

DOI: 10.5534/wjmh.190055

PMID: 31081299

4: Agarwal N, Chandrappa H, Varshney G, Borkar SA. Is conservative treatment really beneficial in elderly patients with unstable odontoid fractures? *Spine (Phila Pa 1976)*. 2019 May 9. doi: 10.1097/BRS.0000000000003105. [Epub ahead of print] PubMed PMID: 31135629.

5: Aggarwal R, Soni KD, Goyal K, Singh GP, Sokhal N, Trikha A. Does Real Time Ultrasonography Confer Any Benefit During Bronchoscopy Guided Percutaneous Tracheostomy: A Preliminary, Randomized Controlled Trial. *Indian J Crit Care Med*. 2019 May;23(5):236-238. doi: 10.5005/jp-journals-10071-23169. PubMed PMID: 31160843; PubMed Central PMCID: PMC6535982.

Background: There are studies comparing USG guided percutaneous dilatational tracheostomy (PDT) with bronchoscopy guided PDT. We have compared USG guided PDT to conventional landmark guided PDT using bronchoscopy in both the groups.

Objective: The primary outcome was the time of procedure and the secondary outcome was incidence of complications in USG guided PDT in comparison to the conventional PDT.

Materials and Methods: Seventy adult patients were randomly allocated in two groups, i.e., conventional landmark percutaneous dilatational tracheostomy (PDT) and ultrasonography (USG) guided PDT. Demographic data, injury severity score, time taken for the procedure, attempts of tracheal puncture, major and minor complications, and outcome were compared.

Results: The median time taken for the procedure was 12 minutes [min., max.; 8, 20] in conventional group 1 and 16 minutes [9, 24] in group 2 (USG guided) which was statistically significant. Minor bleeding was seen in 7 (20%) patients in group 1 and only in 4 patients (11.5%) in group 2. The rate of other complications and the long term outcome were similar in both the groups.

Conclusion: The use of real time USG during PDT may confer advantage over conventional PDT when using bronchoscopy in terms of decreasing the incidence of minor bleeding but duration of the procedure gets prolonged.

How to cite this article: Aggarwal R, Soni KD, Goyal K, Singh GP, Sokhal N, Trikha A. Does Real Time Ultrasonography Confer Any Benefit During Bronchoscopy Guided Percutaneous Tracheostomy: A Preliminary, Randomized Controlled Trial.

Indian J Crit Care Med 2019;23(5):236-238.

DOI: 10.5005/jp-journals-10071-23169

PMCID: PMC6535982

PMID: 31160843

6: Anand S, Jain V, Kandasamy D, Agarwala S. Traumatic perforation of a juxtapancreatic enteric duplication cyst: a paediatric emergency. *BMJ Case Rep.* 2019 May 24;12(5). pii: e227984. doi: 10.1136/bcr-2018-227984. PubMed PMID: 31129635.

This report outlines a rare case of juxtapancreatic duplication cyst in a 5-month-old infant who presented with peritonitis, secondary to traumatic perforation of the cyst. We aim to highlight the role of selective mucosectomy in these cases.

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PMID: 31129635

7: Arumugam V, Saha A, Kaur M, Deepthi B, Basak T, Sengupta S, Bhatt A, Batra VV, Upadhyay AD. Plasma Free Homocysteine Levels in Children with Idiopathic Nephrotic Syndrome. *Indian J Nephrol.* 2019 May-Jun;29(3):186-190. doi: 10.4103/ijn.IJN_293_17. PubMed PMID: 31142965; PubMed Central PMCID: PMC6521775.

Altered metabolism of homocysteine in children with idiopathic nephrotic syndrome leads to raised plasma-free homocysteine levels. Elevated free homocysteine causes endothelial cell dysfunction and promotes early atherosclerosis and glomerulosclerosis. In this analytical study with a longitudinal follow-up, 29 children with first episode of nephrotic syndrome (FENS) aged 1-16 years along with 30 age and gender-matched healthy controls were enrolled. Plasma-free homocysteine was measured using high-performance liquid chromatography (HPLC). Other variables were measured using standard biochemical methods. The primary outcome measure was plasma-free homocysteine level in children with FENS and in controls. The secondary outcome measure was to observe the levels of plasma-free homocysteine in children with FENS at 12 weeks in remission and in steroid resistant states. Plasma-free homocysteine levels were significantly elevated in children with FENS at disease onset [Median (IQR) 2.170 (1.54-2.71); N = 29; P < 0.001], at 12 weeks of steroid-induced remission [Median (IQR) 1.946 (1.53-2.71); N = 22; P < 0.001], and in steroid-resistant states [Median (IQR) 2.262 (1.53-2.74); N = 7; P < 0.001] compared to controls. The levels did not decrease significantly at 12 weeks of steroid-induced remission compared to onset of nephrotic syndrome. Plasma-free homocysteine levels correlated positively with serum total cholesterol (P = 0.005; r = 0.362) and negatively with serum albumin (P = 0.032; r = 0.281). Plasma-free homocysteine levels are raised in children with FENS posing a risk of endothelial dysfunction which persists at least in short term. Long-term effects of raised plasma-free homocysteine needs to be studied.

DOI: 10.4103/ijn.IJN_293_17

PMCID: PMC6521775

PMID: 31142965

8: Bagri N, Jana M, Sundaram DD. Pseudorheumatoid Arthropathy of Childhood: A Mimicker of Juvenile Idiopathic Arthritis. *Indian J Pediatr.* 2019 May 27. doi: 10.1007/s12098-019-02983-8. [Epub ahead of print] PubMed PMID: 31134535.

9: Bahadur T, Chaudhry R, Bamola VD, Agrawal SK, Malhotra P, Chutani AM, Mirdha BR, Das BK, Sharma RK, Thakur CK. Toll like receptors (TLRs) in response to human gut microbiota of Indian obese and lean individuals. *J Family Med Prim Care.* 2019 May;8(5):1567-1570. doi: 10.4103/jfmpc.jfmpc_136_19. PubMed PMID: 31198715;

Background: The rising incidence of obesity is one of the most serious public health issues in the developed as well as in developing countries like India. Obesity and overweight are most important risk factors for many chronic diseases, including cardiovascular diseases, diabetes and cancer. In this study the body mass index (BMI) cut off was taken as 18.5-22.9 kg/m² for normal, 23.0-24.9 kg/m² for Overweight and >25 kg/m² for obese as per WHO recommendation for Asian Indians, which is different for developed and developing countries. Role of gut microbiota mediated immune response in the development of obesity has been studied but the literature on Indian population are lacking. Therefore, a study was conducted to determine Toll like receptors (TLRs) in response to human gut microbiota of Indian obese and lean individuals using viable colonocytes in a Non invasive technique and Flowcytometry.

Methods: A total of 20 healthy volunteer (10 obese and 10 lean) were enrolled in the study as per inclusion and exclusion criteria. Viable colonocytes were isolated from fecal samples using a Non invasive technique (SCSR Method). Toll like receptors (TLRs) and immunoglobulin (IgA & IgG) receptor concentration were measured by standard Flowcytometry methods using specific fluorochrome conjugated antibodies.

Results: Average TLR2 receptor concentration was significantly higher in obese (6.35 %) as compared to lean (2.9 %) (P = 0.01). TLR4 receptor concentration was 1.4 % in obese and 1.65 % in lean although the difference was not statistically significant (P = 0.59). IgA & IgG receptor concentration was 49.6 % & 11.2 % in the obese and 67.15 % & 8.05 % in the lean respectively but the differences among both the group were not statistically significant.

Conclusion: The results of the present study will be helpful for physicians and researchers to find some biomarkers which can determine predisposition of the obesity in Indian population and helps to use alternative therapeutics such as probiotics to maintain gut homeostasis and immune modulation to prevent obesity.

DOI: 10.4103/jfmpc.jfmpc_136_19

PMCID: PMC6559096

PMID: 31198715

10: Bains L, Gupta A, Kori R, Kumar V, Kaur D. Transanal high pressure barotrauma causing colorectal injuries: a case series. *J Med Case Rep.* 2019 May 7;13(1):133. doi: 10.1186/s13256-019-2067-y. PubMed PMID: 31060601; PubMed Central PMCID: PMC6503442.

BACKGROUND: Rectal perforation by foreign bodies is known; however, high-pressure injury leading to rectal blowout has been confined to battlefields and is less often encountered in general medical practice. Apart from iatrogenic injuries during colonoscopy, barotrauma from compressed air is encountered very less frequently. Owing to the infrequent nature of these injuries, the mechanism is still not well understood. We present our experience with treating high-pressure transanal barotrauma to the rectum and colon in three similar cases.

CASE PRESENTATION: The mode of injury was accidental or a cruel, perverted joke played by acquaintances. The high-pressure air jet column overcomes the anal sphincter barrier, pushing enormous amounts of air through the anus into the bowel, which ruptures when the burst pressure is reached. A huge amount of free gas was noted in the peritoneal cavity on x-rays, and a big gush was noted during surgery. All these cases had rectosigmoid junction blowout with multiple colonic injuries. The patients underwent exploratory laparotomy with resection of severely injured segments and proximal ileostomy. They underwent restoration of bowel continuity after 2-3months and were doing well in follow-up.

CONCLUSIONS: Colorectal injuries by pneumatic insufflation through the anus depends on the air pressure, air flow velocity, anal resting pressure, and the distance between the source and anus. The relative fixity of the rectum and the bends of the sigmoid make the rectosigmoid junction more prone to rupture by high-pressure air jet. Education regarding such machines and their safe use must be encouraged because most of these cases are accidental and due to ignorance.

DOI: 10.1186/s13256-019-2067-y

PMCID: PMC6503442
PMID: 31060601

11: Bansal R, Ramakrishnan S, Verma SK. Pulmonary artery from the left main coronary artery. *Ann Pediatr Cardiol*. 2019 May-Aug;12(2):176-177. doi: 10.4103/apc.APC_163_18. PubMed PMID: 31143051; PubMed Central PMCID: PMC6521668.

The usual sources of pulmonary blood flow in pulmonary atresia (PA) with (VSD) are patent ductus arteriosus and aortopulmonary collaterals. However, rarely fistulous collaterals may also arise from the coronary arteries which usually open into the main pulmonary trunk or branch pulmonary arteries. In such cases, selective coronary angiogram may be required for the demonstration of pulmonary arterial anatomy. A case of PA with VSD with failure to demonstrate pulmonary arteries on routine catheterization study (ventricular, aortic root, and descending aortic angiograms) is being presented here. A coronary artery-to-pulmonary artery fistula was suspected in view of dilated left main coronary artery, and pulmonary arteries were well demonstrated with selective coronary angiogram.

DOI: 10.4103/apc.APC_163_18
PMCID: PMC6521668
PMID: 31143051

12: Basu A, Chadda RK, Sood M, Kaur H, Kukreti R. A preliminary association study between serotonin transporter (5-HTTLPR), receptor polymorphisms (5-HTR1A, 5-HTR2A) and depression symptom-clusters in a north Indian population suffering from Major Depressive Disorder (MDD). *Asian J Psychiatr*. 2019 May 17;43:184-188. doi: 10.1016/j.ajp.2019.05.028. [Epub ahead of print] PubMed PMID: 31228794.

INTRODUCTION: Major Depressive Disorder (MDD) is a broad heterogeneous diagnostic construct. Previous studies have shown that it can be resolved into several symptom-clusters which are proposed to be associated with single nucleotide polymorphisms (SNPs) of the serotonergic pathway (5-HTTLPR, 5HTR1A, 5-HTR2A).

METHODS AND MATERIAL: In a cross-sectional study conducted at a tertiary level mental health care set-up in north India, 80 out-patients with MDD were evaluated with Montgomery Asberg Depression Rating Scale (MADRS) and then genotyping was done. The different clinical and genetic variables were compared across the factor structures of MADRS. Also, the comparison of the genetic data of cases was done with the pre-existing database of the non-blood related healthy ethnically-matched controls.

RESULTS: There was no significant association between age, gender, other clinical variables, SNPs like 5-HTTLPR SS/SL, rs6295 CC/CG/GG, rs6311GG/GA/AA, rs6313 CC/CT/TT and different factor-structures like 'detachment' consisting of items like concentration difficulty, lassitude, inability to feel; 'psychic anxiety' consisting of suicidal thoughts and inner tension; 'mood-pessimism' consisting of symptoms like apparent sadness, reported sadness, pessimistic thoughts and 'vegetative symptoms' like decreased sleep, poor appetite. Neither there was any association between genotype of the cases compared with the controls.

CONCLUSIONS: No significant association was obtained between the four-factor structures of depression in MADRS and serotonin transporter and receptor SNPs in a study with a small sample size. This study evaluates whether depression symptom-clusters have distinct genotypic determinants and necessitates more comprehensive studies for unravelling the genetic determinants of depression.

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PMID: 31228794

13: Basu K, Maurya N, Kaur J, Saxena R, Gupta V, Sihota R, Ghosh I. Possible role of differentially expressing novel protein markers (ligatin and fibulin-7) in human aqueous humor and trabecular meshwork tissue in glaucoma progression. *Cell Biol Int*. 2019 Jul;43(7):820-834. doi: 10.1002/cbin.11138. Epub 2019 May 18. PubMed PMID: 30958601.

The pathological mechanism underlying glaucoma has always been a complex aspect of this permanently blinding disease but proteomic studies have been helpful in elucidating it to a great extent in several studies. This study was designed to evaluate the expression and to get an idea about the function of two novel markers (ligatin and fibulin-7) identified in human aqueous humor (hAH) in relation to glaucomatous progression. A significant increase in the protein content of glaucomatous hAH compared to that of non-glaucomatous controls (NG-Ctrls) was observed. Ligatin, fibulin-7, and its proteolysis were revealed in hAH of primary open angle glaucoma (POAG), primary angle closure glaucoma (PACG) and NG-Ctrls. Quantification confirmed no significant difference in expression of ligatin, whereas fibulin-7 was significantly ($P < 0.05$) low in hAH of PACG in comparison to NG-Ctrls and POAG. Importantly the immunohistochemical assay for both indicated their possible involvement in the maintenance of the appropriate structure of TM in vivo. Since oxidative stress is a major contributor to glaucomatous pathogenesis, in vitro analysis of nuclear and cytoplasmic fractions indicated intracellular changes in localization and expression of ligatin upon oxidative insult of human trabecular meshwork (TM) cells. While no such changes were found for fibulin-7 expression. This was also corroborated with the immunocytochemical assay. Though a study with a small sample size, this is the first report which confirms the presence of ligatin and fibulin-7 in hAH, quantified their differential expression, and indicated the possibility of their involvement in the maintenance of the TM structure.

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PMID: 30958601

14: Bhargava P, Verma VK, Malik S, Khan SI, Bhatia J, Arya DS. Hesperidin regresses cardiac hypertrophy by virtue of PPAR- γ agonistic, anti-inflammatory, antiapoptotic, and antioxidant properties. *J Biochem Mol Toxicol*. 2019 May;33(5):e22283. doi: 10.1002/jbt.22283. Epub 2019 Jan 8. PubMed PMID: 30623541.

Hesperidin (HES), a flavanone glycoside, predominant in citrus fruits, has an agonistic activity on peroxisome proliferator-activated receptor gamma (PPAR- γ). PPAR- γ is an inhibitor of cardiac hypertrophy (CH) signaling pathways. In this study, we investigated the cardioprotective effect of HES in isoproterenol (ISO)-induced CH through PPAR- γ agonistic activity. For this, male albino Wistar rats were divided into six groups ($n=6$), that is, normal, ISO-control, HES treatment group (200 mg kg⁻¹ ; p.o.), HES per se (200 mg kg⁻¹ ; p.o.), enalapril treatment group (30 mg kg⁻¹ ; p.o.), and combination group (HES 200 mg kg⁻¹ ; p.o.+enalapril 30 mg kg⁻¹ ; p.o.). ISO (3 mg kg⁻¹ ; s.c.) was administered to all groups except normal and per se to induce CH. HES or enalapril treatment of 28 days significantly attenuated pathological changes, improved cardiac hemodynamics, suppressed oxidative stress, and apoptosis along with an increased PPAR- γ expression. The combination of enalapril with HES exhibited an effect similar to that of HES or enalapril alone on all the aforementioned parameters. Therefore, HES may be further evaluated as a promising molecule for the alleviation of CH.

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PMID: 30623541 [Indexed for MEDLINE]

15: 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 May 17. doi: 10.1111/cei.13310. [Epub ahead of print] PubMed PMID: 31099890.

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)-1 β , 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-1 β , 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.

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DOI: 10.1111/cei.13310

PMID: 31099890

16: Bhatia R, Parambath N, Yadav S, Mridha AR. Rapidly growing targetoid necrotic plaques in an immunocompetent man. *Postgrad Med J*. 2019 May;95(1123):284. doi: 10.1136/postgradmedj-2018-136039. Epub 2019 Apr 12. PubMed PMID: 30979788.

17: Bhattacharjee R, Gupta RK, Patir R, Vaishya S, Ahlawat S, Singh A. Quantitative vs. semiquantitative assessment of intratumoral susceptibility signals in patients with different grades of glioma. *J Magn Reson Imaging*. 2019 May 14. doi: 10.1002/jmri.26786. [Epub ahead of print] PubMed PMID: 31087724.

BACKGROUND: Susceptibility weighted imaging (SWI) provides vascular information and plays an important role in improving the diagnostic accuracy of preoperative glioma grading. Intratumoral susceptibility signal intensities (ITSS) obtained from SWI has been used in glioma grading. However, the current method for estimation of ITSS is semiquantitative, manual count-dependent, and includes hemorrhage as well as vasculature.

PURPOSE: To develop a quantitative approach that calculates the vasculature volume within tumors by filtering out the hemorrhage from ITSS using R2 * values and connected component analysis-based segmentation algorithm; to evaluate the accuracy of the proposed ITSS vasculature volume (IVV) for differentiating various grades of glioma; and compare it with reported semiquantitative ITSS approach.

STUDY TYPE: Retrospective.

SUBJECTS: Histopathologically confirmed 41 grade IV, 19 grade III, and 15 grade II glioma patients. **Field Strength/Sequence:** SWI (four echoes: 5.6, 11.8, 18, 24.2 msec) along with conventional MRI sequences (T2 -weighted, T1 -weighted, 3D-fluid-attenuated inversion recovery [FLAIR], and diffusion-weighted imaging [DWI]) at 3.0T.

ASSESSMENT: R2 * relaxation maps were calculated from multiecho SWI. The R2 * cutoff value for hemorrhage ITSS was determined. A segmentation algorithm was designed, based on this R2 * hemorrhage combined with connected component shape analysis, to quantify the IVV from all slices containing tumor by filtering out hemorrhages. Semiquantitative ITSS scoring as well as total ITSS volume (TIV) including hemorrhages were also calculated.

STATISTICAL TESTS: One-way analysis of variance (ANOVA) and Tukey-Kramer post-hoc tests were performed to see the difference among the three grades of the tumor

(II, III, and IV) in terms of semiquantitative ITSS scoring, TIV, and IVV. Receiver operating characteristic (ROC) curve analysis was used to evaluate the performance of the three methods individually in discriminating between grades of glioma.

RESULTS: One-way ANOVA showed that only the proposed IVV significantly differentiated different grades of gliomas having visible ITSS. ROC analysis showed that IVV provided the highest AUC for the discrimination of grade II vs. III (0.93), grade III vs. IV (0.98), and grade II vs. IV glioma (0.94). IVV also provided the highest sensitivity and specificity for differentiating grade II vs. III (87.44, 98.41), grade III vs. IV (97.15, 94.12), and grade II vs. IV (98.72, 92.31).

DATA CONCLUSION: The proposed quantitative method segregates hemorrhage from tumor vasculature. It scores above the existing semiquantitative method in terms of ITSS estimation and grading accuracy.

LEVEL OF EVIDENCE: 4 Technical Efficacy: Stage 2 J. Magn. Reson. Imaging 2019.

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18: Bhushan S, Bazaz R, Naalla R, Singhal M. Think before throwing away the amputated part! BMJ Case Rep. 2019 May 8;12(5). pii: e230271. doi: 10.1136/bcr-2019-230271. PubMed PMID: 31068356.

19: Biswas A, Raza A, Das S, Kapoor M, Jayarajan R, Verma A, Shamsudheen KV, Murry B, Seth S, Bhargava B, Scaria V, Sivasubbu S, Rao VR. Loss of function mutation in the P2X7, a ligand-gated ion channel gene associated with hypertrophic cardiomyopathy. Purinergic Signal. 2019 May 31. doi: 10.1007/s11302-019-09660-7. [Epub ahead of print] PubMed PMID: 31152337.

Hypertrophic cardiomyopathy (HCM) is an inherited heart failure condition, mostly found to have genetic abnormalities, and is a leading cause of sudden death in young adults. Whole exome sequencing should be given consideration as a molecular diagnostic tool to identify disease-causing mutation/s. In this study, a HCM family with multiple affected members having history of sudden death were subjected to exome sequencing along with unaffected members. Quality passed variants obtained were filtered for rarity (MAF > 0.5%), evolutionary conservation, pathogenic prediction, and segregation in affected members after removing shared variants present in unaffected members. Only one non-synonymous mutation (p. Glu186Lys or E186K) in exon 6 of P2X7 gene segregated in HCM-affected individuals which was absent in unaffected family members and 100 clinically evaluated controls. The site of the mutation is highly conserved and led to complete loss of function which is in close vicinity to ATP-binding site-forming residues, affecting ATP binding, channel gating, or both. Mutations in candidate genes which were not segregated define clinical heterogeneity within affected members. P2X7 gene is highly expressed in the heart and shows direct interaction with major candidate genes for HCM. Our results reveal a significant putative HCM causative gene, P2X7, for the first time and show that germ-line mutations in P2X7 may cause a defective phenotype, suggesting purinergic receptor involvement in heart failure mediated through arrhythmias which need further investigations to be targeted for therapeutic interventions.

DOI: 10.1007/s11302-019-09660-7

PMID: 31152337

20: Biswas S, Ray A. Dextrocardia with pulmonary hypoplasia: an unusual cause of unilateral lung white-out. BMJ Case Rep. 2019 May 28;12(5). pii: e229413. doi: 10.1136/bcr-2019-229413. PubMed PMID: 31142489.

Pulmonary agenesis is a rare developmental disorder with many syndromic associations. Type III agenesis presents with variable amounts of bronchial tree, pulmonary parenchyma and supporting vasculature. It is also reported to be

associated with dextrocardia due to shifting of the heart to occupy the space left by the underdeveloped lung, which occurs as early as the fourth week of gestation. Right lung agenesis is considered rarer than its left-sided counterpart and also has a poorer prognosis due to increased chances of respiratory infections. We report a case of isolated right-sided lung hypoplasia with dextrocardia without situs inversus or heterotaxy.

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PMID: 31142489

21: Chandran N, Mahapatra A, Tak NK, Nanda Patra B, Sagar R. Anticholinergic induced mania-A case report. *Asian J Psychiatr*. 2019 May 7;43:53-54. doi: 10.1016/j.ajp.2019.05.014. [Epub ahead of print] PubMed PMID: 31082623.

22: Chattopadhyay K, Chandrasekaran AM, Praveen PA, Manchanda SC, Madan K, Ajay VS, Singh K, Tillin T, Hughes AD, Chaturvedi N, Ebrahim S, Pocock S, Reddy KS, Tandon N, Prabhakaran D, Kinra S. Development of a Yoga-Based Cardiac Rehabilitation (Yoga-CaRe) Programme for Secondary Prevention of Myocardial Infarction. *Evid Based Complement Alternat Med*. 2019 May 2;2019:7470184. doi: 10.1155/2019/7470184. eCollection 2019. PubMed PMID: 31186666; PubMed Central PMCID: PMC6521480.

Cardiac rehabilitation (CR) after myocardial infarction is highly effective. It is unavailable in public hospitals in India due to limited resources. Our objective was to develop a scalable model of CR for India based on yoga, which could also appeal to some groups with low uptake of CR (e.g., ethnic minorities, women, and older people) globally. The intervention was developed using a structured process. A literature review and consultations with yoga experts, CR experts, and postmyocardial infarction patients were conducted to systematically identify and shortlist appropriate yoga exercises and postures, breathing exercises, meditation and relaxation practices, and lifestyle changes, which were incorporated into a conventional CR framework. The draft intervention was further refined based on the feedback from an internal stakeholder group and an external panel of international experts, before being piloted with yoga instructors and patients with myocardial infarction. A four-phase yoga-based CR (Yoga-CaRe) programme was developed for delivery by a single yoga instructor with basic training. The programme consists of a total of 13 instructor-led sessions (2 individual and 11 group) over a 3-month period. Group sessions include guided practice of yoga exercises and postures, breathing exercises, and meditation and relaxation practices, and support for the lifestyle change and coping through a moderated discussion. Patients are encouraged to self-practice daily at home and continue long-term with the help of a booklet and digital video disc (DVD). Family members/carers are encouraged to join throughout. In conclusion, a novel yoga-based CR programme has been developed, which promises to provide a scalable CR solution for India and an alternative choice for CR globally. It is currently being evaluated in a large multicentre randomised controlled trial across India.

DOI: 10.1155/2019/7470184

PMCID: PMC6521480

PMID: 31186666

23: Chawla D, Deorari A. Chapter 4. ROP prevention, screening and treatment programmes. *Semin Perinatol*. 2019 May 11. pii: S0146-0005(19)30066-7. doi: 10.1053/j.semperi.2019.05.006. [Epub ahead of print] Review. PubMed PMID: 31174875.

India is home to largest number of preterm births and neonates at risk of developing retinopathy of prematurity. Being a large heterogenous country, different approaches including training of local ophthalmologists, tele-screening by ophthalmic technicians carrying wide-angle retinal cameras and use of low-cost retinal cameras by neonatal unit healthcare providers are being tested to expand

the coverage of screening.

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DOI: 10.1053/j.semperi.2019.05.006

PMID: 31174875

24: 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 May 16. doi: 10.1007/s00586-019-06003-3. [Epub ahead of print] 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

25: Choudhary V, Satapathy S, Sagar R. Qualitative Study on the Impact of Child Sexual Abuse: Perspectives of Children, Caregivers, and Professionals in Indian Context. *J Child Sex Abus*. 2019 May-Jun;28(4):489-510. doi: 10.1080/10538712.2018.1563262. Epub 2019 Jan 25. PubMed PMID: 30681937.

With an alarming increase in reported cases of Child Sexual Abuse (CSA) in India, the present study was conceived in an attempt to unearth the impact of CSA from the perspective of children, their caregivers, and the professionals dealing with them using qualitative research methodology. The secondary objective of the study was to discuss the clinical implications of the obtained findings for conducting culturally sensitive psychological assessment and intervention for CSA in India. Thus, in-depth interviews with 11 children and 7 Focused Group Discussions (FGDs) with 21 caregivers and 27 professionals were conducted. A total of 59 sample participants were recruited, and a thematic analysis was done. Six broad themes were identified from 223 generated codes-impact on behavioral, emotional, cognitive functioning and academics, psychopathology, biological, and social functioning. Four essential recommendations were concluded from the study, i.e., multidimensional impact assessment as a mandatory clinical practice, developing and utilizing culturally sensitive assessment & intervention protocols, incorporation of family-focused approach and multidisciplinary treatment team

approach to ensure the holistic well-being of each child in India.

DOI: 10.1080/10538712.2018.1563262

PMID: 30681937

26: Claudino AM, Pike KM, Hay P, Keeley JW, Evans SC, Rebello TJ, Bryant-Waugh R, Dai Y, Zhao M, Matsumoto C, Herscovici CR, Mellor-Marsá B, Stona AC, Kogan CS, Andrews HF, Monteleone P, Pilon DJ, Thiels C, Sharan P, Al-Adawi S, Reed GM. The classification of feeding and eating disorders in the ICD-11: results of a field study comparing proposed ICD-11 guidelines with existing ICD-10 guidelines. *BMC Med.* 2019 May 14;17(1):93. doi: 10.1186/s12916-019-1327-4. PubMed PMID: 31084617; PubMed Central PMCID: PMC6515596.

BACKGROUND: The World Health Organization (WHO) International Classification of Diseases and Related Health Problems (ICD) is used globally by 194 WHO member nations. It is used for assigning clinical diagnoses, providing the framework for reporting public health data, and to inform the organization and reimbursement of health services. Guided by overarching principles of increasing clinical utility and global applicability, the 11th revision of the ICD proposes major changes that incorporate empirical advances since the previous revision in 1992. To test recommended changes in the Mental, Behavioral, and Neurodevelopmental Disorders chapter, multiple vignette-based case-controlled field studies have been conducted which examine clinicians' ability to accurately and consistently use the new guidelines and assess their overall clinical utility. This manuscript reports on the results from the study of the proposed ICD-11 guidelines for feeding and eating disorders (FEDs).

METHOD: Participants were 2288 mental health professionals registered with WHO's Global Clinical Practice Network. The study was conducted in Chinese, English, French, Japanese, and Spanish. Clinicians were randomly assigned to apply either the ICD-11 or ICD-10 diagnostic guidelines for FEDs to a pair of case vignettes designed to test specific clinical questions. Clinicians selected the diagnosis they thought was correct for each vignette, evaluated the presence of each essential feature of the selected diagnosis, and the clinical utility of the diagnostic guidelines.

RESULTS: The proposed ICD-11 diagnostic guidelines significantly improved accuracy for all FEDs tested relative to ICD-10 and attained higher clinical utility ratings; similar results were obtained across all five languages. The inclusion of binge eating disorder and avoidant-restrictive food intake disorder reduced the use of residual diagnoses. Areas needing further refinement were identified.

CONCLUSIONS: The proposed ICD-11 diagnostic guidelines consistently outperformed ICD-10 in distinguishing cases of eating disorders and showed global applicability and appropriate clinical utility. These results suggest that the proposed ICD-11 guidelines for FEDs will help increase accuracy of public health data, improve clinical diagnosis, and enhance health service organization and provision. This is the first time in the revision of the ICD that data from large-scale, empirical research examining proposed guidelines is completed in time to inform the final diagnostic guidelines.

27: Dadhwal V, Sharma AK, Deka D, Chawla L, Agarwal N. Selective fetal reduction in monozygotic twins: Preliminary experience. *J Turk Ger Gynecol Assoc.* 2019 May 28;20(2):79-83. doi: 10.4274/jtgga.galenos.2018.2018.0052. Epub 2018 Oct 9. PubMed PMID: 30299263; PubMed Central PMCID: PMC6558353.

Objective: In complicated mono-chorionic twin pregnancies, vaso-occlusive techniques like bipolar cord coagulation (BPCC), radiofrequency ablation (RFA), interstitial laser ablation (ILA) of cord and fetoscopy guided cord coagulation with lasers are the methods proposed for selective fetal reduction. This study brings forth preliminary data of selective fetal reduction procedures at a tertiary care center in India.

Material and Methods: This was a prospective observational study of 31 patients with complicated mono-chorionic twin pregnancies. Methods used were ILA, RFA and BPCC. Outcome measures included overall co-twin survival after selective fetocide, survival rates with each method, miscarriage (defined as all fetal loss

before 24 weeks), early fetal death (<24 hours after procedure) and late fetal death (>24 hours after the procedure) of co-twin.
Results: Technical success was achieved in 30/31 (96.8%) of pregnancies. Over all take home baby rate was 63.3%. Live birth rates were 50%, 71.4% and 75% with ILA, RFA and BPCC respectively.
Conclusion: Data from initial cases of selective fetal reduction in complicated mono-chorionic twins suggests that these procedures are feasible but are associated with high adverse perinatal outcome.

DOI: 10.4274/jtgga.galenos.2018.2018.0052

PMCID: PMC6558353

PMID: 30299263

28: Dang S, Sharma P, Shekhawat LS. Cognitive Schemas among Mental Health Professionals and Other Health Professionals. *Indian J Psychol Med.* 2019 May-Jun;41(3):258-265. doi: 10.4103/IJPSYM.IJPSYM_194_18. PubMed PMID: 31142928; PubMed Central PMCID: PMC6532379.

Objective: Research has demonstrated that dysfunctional cognitive schemas among mental health professionals (MHPs) may influence the ability to process clients' information in an unbiased manner, may be a substantial source of error in psychotherapeutic ratings, hinder accurate reporting of clients' cognitive schemas, and have a detrimental effect on therapeutic alliance. The present study compared cognitive schemas among MHPs and other health professionals (OHPs).
Materials and Method: A sample of 128 professionals (64 MHPs and 64 OHPs) was chosen using a purposive sampling technique. The study used a cross-sectional observational research design. The Young Schema Questionnaire Short Form 3rd version was administered on the consenting participants.
Results: OHPs had higher maladaptive schemas on the domains of abandonment and defectiveness. Overall, males had more maladaptive schemas in the domains of abandonment, mistrust, entitlement/superiority, admiration/recognition seeking, and emotional inhibition. Among MHPs, a weak positive correlation of years of experience with vulnerability to harm or illness was seen. Among other health professionals, a significant but weak positive correlation of age with admiration/recognition seeking was seen.
Conclusion: This study highlights the presence of maladaptive schemas in health professionals and the need for incorporation of training modules to address these.

DOI: 10.4103/IJPSYM.IJPSYM_194_18

PMCID: PMC6532379

PMID: 31142928

29: Das CJ, Razik A, Sharma S, Verma S. Prostate biopsy: when and how to perform. *Clin Radiol.* 2019 May 9. pii: S0009-9260(19)30160-6. doi: 10.1016/j.crad.2019.03.016. [Epub ahead of print] Review. PubMed PMID: 31079953.

Prostate cancer, unlike other cancers, has been sampled in a non-targeted, systematic manner in the past three decades. On account of the low volume of prostate sampled despite the multiple cores acquired, systematic transrectal (TRUS) biopsy suffered from low sensitivity in picking up clinically significant prostate cancer. In addition, a significant number of cancers of the anterior, lateral peripheral zone, and the apex were missed as these areas were undersampled or missed during this biopsy protocol. Subsequently, the number of cores acquired was increased with special focus given to targeting the previously undersampled areas. These procedures led to an increase in the complication rates as well as detection of more clinically insignificant cancers. The advent of multiparametric magnetic resonance imaging (MRI) and its high intrinsic tissue contrast enabled better detection of prostate cancer. This led to the introduction of MRI-targeted biopsies with either MRI-TRUS fusion or under direct (in-gantry) guidance. MRI-targeted biopsies increased the percentage of positive cores and detection of clinically significant prostate cancers; however, these are expensive, time-intensive, require significant capital investment and operator expertise. This article describes the indications, workflow,

complications, advantages, and disadvantages of TRUS-guided biopsy followed by MRI-guided biopsies.

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DOI: 10.1016/j.crad.2019.03.016

PMID: 31079953

30: Dawani A, Gupta AK, Jana M. Imaging in Pediatric Extra-Pulmonary Tuberculosis. *Indian J Pediatr.* 2019 May;86(5):459-467. doi: 10.1007/s12098-019-02858-y. Epub 2019 Jan 30. PubMed PMID: 30697676.

Extrapulmonary tuberculosis in children tends to be more severe than the adults. It can affect almost any organ system of the body. The clinical manifestations are often non-specific. Imaging findings are also not always very specific. This article describes the imaging spectrum of pediatric extrapulmonary tuberculosis.

DOI: 10.1007/s12098-019-02858-y

PMID: 30697676

31: Dharmshaktu P, Saha S, Kar P, Sreenivas V, Ramakrishnan L, Goswami R. Absence of vitamin D deficiency among common outdoor workers in Delhi. *Clin Endocrinol (Oxf).* 2019 May 14. doi: 10.1111/cen.14012. [Epub ahead of print] PubMed PMID: 31087795.

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.

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DOI: 10.1111/cen.14012

PMID: 31087795

32: Dhingra A, Ganie MA, Dharmshaktu P, Chakraborty S, Jyotsna VP, Gupta N. Pattern of Lipid Abnormalities Among South Asian Indians With Cushing's Syndrome and the Short Term Impact of Surgical Correction of Hypercortisolism. *Horm Metab Res.* 2019 May;51(5):309-314. doi: 10.1055/a-0879-5122. Epub 2019 May 9. PubMed PMID: 31071735.

Atherosclerotic cardiovascular events are one of the common causes of mortality in patients with Cushing's syndrome (CS). Atherogenic dyslipidemia is more common among South Asian Indians as compared to other ethnicities and is likely to

worsen among patients with CS. This retrospective study was done over 5 years at a single institute to evaluate the pattern of lipid abnormalities in subjects with CS and the changes in lipid parameters after surgical control of hypercortisolemia. The study was done in two parts. In the first part, records of patients with CS diagnosed over 3 years were retrospectively reviewed. Hormonal and metabolic parameters including fasting plasma glucose (FPG), post prandial plasma glucose (PPPG), HbA1c, serum lipids, serum cortisol and plasma ACTH were recorded. In the second part, lipid parameters were rechecked among patients who underwent surgery and a median follow up of 4±2 months after remission. Out of the 126 patients diagnosed with endogenous CS over 3 years, 100 patients were eligible for inclusion in the study. At baseline, sixty five (65%) patients had dyslipidemia as defined by the NCEP-ATPIII criteria. 47 out of 63 (74.6%) subjects achieved remission after surgical management of CS. 32 (68.1%) of these patients had dyslipidemia prior to surgery. After excluding 1 death, 26 of 46 (56.5%) subjects had dyslipidemia after the follow up period. Lipid abnormalities are common among South Asian Indian subjects with endogenous CS and the pattern persists in most of them, 3 months after surgical correction of hypercortisolism.

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DOI: 10.1055/a-0879-5122

PMID: 31071735

33: Dongare PA, Bhaskar SB, Harsoor SS, Kalaivani M, Garg R, Sudheesh K, Goneppanavar U. Development and validation of a questionnaire for a survey on perioperative fasting practices in India. *Indian J Anaesth.* 2019 May;63(5):394-399. doi: 10.4103/ija.IJA_118_19. PubMed PMID: 31142884; PubMed Central PMCID: PMC6530289.

Background and Aims: Perioperative fasting guidelines have been published and updated to standardise practices. Hence, Indian Society of Anaesthesiologists decided to conduct a survey to assess the fasting practices and the food habits across India, which would be subsequently used for developing preoperative fasting guidelines for the Indian population. We detail and discuss herewith the content validity of the questionnaire developed for the survey.

Methods: Thirty-six questions related to perioperative fasting practices were framed based on the collected evidence and relevance to regional diet and concerns. Subsequently, an information sheet was prepared and sent to 10 experts to grade each question. The responses were tabulated, and item-wise content validity index (I-CVI), scale-wise content validity index (S-CVI) and modified kappa statistic were calculated in Microsoft Excel™ sheet.

Results: Seven of the 10 experts completed the assessment and grading as per the instructions provided and submitted a completed proforma. S-CVI for relevance, simplicity, clarity and ambiguity was 0.72, 0.86, 0.72 and 0.72, respectively. S-CVI/average or average congruency percentagewas 0.95, 0.97, 0.95 and 0.95 for relevance, simplicity, clarity and ambiguity, respectively. Question 2 received an I-CVI of 0.71 in terms of clarity and question 23 received an I-CVI of 0.71. They were modified as persuggestions of the experts.

Conclusion: We conclude that our questionnaire designed to ascertain the preoperative fasting practices for a surveymet the content validity criteria both by qualitative and quantitative analyses.

DOI: 10.4103/ija.IJA_118_19

PMCID: PMC6530289

PMID: 31142884

34: Ferrone G, Spinazzola G, Hadda V, Esquinas A. Proportional assist ventilation plus (PAV+) from weaning to assist control ventilation: insights for caution on issue. *Minerva Anesthesiol.* 2019 May 21. doi: 10.23736/S0375-9393.19.13733-9. [Epub ahead of print] PubMed PMID: 31124627.

35: Garfin DR, Shin SS, Ekstrand ML, Yadav K, Carpenter CL, Sinha S, Nyamathi AM.

Depression, social support, and stigma as predictors of quality of life over time: results from an Asha-based HIV/AIDS intervention in India. *AIDS Care*. 2019 May;31(5):563-571. doi: 10.1080/09540121.2018.1563281. Epub 2019 Feb 3. PubMed PMID: 30714386.

Quality of life (QOL) is associated with better outcomes in HIV/AIDS populations. We explored predictors of improved QOL over time in 600 Women Living with HIV/AIDS (WLH/A) in India [mean age = 34.31, SD = 6.97], enrolled in a nurse-led-Asha (Accredited Social Health Activist) intervention. Trained local interviewers ascertained self-report data at baseline and six-month follow-up (post-intervention). Latent Class Analysis (LCA) identified constellations of responses on psychosocial indicators (depression, social support, internalized stigma and stigma fears); their relationship with QOL over time was examined. We identified three classes: Class 1) Highest Social Resources/Lowest Depression; Class 2) Some Social Resources/Highest Depression; and Class 3) Lowest Social Resources/Higher Depression. At baseline, Class 3 reported the lowest QOL (M = 0.25, SD = 0.26); Class 1 reported the highest (M = 0.37, SD = 0.33). Class 2's QOL did not differ from Class 3's QOL, likely due to the potent effects of high depression. At six-month follow-up, all groups reported improved QOL; class membership no longer predicted variability (contrast between Class 2 and 1 = -0.05, 95% CI = -0.14, 0.04; contrast between Class 3 and 1 = 0.01, 95% CI = -0.03, 0.05; contrast between Class 3 and 2 = 0.07, 95% CI = -0.02, 0.16). Psychosocial indicators are important predictors of QOL; an Asha-supported approach may have broad applicability to improve QOL in WLH/A in India.

DOI: 10.1080/09540121.2018.1563281
PMID: 30714386

36: Garg D, Pedapati R, Nakra T, Singh RK, Prabhakar A, Dash D, Bhatia R, Tripathi M. Langerhans cell histiocytosis presenting as a rapidly evolving frontotemporal syndrome. *Neurol Sci*. 2019 May;40(5):1055-1058. doi: 10.1007/s10072-019-3709-y. Epub 2019 Jan 10. PubMed PMID: 30631989.

Langerhans cell histiocytosis (LCH) is a rare disorder in adults which usually manifests with involvement of multiple organ systems, including the central nervous system. We describe an unusual case of biopsy-proven LCH presenting with frontotemporal-dominant cognitive impairment with hypothalamic involvement, along with multisystem disease. We propose that the dementia was probably an immune-mediated process triggered by LCH which responded dramatically to high-dose steroids.

DOI: 10.1007/s10072-019-3709-y
PMID: 30631989 [Indexed for MEDLINE]

37: Garg PK, Meena D, Babu D, Padhan RK, Dhingra R, Krishna A, Kumar S, Misra MC, Bansal VK. Endoscopic versus laparoscopic drainage of pseudocyst and walled-off necrosis following acute pancreatitis: a randomized trial. *Surg Endosc*. 2019 May 28. doi: 10.1007/s00464-019-06866-z. [Epub ahead of print] PubMed PMID: 31140002.

BACKGROUND: Pancreatic fluid collections (PFC) may develop following acute pancreatitis (AP). Endoscopic and laparoscopic internal drainage are accepted modalities for drainage of PFCs but have not been compared in a randomized trial. Our objective was to compare endoscopic and laparoscopic internal drainage of pseudocyst/walled-off necrosis following AP.

PATIENTS AND METHODS: Patients with symptomatic pseudocysts or walled-off necrosis suitable for laparoscopic and endoscopic transmural internal drainage were randomized to either modality in a randomized controlled trial. Endoscopic drainage comprised of per-oral transluminal cystogastrostomy. Additionally, endoscopic lavage and necrosectomy were done following a step-up approach for infected collections. Surgical laparoscopic cystogastrostomy was done for drainage, lavage, and necrosectomy. Primary outcome was resolution of PFCs by the intended modality and secondary outcome was complications.

RESULTS: Sixty patients were randomized, 30 each to laparoscopic and endoscopic drainage. Both groups were comparable for baseline characteristics. The initial

success rate was 83.3% in the laparoscopic and 76.6% in the endoscopic group (p=0.7) after the index intervention. The overall success rate of 93.3% (28/30) and 90% (27/30) in the laparoscopic and endoscopic groups respectively was also similar (p=1.0). Two patients in the laparoscopic group required endoscopic cystogastrostomy for persistent collections. Similarly, two patients in the endoscopic group required laparoscopic drainage. Postoperative complications were comparable between the groups except for higher post-procedure infection in the endoscopic group (19 vs. 9; p=0.01) requiring endoscopic re-intervention. CONCLUSIONS: Endoscopic and laparoscopic techniques have similar efficacy for internal drainage of suitable pancreatic fluid collections with <30% debris. The choice of procedure should depend on available expertise and patient preference.

DOI: 10.1007/s00464-019-06866-z
PMID: 31140002

38: Garg PK, Singh VP. Organ Failure Due to Systemic Injury in Acute Pancreatitis. *Gastroenterology*. 2019 May;156(7):2008-2023. doi: 10.1053/j.gastro.2018.12.041. Epub 2019 Feb 12. Review. PubMed PMID: 30768987; PubMed Central PMCID: PMC6486861.

Acute pancreatitis may be associated with both local and systemic complications. Systemic injury manifests in the form of organ failure, which is seen in approximately 20% of all cases of acute pancreatitis and defines "severe acute pancreatitis." Organ failure typically develops early in the course of acute pancreatitis, but also may develop later due to infected pancreatic necrosis-induced sepsis. Organ failure is the most important determinant of outcome in acute pancreatitis. We review here the current understanding of the risk factors, pathophysiology, timing, impact on outcome, and therapy of organ failure in acute pancreatitis. As we discuss the pathophysiology of severe systemic injury, the distinctions between markers and mediators of severity are highlighted based on evidence supporting their causality in organ failure. Emphasis is placed on clinically relevant end points of organ failure and the mechanisms underlying the pathophysiological perturbations, which offer insight into potential therapeutic targets to treat.

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PMCID: PMC6486861 [Available on 2020-05-01]
PMID: 30768987 [Indexed for MEDLINE]

39: Garg R, Nandi R, Hadda V, Mohan A. Conventional laryngoscopy as a rescue for fiber-optic-assisted tracheal intubation in a patient with perilaryngeal edema after rigid bronchoscopy: A case report. *Lung India*. 2019 May-Jun;36(3):253-254. doi: 10.4103/lungindia.lungindia_251_17. PubMed PMID: 31031350; PubMed Central PMCID: PMC6503725.

40: 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 May 18. doi: 10.1007/s00125-019-4903-4. [Epub ahead of print] 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 \pm SD age of 32.4 \pm 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 \pm SD age of 36.4 \pm 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

41: Guleria R, Korukonda K; DUSS Investigators. Clinical Impact of a Digital Dose Counter Pressurized Metered-Dose Inhaler on Uncontrolled Asthma: Cross-Sectional, Observational, Surveillance Study. *Interact J Med Res.* 2019 May 5;8(2):e13530. doi: 10.2196/13530. PubMed PMID: 31066694; PubMed Central PMCID: PMC6528432.

BACKGROUND: In India, control of asthma with persistent symptoms remains a clinical enigma with likely incriminating factors including non- and pseudo-adherence to the inhaled corticosteroids and long-acting beta2-agonists. The United States Food and Drug Administration guidance recommends the use of dose counter pressurized metered-dose inhalers (pMDIs) with further mechanisms to track adherence and pseudo-adherence in real-world settings.

OBJECTIVE: Digital dose counter pMDIs (dpMDIs) offer simplified, reliable tracking of individual "actuated" dosages with "END" display at completion of the labelled therapeutic aerosol spray. The translational impact on symptom persistence with likely unwarranted exposure to the "Step up" strategy is often prevented if not treated, as in the cases of "pseudo" severe asthma. To further assess the real-world acceptance and clinical impact of dpMDIs in bronchial asthma including poorly controlled or uncontrolled bronchial asthma cases, a non-interventional observational study was performed.

METHODS: This cross-sectional, retrospective, case cohort, observational study-the Drug Utilization Surveillance-of dpMDIs in bronchial asthma was conducted in September 2016 in an outpatient setting in India. The retrospective analysis was initiated and conducted as per the International Conference on Harmonization Good Clinical Practice principles and Declaration of Helsinki, following approval from the local ethics committee and registration in the Clinical Trial Registry of India.

RESULTS: Consecutive cases of moderate-to-severe asthma with poor control (n=4575), diagnosed as per the Global Initiative for Asthma symptom scale at baseline and follow-up, were included. Patients under treatment using dpMDIs were enrolled from 500 centers across India and assessed by respiratory care specialists. Baseline asthma control was assessed as partly controlled (n=4575) or poorly controlled (n=2942). Per protocol analyses showed that asthma was well controlled with dpMDIs at 8 weeks in 92.7% of the cases (2727/2942, P<.001). Adverse events (n=106, 2%) of mild-to-moderate intensity were reported. Nebulization was required in two patients with episodic breathlessness who were discharged with no consequent sequelae. Post hoc analyses for patients with baseline poorly controlled asthma who "switched" exclusively to dpMDI monotherapy

or a combination with xanthines or long-acting beta2-agonists showed a "well controlled" asthma status in 85.9% (500/582, P=.04), 95.4% (395/414, P=.048), and 80.3% (106/132, P=.28) of the cases, respectively. The patient acceptability criteria for an "empty" canister was well correlated with the clinical strategy to identify and avoid pseudo-adherence in poorly controlled or difficult-to-treat asthma cases, especially in patients who "switched" exclusively to dpMDIs (n=582) and demonstrated responses of "Use till twenty dose display" (65/156, 41.6%), "Use till END display" (83/156, 53.2%), and "Use till LAST spray" (8/156, 5.1%). CONCLUSIONS: dpMDIs offer simple, accurate, and reliable tracking of non- and pseudo-adherence while highlighting incremental asthma-control rates in severe and pseudo-severe asthma cases before risk assessment for further "add-on" therapy. TRIAL REGISTRATION: Clinical Trials Registry - India CTRI/2018/06/014595; <http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=24583>.

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PMCID: PMC6528432
PMID: 31066694

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One hundred and fifty infertile polycystic ovary syndrome (PCOS) women were classified into four phenotypes on the basis of Rotterdam criteria. Homeostatic model assessment of insulin resistance (HOMA-IR) with a cutoff ≥ 2.5 was considered as a measure of insulin resistance (IR). Maximum number of patients, 57 (38%) in our cohort belonged to phenotype A or the classical phenotype with all 3 features of Rotterdam criteria. Mean body mass index (BMI) in all phenotypes was more than 25kg/m² and the highest was seen in phenotype B. According to BMI categories in the four phenotypes, more number of women was in the obese category in phenotype A (24.5%) and B (56.5%) in comparison to phenotype C (18.2%) and D (10.8%) (p<.001). There was no difference in median HOMA-IR among different phenotype categories (p=.718). The median value of anti-mullerian hormone (AMH) was highest in phenotype A (11.68ng/ml [7.94-16.46]) and significantly more in comparison to B phenotype (Kruskal-Wallis, p=.018). Thus there is heterogeneity in AMH levels and BMI in different PCOS phenotypes with higher levels in the most severe phenotypes. There is, however, no correlation of IR among the different phenotype groups and further investigation is needed to characterize its role in phenotypic classification.

DOI: 10.1080/09513590.2019.1613640
PMID: 31081410

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Computed tomography has an established role in the evaluation of a variety of cardiac disorders, including congenital heart diseases. The current generation of high-speed scanners produces volumetric data at low doses of radiation. The interpretation of cardiac anatomy, however, is generally limited to multiplanar assessment of two-dimensional images. The volume rendering technique provides an excellent three-dimensional demonstration of external morphology but offers little information about the intracardiac anatomy. The alternative approach of virtual cardiac dissection, which is a modification of volume rendering, on the other hand, provides crucial insights regarding the intracardiac anatomy. At

present, virtual cardiac dissection requires expensive software packages. These software packages are not available in all countries, thus limiting its use in routine clinical care. We present here the details of a newly developed technique that permits virtual cardiac dissection using a personal computer and open-source software. Our technique involves no additional cost and can be achieved in the comfort of the office or operating room of the cardiologist, radiologist, or cardiac surgeon. This enhanced three-dimensional visualization of intracardiac anatomy will surely improve the understanding of the morphological details of both normal and malformed hearts. In addition, by permitting assessment in projections with which modern-day cardiologists and cardiac surgeons are conversant, it is likely to improve clinical decision-making. We illustrate here its potential utility in the morphologic assessment of the atrial septum and its deficiencies, along with malformations of the ventricular outflow tracts, including common arterial trunk.

DOI: 10.4103/apc.APC_167_18

PMCID: PMC6521663

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INTRODUCTION: Pregnancy is characterised by a high rate of metabolic shifts from early to late phases of gestation in order to meet the raised physiological and metabolic needs. This change in levels of metabolites is influenced by gestational weight gain (GWG), which is an important characteristic of healthy pregnancy. Inadequate/excessive GWG has short-term and long-term implications on maternal and child health. Exploration of gestational metabolism is required for understanding the quantitative changes in metabolite levels during the course of pregnancy. Therefore, our aim is to study trimester-specific variation in levels of metabolites in relation to GWG and its influence on fetal growth and newborn anthropometric traits at birth.

METHODS AND ANALYSIS: A prospective longitudinal study is planned (start date: February 2018; end date: March 2023) on pregnant women that are being recruited in the first trimester and followed in subsequent trimesters and at the time of delivery (total 3 follow-ups). The study is being conducted in a hospital located in Bikaner district (66% rural population), Rajasthan, India. The estimated sample size is of 1000 mother-offspring pairs. Information on gynaecological and obstetric history, socioeconomic position, diet, physical activity, tobacco and alcohol consumption, depression, anthropometric measurements and blood samples is being collected for metabolic assays in each trimester using standardised methods. Mixed effects regression models will be used to assess the role of gestational weight in influencing metabolite levels in each trimester. The association of maternal levels of metabolites with fetal growth, offspring's weight and body composition at birth will be investigated using regression modelling.

ETHICS AND DISSEMINATION: The study has been approved by the ethics committees of the Department of Anthropology, University of Delhi and Sardar Patel Medical College, Rajasthan. We are taking written informed consent after discussing the various aspects of the study with the participants in the local language.

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30724000.

Maffucci syndrome is characterized by multiple benign vascular anomalies and enchondromas present on the distal extremities. Effective treatment options are currently not available for Maffucci syndrome-associated vascular lesions. Sirolimus is a mTOR pathway inhibitor, and has been tried successfully in the treatment of various vascular anomalies. We treated a 23-year-old female with Maffucci syndrome-associated spindle cell hemangiomas with oral sirolimus (2mg/day, 0.04mg/kg/day). There was improvement in pain, but no change in colour or size of the vascular nodules. In view of unsatisfactory response and treatment-related adverse effects (oral aphthae, mild transaminitis), sirolimus was stopped after 6 months.

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DOI: 10.1111/dth.12851
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This article presents the case of a 3-month-old male child, who while on bolus jejunostomy tube feeds, developed recurrent episodes of hypoglycaemia. This infant had presented with failure to thrive with moderate gastroesophageal reflux necessitating a feeding jejunostomy. The infant was started on bolus feeds through the jejunostomy tube but developed recurrent episodes of hypoglycaemia. On evaluation, these episodes were hyperinsulinaemic and the baby was subsequently diagnosed with a late dumping syndrome. On changing the feeds to a continuous infusion and by eliminating added sugar from the feeds, the glucose fluctuations resolved. Dumping syndrome is a well-known complication in adults undergoing gastric surgeries. In the paediatric age group, dumping syndrome has been reported rarely, most commonly as a complication of Nissen fundoplication.

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49: Jain D, Nambirajan A, Borczuk A, Chen G, Minami Y, Moreira AL, Motoi N, Papotti M, Rekhtman N, Russell PA, Savic Prince S, Yatabe Y, Bubendorf L; IASLC Pathology Committee. Immunocytochemistry for predictive biomarker testing in lung cancer cytology. *Cancer Cytopathol*. 2019 May;127(5):325-339. doi: 10.1002/cncy.22137. Epub 2019 May 3. Review. PubMed PMID: 31050216.

With an escalating number of predictive biomarkers emerging in non-small cell lung carcinoma (NSCLC), immunohistochemistry (IHC) is being used as a rapid and cost-effective tool for the screening and detection of many of these markers. In particular, robust IHC assays performed on formalin-fixed, paraffin-embedded (FFPE) tumor tissue are widely used as surrogate markers for ALK and ROS1 rearrangements and for detecting programmed death ligand 1 (PD-L1) expression in patients with advanced NSCLC; in addition, they have become essential for treatment decisions. Cytology samples represent the only source of tumor in a significant proportion of patients with inoperable NSCLC, and there is increasing demand for predictive biomarker testing on them. However, the wide variation in

the types of cytology samples and their preparatory methods, the use of alcohol-based fixatives that interfere with immunochemistry results, the difficulty in procurement of cytology-specific controls, and the uncertainty regarding test validity have resulted in underutilization of cytology material for predictive immunocytochemistry (ICC), and most cytopathologists limit such testing to FFPE cell blocks (CBs). The purpose of this review is to: 1) analyze various preanalytical, analytical, and postanalytical factors influencing ICC results; 2) discuss measures for validation of ICC protocols; and 3) summarize published data on predictive ICC for ALK, ROS1, EGFR gene alterations and PD-L1 expression on lung cancer cytology. Based on our experience and from a review of the literature, we conclude that cytology specimens are in principal suitable for predictive ICC, but proper optimization and rigorous quality control for high-quality staining are essential, particularly for non-CB preparations.

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PMID: 31050216

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Hyoid bone syndrome is a type of cervicofacial pain that is caused by degeneration of the greater cornu of the hyoid at the attachment of the stylohyoid ligament. We report four patients who presented with deep-seated, dull, aching, temporomandibular (TMJ) pain that radiated from the greater cornu of the hyoid bone and did not respond to conservative management. Diagnostic tests included a local anaesthetic block and digital palpation of the greater cornu of the hyoid bone. All four patients responded well to methylprednisolone 40mg/ml at the greater cornu of the hyoid bone, which resulted in complete resolution of their symptoms. No patients developed postoperative complications. Oral and maxillofacial surgeons involved in the treatment of orofacial pain should consider this less documented condition in their differential diagnosis when treating temporomandibular disorders.

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DOI: 10.1016/j.bjoms.2019.01.022

PMID: 31054794

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BACKGROUND: The health and economic consequences of alcohol consumption have been assessed mainly in developed countries. This study aims to estimate health impact and economic burden attributable to alcohol use in India.

METHODS: A combination of decision tree and mathematical markov model was parameterized to assess the health effects and economic cost attributable to alcohol consumption. Health effect of alcohol was modelled for a time period of 2011 to 2050 on three sets of conditions - liver disease, cancers and road traffic accidents. Estimates of illness, death, life years lost and quality adjusted life years (QALYs) gained were estimated as a result of alcohol consumption. Both direct and indirect costs were estimated to determine economic burden. Future costs and consequences were discounted at 3% for time preferences of cost and utility. Uncertainties in parameters were assessed using probabilistic sensitivity analysis.

RESULTS: Between 2011 and 2050, alcohol attributable deaths would lead to a loss of 258 million life years. In contrast, 552 million QALYs would be gained by eliminating alcohol consumption. Treatment of these conditions will impose an economic burden of INR 3127 billion (US\$ 48.11 billion) on the health system. Societal burden of alcohol, inclusive of health system cost, out of pocket expenditure and productivity losses will be INR 121,364 billion (US\$ 1867 billion). Even after adjusting for tax receipts from sale of alcohol, alcohol poses a net economic loss of INR 97,895 billion (US\$ 1506 billion). This amounts to an average loss of 1.45% of the gross domestic product (GDP) per year to the Indian economy.

CONCLUSION: Alcohol causes significant negative health impact and economic burden on Indian society and evidence informed policy interventions are needed to control alcohol attributable harm.

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DOI: 10.1016/j.drugpo.2019.04.005

PMID: 31055044

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Platelets play a major role in primary hemostasis and thrombus formation. After vascular injury, platelets adhere to injured site and rapidly change their shape that switches the resting platelets to active state. Activated platelets aggregate and secrete biologically active intermediate substances that further potentiate platelet activation through autocrine as well as paracrine mechanisms. The activated platelet expresses certain proteins that are not seen on the resting platelets, thus these proteins serve as markers of platelet activation. Other subsequent events of platelet activation include release of microvesicles and formation of complexes with other circulating cells, like monocytes and neutrophils. Platelet activation markers are useful tools in evaluating risk factors of thrombosis in a variety of clinical conditions. Increased platelet activation has been associated with various pathological conditions such as acute coronary syndrome, stroke, peripheral vascular disease and other inflammatory diseases. The advancement in technologies helps in determining the status of platelet activation in such clinical conditions. This article focuses on the sources, mechanism and diagnosis of platelet activation and their clinical implications.

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DOI: 10.1016/j.blre.2019.05.007

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Anemia is a major public health problem in India with prevalence of more than 50% amongst children and adolescents. The decline in the burden of anemia has been insignificant over the past 5 decades. The present review assesses the National Guidelines for Prevention and Control of Anemia in India, the current status of the program implementation and possible reasons for the continued high prevalence of anemia in the country.

DOI: 10.1007/s12098-019-02932-5

PMID: 31079321

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OBJECTIVE: Orthodontic force application releases multiple enzymes in gingival crevicular fluid (GCF) for activation, resorption, reversal, deposition of osseous elements and extracellular matrix degradation. The current systematic review critically evaluated all existing evidence on enzymes in orthodontic tooth movement.

METHODS: Literature was searched with predetermined search strategy on electronic databases (PubMed, Scopus, Embase), along with hand search.

RESULTS: Initial search identified 652 studies, shortlisted to 52 studies based on PRISMA. Quality assessment further led to final inclusion of 48 studies (13 moderately and 35 highly sensitive studies). Primary outcomes are significant upregulation in GCF levels of enzymes-aspartate aminotransferase (AST), alkaline phosphatase (ALP), matrix metalloproteinases (MMPs), lactate dehydrogenase (LDH), β -glucuronidase (β G), tartrate resistant acid phosphatase (TRAP), acid phosphatase (ACP) and down regulation in cathepsin B (Cb). Site specificity is shown by ALP, TRAP, AST, LDH, MMP9 with levels at compression site increasing earlier and in higher quantities compared with tension site. ALP levels are higher at tension site only in retention. A positive correlation of LDH, ALP and AST is also observed with increasing orthodontic force magnitude.

CONCLUSIONS: A strong evidence of variation in enzymes (ALP, AST, ACP TRAP, LDH, MMPs, Cb) in GCF is found in association with different magnitude, stages and sites of orthodontic force application.

DOI: 10.1590/2177-6709.24.2.40.e1-22.onl

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In this study, we examined the relative immune response of T-lymphocytes and its intracellular cholesterol homeostasis, in a mouse model system, after treatment with immunogen, mitogen, and carcinogen. We studied the T-lymphocyte percentage, their LDL-receptor expression, along with the levels of serum interleukins (IL-2, IFN γ , IL-4, and IL-10) and intracellular cholesterol concentration (cytoplasmic and nuclear). The mitogen was found to be a better stimulator of T-cell marker expressions than the immunogen; though the immunogen was more effective on immunogenic response as was marked from interleukin levels. The chemical carcinogen benzo- α -pyrene at low concentration acted potentially like a mitogen but a reduced immune response was apparent at a carcinogenic dose. The findings in our study focus on the effect of carcinogenic dose of benzo- α -pyrene (BaP) on T-cell immunity. Benzo- α -pyrene causes immunosuppression through restriction of the T-cell population by targeting intracellular cholesterol.

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PMID: 30664314 [Indexed for MEDLINE]

58: Kaur K, Jha P, Pathak P, Suri V, Sharma MC, Garg A, Suri A, Sarkar C. Approach to molecular subgrouping of medulloblastomas: Comparison of NanoString nCounter assay versus combination of immunohistochemistry and fluorescence in-situ hybridization in resource constrained centres. *J Neurooncol*. 2019 Jul;143(3):393-403. doi: 10.1007/s11060-019-03187-y. Epub 2019 May 18. PubMed PMID: 31104222.

INTRODUCTION: Molecular classification of medulloblastomas (MB) is prognostically and therapeutically relevant and helps in better risk-stratification. Translation of this subgrouping to routine practice still remains a challenge. The most pathologist accessible techniques for molecular subgrouping include immunohistochemistry (IHC), fluorescent in-situ hybridization (FISH) and NanoString.

OBJECTIVES: (1) Molecular subgrouping of MBs by IHC and FISH, and NanoString assay (2) To compare their efficacy and cost for applicability in resource constrained centers.

METHODS: Ninety-five cases of MB with adequate tissue were included. Molecular subgrouping was performed by IHC for β -catenin, GAB1 and YAP1; FISH for MYC amplification, and sequencing for CTNNB1, and by NanoString Assay on the same set of MBs. A subset of cases was subjected to 850k DNA methylation array.

RESULTS: IHC+FISH classified MBs into 15.8% WNT, 16.8% SHH, and 67.4% non-WNT/non-SHH subgroups; with MYC amplification identified in 20.3% cases of non-WNT/non-SHH. NanoString successfully classified 91.6% MBs into 25.3% WNT, 17.2% SHH, 23% Group 3 and 34.5% Group 4. However, NanoString assay failure was seen in eight cases, all of which were >8-years-old formalin-fixed paraffin-embedded tissue blocks. Concordant subgroup assignment was noted in 88.5% cases, while subgroup switching was seen in 11.5% cases. Both methods showed prognostic correlation. Methylation profiling performed on discordant cases revealed 1 out of 4 extra WNT identified by NanoString to be WNT, others aligned with IHC subgroups; extra SHH by NanoString turned out to be SHH by methylation.

CONCLUSIONS: Both IHC supplemented by FISH and NanoString are robust methods for molecular subgrouping, albeit with few disadvantages. IHC cannot differentiate between Groups 3 and 4, while NanoString cannot classify older-archived tumors, and is not available at most centres. Thus, both the methods complement each other and can be used in concert for high confidence allotment of molecular subgroups in clinical practice.

DOI: 10.1007/s11060-019-03187-y

PMID: 31104222

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OBJECTIVE: Extranodal natural killer/T-cell lymphoma, nasal type (ENKTL) is an aggressive extranodal lymphoma of NK-cell or T-cell lineage. Its clinical features overlap with those of several sinonasal mass lesions. While the histopathological features are well described, diagnosis is often difficult, owing to presence of extensive coagulative necrosis, so that repeated biopsies may sometimes be necessary for correct diagnosis. Literature on cytological findings of ENKTL is limited.

METHODS: Cytomorphological features of cases of histologically confirmed ENKTL having corresponding cytology samples were reviewed retrospectively, to identify distinctive features that could possibly suggest this entity.

RESULTS: Aspirates from five patients were studied: four from cervical nodes, one from cheek swelling and one from pleural fluid. Two aspirates were reported as positive for malignancy, two as atypical lymphoid proliferation and one was non-diagnostic. Pleural fluid was reported as malignant, favouring a diagnosis of carcinoma. On cytology, aspirates showed medium to large cells with folded, indented nuclei and abundant pale cytoplasm, some with tongue-like cytoplasmic protrusions. A distinctive feature was presence of large loose clusters of tumour cells with arborising capillaries running through them. Interestingly, necrosis was consistently absent. Subsequent biopsies from palate (three cases) and nasal masses (two cases) confirmed the diagnosis of ENKTL.

CONCLUSIONS: Suspicion of ENKTL on cytology is crucial for timely diagnosis to avoid diagnostic delay, especially when only highly necrotic biopsy samples are available. Awareness of distinctive cytomorphological features is required to make fine needle aspiration an effective diagnostic tool for initial diagnosis

and for evaluation of possible recurrences.

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PMID: 30980430

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Skeletal muscle atrophy/wasting is associated with impaired protein metabolism in diverse physiological and pathophysiological conditions. Elevated levels of reactive oxygen species (ROS), disturbed redox status, and weakened antioxidant defense system are the major contributing factors toward atrophy. Regulation of protein metabolism by controlling ROS levels and its associated catabolic pathways may help in treating atrophy and related clinical conditions. Although cinnamaldehyde (CNA) enjoys the established status of antioxidant and its role in ROS management is reported, impact of CNA on skeletal muscle atrophy and related pathways is still unexplored. In the current study, the impact of CNA on C2C12 myotubes and the possible protection of cultured cells from H₂O₂-induced atrophy is examined. Myotubes were treated with H₂O₂ in the presence and absence of CNA and the changes in the antioxidative, proteolytic systems, and mitochondrial functions were scored. Morphological analysis showed significant protective effects of CNA on length, diameter, and nuclei fusion index of myotubes. The evaluation of biochemical markers of atrophy; creatine kinase, lactate dehydrogenase, succinate dehydrogenase along with the study of muscle-specific structural protein (i.e., myosin heavy chain-fast [MHCf] type) showed significant protection of proteins by CNA. CNA pretreatment not only checked the activation of proteolytic systems (ubiquitin-proteasome E3-ligases [MuRF1/Atrogin1]), autophagy [Beclin1/LC3B], cathepsin L, calpain, caspase), but also prevented any alteration in the activities of antioxidative defense enzymes (catalase, glutathione-S-transferase, glutathione-peroxidase, superoxide dismutase, glutathione reductase). The results suggest that CNA protects myotubes from H₂O₂-induced atrophy by inhibiting/resisting the amendments in proteolytic systems and maintains cellular redox-balance.

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PMID: 30317570

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Purpose: To prospectively evaluate the diagnostic yield of multiparametric magnetic resonance imaging (mpMRI)-fusion, transrectal ultrasound (TRUS)-guided prostate biopsies for detection of prostate cancer in an Asian population with a low incidence of prostate cancer.

Materials and Methods: A total of 131 males with suspected prostate cancer were recruited to undergo fusion biopsy with the Artemis prostate fusion biopsy device (Eigen, Grass Valley, CA, USA). All patients underwent standard 12-core systematic biopsies in addition to biopsies targeted at the mpMRI-identified abnormal regions. Yield from the standard cores was compared with that from the targeted cores. Gleason scores of 4+3 or higher were considered significant.

Results: The mean age of the patients was 63.54±7.96 years and the mean prostate-specific antigen value was 9.75±5.35 ng/mL. A total of 36 patients had cancer, of which 3 (8.3%) were detected only on standard cores and 3 (8.3%) only on targeted cores. Of the clinically significant cancers (n=30), targeted biopsy detected a higher number (28/30, 93.3%) than standard biopsy (21/30, 70.0%). A total of 6 of 8 cancers (75.0%) that were insignificant on standard biopsy were upgraded to significant cancer on targeted cores.

Conclusions: Eight percent of cancers were detected only on MRI-TRUS fusion-targeted biopsies, whereas the method upgraded more than two-thirds of insignificant cancers to significant cancers. Fusion biopsies thus provide incremental information over standard TRUS biopsies in the diagnosis of significant prostate cancer in populations with a low incidence of prostate cancer.

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PMCID: PMC6495042

PMID: 31098422

63: Khanna U, Khandpur S. What Is New in Narrow-Band Ultraviolet-B Therapy for Vitiligo? *Indian Dermatol Online J.* 2019 May-Jun;10(3):234-243. doi: 10.4103/idoj.IDOJ_310_18. Review. PubMed PMID: 31149564; PubMed Central PMCID: PMC6536079.

Vitiligo is an acquired disorder of skin pigmentation that produces significant psychological impact especially in those with skin of color. Narrow-band ultraviolet B (NB-UVB) therapy, which was first used in vitiligo in 1997 by Westerhof and Nieuweboer-Krobotova, has emerged as one of the safest and most effective therapy for this dermatosis. The light source used for NB-UVB phototherapy is the TL-01 lamp, and the most common model of the NB-UVB phototherapy device is the upright in-office booth or chamber which has 24-48 such lamps. In recent years, there have been several advances in the understanding of the mechanism of action of NB-UVB and the use of combination treatments, many of which increase the efficacy of NB-UVB. In 2017, the Vitiligo Working Group made vital recommendations on the dosage, frequency, and safety of NB-UVB in vitiligo. Furthermore, home phototherapy devices are gaining popularity as they lead to an improved patient compliance. There is still need for large multicenter randomized controlled trials to assess benefits of home phototherapy in vitiligo and studies investigating additional benefits of phototherapy following surgical therapy.

DOI: 10.4103/idoj.IDOJ_310_18

PMCID: PMC6536079

PMID: 31149564

64: Khokhar S, Sen S, Dhull C. Active-fluidics-based torsional phacoemulsification in diabetic eyes: A prospective interventional study. *Indian J Ophthalmol.* 2019 May;67(5):619-624. doi: 10.4103/ijo.IJO_1146_18. PubMed PMID: 31007221; PubMed Central PMCID: PMC6498917.

Purpose: To compare the outcomes of active-fluidics based torsional phacoemulsification in diabetics and nondiabetics using a balanced tip. Methods: Two hundred and forty-eight patients undergoing senile cataract surgery using torsional phacoemulsification on an active-fluidics-based platform from December 2016 to August 2017 were included in this prospective, nonrandomized, interventional cohort study; of the 248 patients, 54 were controlled diabetics and 194 were nondiabetics. Intraoperative parameters such as cumulative dissipated energy (CDE), total ultrasound time, torsion usage time, torsion amplitude, aspiration time, and fluid usage were documented and compared. Endothelial cell loss (ECL) and central corneal thickness (CCT) were evaluated at 1 month postoperatively.

Results: Diabetics and nondiabetics did not differ in CDE, total ultrasound time, torsion amplitude, aspiration time, fluid usage, endothelial cell count, and CCT. ECL on Day 1 (10.2 ± 8.0%) and Day 30 (11.05 ± 8.3%) were significantly higher in diabetics (P = 0.025 and P = 0.045, respectively). There was an increase in CCT

on Day 1 ($P = 0.018$), which settled by Day 30. Grade 4 cataracts in diabetics had significantly higher CCT at Day 1 ($P = 0.032$) and Day 30 ($P = 0.007$). In the diabetic subgroup, Grades 3 and 4 cataracts required lower CDE ($P < 0.001$) and Grade 4 cataracts showed higher ECL than others till 1 month of follow-up ($P < 0.05$).

Conclusion: Intraoperative and postoperative parameters after torsional phacoemulsification are comparable in diabetics and nondiabetics. Endothelial changes and pachymetry may be related to the grade of cataract in diabetics.

DOI: 10.4103/ijo.IJO_1146_18

PMCID: PMC6498917

PMID: 31007221

65: 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 May 22. doi: 10.1097/SLE.0000000000000682. [Epub ahead of print] 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

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67: Kumar A, Das S, Chauhan S, Kiran U, Satapathy S. Perioperative Anxiety and Stress in Children Undergoing Congenital Cardiac Surgery and Their Parents: Effect of Brief Intervention-A Randomized Control Trial. J Cardiothorac Vasc Anesth. 2019 May;33(5):1244-1250. doi: 10.1053/j.jvca.2018.08.187. Epub 2018 Aug 22. PubMed PMID: 30243867.

OBJECTIVE: To know the effects of psychological preparation on perioperative stress, anxiety, and mood in children undergoing cardiac surgery and their parents.

DESIGN: Prospective randomized control nonblinded trial.

SETTING: Single-center tertiary teaching hospital.

PARTICIPANTS: A total of 60 children aged 5 to 15 years undergoing cardiac surgery were included in the study. One of the parents, preferably the father, was selected from the respective children.

INTERVENTIONS: Subjects were randomized into 2 groups: noninterventional (group 1) and interventional (group 2). Intervention was in the form of toys and video games in children, and counseling and information in parents. Preoperative and postoperative anxiety in parents was measured using the State-Trait Anxiety Inventory (STAI), stress using the Index of Clinical Stress (ICS) scale by Abell, and the Ottawa mood scale. In children, the STAI-C (child version of STAI), Ottawa mood and Ottawa stress scales, and Wong-Baker faces pain scale were applied and serum cortisol was measured.

MEASUREMENTS AND MAIN RESULTS: Group 2 children had significantly less ($p < 0.001$) stress, anxiety, and pain and improved mood. Group 2 parents had a significant reduction in state anxiety (42 ± 4.4 v 54.5 ± 7.8 ; $p < 0.001$) and ICS score (68.1 ± 9.6 v 84.2 ± 9.2 ; $p < 0.001$) and an improvement in mood (7.5 ± 0.7 v 5.9 ± 1 ; $p < 0.001$) compared with group 1. Postoperatively, cortisol levels in group 2 were lower than group 1 (571.3 nmol/L [123.3 - 1247.14] v 718.9 nmol/L [53 - 1642.0]).

CONCLUSION: Providing video games and toys preoperatively reduced postoperative stress and anxiety and improved mood in children undergoing congenital cardiac surgery. Parents were relieved of anxiety and stress with proper counseling and information.

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DOI: 10.1053/j.jvca.2018.08.187

PMID: 30243867

68: Kumar B, Jensen MM, Strielkowski W, Johnston JT, Sharma V, Dandara C, Shehata MM, Struett MM, Nikolaou A, Szymanski DW, Abdul-Ghani R, Cao B, Varzinczak LH, Kerman BE, Arthur PK, Oda FS, Bohon W, Ellwanger JH, Tyner S, Jordan EJ, Murphy C. NextGen Voices: Science-inspired sustainable behavior. *Science*. 2019 May 31;364(6443):822-824. doi: 10.1126/science.aax8945. PubMed PMID: 31147504.

69: Kumar P, Misra P, Yadav NK, Joshi S, Sahasrabudde AA, Dube A, Rishi N, Mitra DK. Prophylactic interferon- γ and interleukin-17 facilitate parasite clearance in experimental visceral leishmaniasis. *Trop Parasitol*. 2019 Jan-Jun;9(1):30-35. doi: 10.4103/tp.TP_32_18. Epub 2019 May 22. PubMed PMID: 31161090; PubMed Central PMCID: PMC6542311.

Background and Objective: The synergy of interleukin (IL)-17 along with other pro-inflammatory cytokines is well known in various autoimmune and infectious diseases. A longitudinal study in the Sudanese population showed an association of IL-17 with the protection of kala-azar outbreak. The protective role of IL-17 is also known in terms of expansion of IL-17-producing cells in vaccine-induced immunity. However, the prophylactic role of IL-17 in visceral leishmaniasis has still not been validated. In the present study, we evaluated the prophylactic efficacy of IL-17A and interferon (IFN)- γ in *Leishmania donovani*-challenged Balb/c mice.

Materials and Methods: Two doses of recombinant IL (rIL)-17A and/or IFN- γ were administered intraperitoneally after/at 1 week interval and then the mice were challenged with amastigote form of *L. donovani*. At 45 days of postchallenge, mice were sacrificed and evaluated for change in the body and organ weight, parasitic load in visceral organs, and fold change in gene expression of cytokines.

Results: We observed that the prophylactic use of rIL-17A and IFN- γ alone or in combination significantly inhibited the parasitic load in visceral organs. Furthermore, pro-inflammatory cytokine gene expression increased up to 2-4-folds in mice treated with recombinant cytokines.

Conclusion: Our results suggest that prophylactic use of recombinant IFN- γ and IL-17A inhibits parasitic growth in visceral organs of *L. donovani*-challenged experimental mice model, especially through upregulation of pro-inflammatory cytokines' gene expression.

DOI: 10.4103/tp.TP_32_18
PMCID: PMC6542311
PMID: 31161090

70: Kumar P, Malla S, Singh A, Razik A, Madhusudhan KS. Demystifying the mesenteric root lesions. *Abdom Radiol (NY)*. 2019 Aug;44(8):2708-2720. doi: 10.1007/s00261-019-02053-9. Epub 2019 May 11. Review. PubMed PMID: 31079195.

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

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72: Kumari S, Deka D, Dadhwal V, Perumal V. Correlation of fetal blood vessel Doppler measurements with fetal anemia among Rhesus isoimmunized pregnancies after two intrauterine transfusions. *Int J Gynaecol Obstet*. 2019 Aug;146(2):218-222. doi: 10.1002/ijgo.12825. Epub 2019 May 7. PubMed PMID: 31004522.

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.

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DOI: 10.1002/ijgo.12825
PMID: 31004522

73: Kumawat D, Alam T, Sahay P, Chawla R. Ocular abnormalities and complications

in anterior megalophthalmos: a case series. *Eye (Lond)*. 2019 May;33(5):826-832. doi: 10.1038/s41433-018-0329-3. Epub 2019 Jan 7. PubMed PMID: 30617289.

OBJECTIVES: To describe the clinical and Scheimpflug imaging features in cases of anterior megalophthalmos (AM).

METHODS: Retrospective record review was performed for patients with AM who presented between June 2017 and May 2018. Clinical history, slit lamp examination, Scheimpflug imaging indices (Pentacam-HR, Oculus, GmbH), dilated fundus examination and treatment records were reviewed.

RESULTS: The study included eight eyes of four male patients (mean age 6.5 years, range 4-10 years). Corrected distance visual acuity ranged from finger counting to 20/80. The mean horizontal corneal diameter, central corneal thickness, steep keratometry, flat keratometry, anterior chamber (AC) angle, AC depth, maximum pupil diameter and axial length were 13.8 ± 0.5 mm, 538.7 ± 68.9 µm, 42.8 ± 1.6 D, 41.4 ± 0.9 D, 47.0 ± 4.2 degree, 3.8 ± 0.3 mm, 3.9 ± 0.1 mm, and 24.9 ± 0.9 mm, respectively. Posterior dislocation of crystalline lens, vitreous degeneration and rhegmatogenous retinal detachment (consequent of retinal dialysis/atrophic hole/lattice with hole) were noted in seven, eight and five eyes, respectively. Pigment dispersion glaucoma was noted in both eyes of one patient, which was managed with topical anti-glaucoma medication. Vitrectomy with silicone oil tamponade was successful in retinal reattachment in all three eyes that underwent surgery.

CONCLUSION: Scheimpflug imaging helps in demonstrating the corneal and anterior segment pathological changes in AM. The disease extends to involve the zonules, vitreous and retina as well. Ophthalmologists should be able to identify this disorder, recognise and manage the associations and complications.

DOI: 10.1038/s41433-018-0329-3
PMID: 30617289

74: Kumawat D, Kumar V. Resolution of arterial aneurysms in idiopathic retinal vasculitis, aneurysms and neuroretinitis: a case report and review of literature. *Int Ophthalmol*. 2019 May;39(5):1155-1161. doi: 10.1007/s10792-018-0913-3. Epub 2018 Mar 28. Review. PubMed PMID: 29594790.

PURPOSE: To report a case of resolution of retinal arterial aneurysms in a patient of idiopathic retinal vasculitis, aneurysms and neuroretinitis (IRVAN) treated with oral steroids.

METHODS: This study contains case report and review of literature.

RESULTS: A 16-year-old girl with stage 2 IRVAN was treated with oral steroids alone. Fluorescein angiography confirmed the presence of aneurysms and absence of neovascularization in both eyes. The aneurysms resolved gradually over 4-month follow-up.

CONCLUSIONS: This case demonstrates previously unreported reversibility of arterial aneurysms with steroid therapy alone in early stages of IRVAN.

DOI: 10.1007/s10792-018-0913-3
PMID: 29594790 [Indexed for MEDLINE]

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BACKGROUND: Sleeping under insecticide-treated mosquito nets/long-lasting insecticidal nets (ITNs/LLINs henceforth referred to as ITNs) is one of the core interventions recommended by the World Health Organization to reduce malaria transmission and prevent malaria in high-risk communities, such as migrants, by preventing mosquito bites. The malaria burden among the migrant population is a big challenge for malaria elimination in Myanmar. In this context, this study aimed to assess the ownership and utilization of ITNs and to understand the barriers to distribution and utilization of ITNs among the high-risk migrant communities in the Regional Artemisinin Resistance Initiative (RAI) project areas

of Myanmar.

METHODS: A sequential mixed methods study (quantitative component: cross-sectional study involving analysis of secondary data available from a survey conducted among migrant households in the RAI project areas of Myanmar in 2016 followed by a descriptive qualitative component in 2018). A total of 17 focus group discussions (involving 121 participants) with different groups of migrants and 17 key-informant interviews with key programme stakeholders were conducted in 4 selected townships of RAI project areas.

RESULTS: Of 3230 migrant households, 63.3% had at least one ITN while 36% had sufficient ITNs (i.e., 1 ITN per 2 persons). Regarding ITN utilization, about 52% of household members reported sleeping under an ITN the previous night, which is similar among under-fives and pregnant women. Over half of all bed nets were ITNs, with nearly one-third having holes or already undergone repairs. The qualitative findings revealed that the key challenges for ITN utilization were insufficient ITNs in households and dislike of ITNs. The barriers to ITN distribution were incomplete migrant mapping due to resource constraints (time, money, manpower) and difficulties in transportation and carrying ITNs.

CONCLUSION: This study highlights poor ownership and utilization of ITNs among migrants in the RAI project areas of Myanmar and barriers to their ownership and utilization. To achieve universal coverage and utilization, more programmatic support by the programme is needed to carry out complete migrant mapping and continuous ITN distribution in remote locations.

DOI: 10.1186/s12936-019-2800-4

PMCID: PMC6518764

PMID: 31088451

76: Lopes BA, Meyer C, Barbosa TC, Poubel CP, Mansur MB, Duployez N, Bashton M, Harrison CJ, Zur Stadt U, Horstmann M, Pombo-de-Oliveira MS, Palmi C, Cazzaniga G, Venn NC, Sutton R, Alonso CN, Tsaour G, Gupta SK, Bakhshi S, Marschalek R, Emerenciano M. IKZF1 Deletions with COBL Breakpoints Are Not Driven by RAG-Mediated Recombination Events in Acute Lymphoblastic Leukemia. *Transl Oncol.* 2019 May;12(5):726-732. doi: 10.1016/j.tranon.2019.02.002. Epub 2019 Mar 13. PubMed PMID: 30877974; PubMed Central PMCID: PMC6423364.

IKZF1 deletion (Δ IKZF1) is an important predictor of relapse in both childhood and adult B-cell precursor acute lymphoblastic leukemia (B-ALL). Previously, we revealed that COBL is a hotspot for breakpoints in leukemia and could promote IKZF1 deletions. Through an international collaboration, we provide a detailed genetic and clinical picture of B-ALL with COBL rearrangements (COBL-r). Patients with B-ALL and IKZF1 deletion (n=133) were included. IKZF1 Δ 1-8 were associated with large alterations within chromosome 7: monosomy 7 (18%), isochromosome 7q (10%), 7p loss (19%), and interstitial deletions (53%). The latter included COBL-r, which were found in 12% of the IKZF1 Δ 1-8 cohort. Patients with COBL-r are mostly classified as intermediate cytogenetic risk and frequently harbor ETV6, PAX5, CDKN2A/B deletions. Overall, 56% of breakpoints were located within COBL intron 5. Cryptic recombination signal sequence motifs were broadly distributed within the sequence of COBL, and no enrichment for the breakpoint cluster region was found. In summary, a diverse spectrum of alterations characterizes Δ IKZF1 and they also include deletion breakpoints within COBL. We confirmed that COBL is a hotspot associated with Δ IKZF1, but these rearrangements are not driven by RAG-mediated recombination.

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DOI: 10.1016/j.tranon.2019.02.002

PMCID: PMC6423364

PMID: 30877974

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

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

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PMID: 30820981 [Indexed for MEDLINE]

78: Madan K, Mittal S, Hadda V, Mohan A. Cryoprobe transbronchial lung biopsy with flexible bronchoscope using Arndt endobronchial blocker. *Lung India*. 2019 May-Jun;36(3):241-243. doi: 10.4103/lungindia.lungindia_35_18. PubMed PMID: 31031348; PubMed Central PMCID: PMC6503724.

Cryoprobe transbronchial lung biopsy (TBLB)/transbronchial lung cryobiopsy (TBLC) is increasingly being described as an alternative to surgical lung biopsy and provides larger lung biopsy samples as compared with conventional TBLB in patients with diffuse parenchymal lung diseases. The technique for cryoprobe TBLB procedure has not yet been standardized, and various authors describe different modalities. However, the use of an artificial airway (rigid bronchoscope or endotracheal tube) is preferred for airway protection. In addition, the use of an occlusion balloon provides safety to prevent excessive bleeding. The exclusive use of rigid bronchoscopy may limit the widespread adoption of this diagnostic modality. We describe a method to perform cryoprobe TBLB with exclusive use of a flexible bronchoscope and utilization of Arndt endobronchial blocker as an occlusion balloon. The procedure was performed in two patients under moderate conscious sedation. Adequate lung biopsies were obtained in both the cases without any complications. This modality may allow safe performance of cryoprobe TBLB with a flexible bronchoscope. Herein, we describe the technical and procedural considerations of this modality.

DOI: 10.4103/lungindia.lungindia_35_18

PMCID: PMC6503724

PMID: 31031348

79: Madasu S, Malhotra S, Kant S, Sagar R, Mishra AK, Misra P, Ahamed F. Prevalence and determinants of anxiety disorders among adolescents in a rural community from northern India. *Asian J Psychiatr*. 2019 May 3;43:137-142. doi: 10.1016/j.ajp.2019.05.009. [Epub ahead of print] PubMed PMID: 31146170.

INTRODUCTION: There is scarce data available on community based prevalence of Anxiety Disorders (ADs) amongst adolescents in north Indian settings.

OBJECTIVE: To determine the prevalence of anxiety disorders, and associated factors amongst adolescents in a rural community of Ballabgarh block, district Faridabad, Haryana.

METHODS: Participants (10-19 years) were enrolled through simple random sequence from a sampling frame of adolescents residing in 28 villages of Ballabgarh block

using household survey technique. They were screened using Screen for Childhood Anxiety Related Emotional Disorders (SCARED) tool and then subjected to confirmatory diagnosis using Mini-International Neuropsychiatric Interview for Children/Adolescent (MINI KID). All adolescents with ADs were assessed for co-psychiatric morbidities using MINI-KID and functional impairment using Children Global Assessment Scale (CGAS). Prevalence and 95% Confidence intervals are reported. Additionally, socio-demographic factors were elicited using a semi-structured interview schedule and associations were determined using multivariable logistic regression analysis.

RESULTS: A total of 678 adolescents participated in this study with mean age (SD) as 14.2 (2.5) years. The age adjusted prevalence of anxiety disorders was found to be 16.6% (95% CI: 16.0-17.2). The most prevalent anxiety disorder among participants was social anxiety disorders followed by specific phobias. Female sex and low socio-economic status were associated with anxiety disorders. Two third of adolescents with ADs had no functional impairment and almost one third were found to have one or more co-existing psychiatric co-morbidity.

CONCLUSION: We found a high prevalence of ADs in rural north Indian community settings warranting adequate health system response at primary care level.

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PMID: 31146170

80: Mahapatra SJ, Jain S, Bopanna S, Gupta S, Singh P, Trikha A, Sreenivas V, Shalimar, Garg PK. Pentazocine, a Kappa-Opioid Agonist, Is Better Than Diclofenac for Analgesia in Acute Pancreatitis: A Randomized Controlled Trial. *Am J Gastroenterol.* 2019 May;114(5):813-821. doi: 10.14309/ajg.0000000000000224. PubMed PMID: 31008736.

OBJECTIVES: The ideal analgesic is not known for patients with acute pancreatitis (AP). Concerns have been raised about serious adverse effects of opioid analgesics increasing the severity of AP. We hypothesized that nonsteroidal anti-inflammatory drugs might be better analgesics because of their anti-inflammatory effect. Our objective was to compare pentazocine, an opioid, and diclofenac, a nonsteroidal anti-inflammatory drug, for adequate analgesia in patients with AP.

METHODS: In a double-blind randomized controlled trial, patients with AP were randomized to either intravenous diclofenac 75 mg or pentazocine 30 mg. Fentanyl was given as a rescue analgesic through a patient-controlled analgesia pump. Primary outcome was pain relief measured objectively by the dose of fentanyl required as the rescue analgesic, pain-free period, and numbers of effective and ineffective demands of fentanyl. Secondary outcome was adverse events.

RESULTS: Fifty patients were randomized, 24 to the pentazocine group and 26 to the diclofenac group. Baseline characteristics were comparable between the groups. Pentazocine was found to be better than diclofenac in terms of significantly lower dose of the rescue analgesic (fentanyl) required (126 µg (interquartile range (IQR) 65-218 µg) vs 225.5 µg (IQR 133-427 µg); P = 0.028) and longer pain-free period (31.1 ± 8.2 vs 27.9 ± 6.6 hours, P = 0.047). The number of effective and ineffective demands was lower in the pentazocine group compared with the diclofenac group (11.5 (IQR 8-15) vs 16 (IQR 13-20), P = 0.098) although not statistically significant. Adverse events were similar between the groups.

CONCLUSIONS: Pentazocine, a kappa-opioid receptor agonist, was significantly better than diclofenac for pain relief in AP (Trial registration number: CTRI/2016/09/007326).

DOI: 10.14309/ajg.0000000000000224

PMID: 31008736

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A 43-year-old man presented with acute onset rapidly progressive weakness in all four limbs (proximal greater than distal), following an episode of binge alcohol ingestion, and was admitted for evaluation and management. There was a history of decreased urine output since 2 days with dark-coloured urine. He was found to have severe hypokalemia and renal dysfunction. Serum creatine kinase was significantly high, and further investigation revealed significantly elevated serum and urine myoglobin levels suggestive of rhabdomyolysis, which was secondary to severe hypokalemia. Following supplementation with intravenous and oral potassium and supportive care, the weakness improved significantly, and he was subsequently discharged. This case describes severe hypokalemia, resulting in rhabdomyolysis and generalised lower motor neuron weakness, in a setting of binge alcohol ingestion, which is an entity rarely described in literature.

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DOI: 10.1136/bcr-2019-229307
PMID: 31126931

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84: Malhotra R, Gautam D. Acute total hip arthroplasty in acetabular fractures using modern porous metal cup. *J Orthop Surg (Hong Kong).* 2019 May-Aug;27(2):2309499019855438. doi: 10.1177/2309499019855438. PubMed PMID: 31221006.

PURPOSE: The aim of this study was to report the clinical and radiological outcome of using the modern porous metal cup in patients undergoing acute total hip arthroplasty (THA) for selected subset of acetabular fractures.

PATIENT AND METHODS: Eighteen patients with acetabular fracture underwent acute THA with modern porous metal cup from a single manufacturer. Fifteen males and three females with a mean age of 46.4 years (range 21-57 years) were ambispectively followed up for a minimum period of 48 months. All patients were evaluated clinically with Harris Hip Scores (HHS) and radiographically with serial X-rays.

RESULTS: No patient was lost to follow-up. The HHS was excellent in nine patients, good in six patients, fair in two patients, and poor in one patient. All the fractures were united and the cups were well integrated. There was no lucent line seen in any acetabular zones on the X-rays. One patient had infection, which resolved with debridement. There was one dislocation following fall, which was reduced by closed means and remained stable. One of the two patients with heterotopic ossification had restricted movement of hip but not restricting the activities of daily living. No failures of acetabular component were seen in the study.

CONCLUSION: The current study showed that the modern porous metal cup provides sufficient primary stability and appear suitable for primary THA in acute acetabular fractures at mid-term follow-up: (i) In selected fractures, acute THA can be extended to young adult patients as well. (ii) Modern porous metal cup may provide sufficient stability with or without additional fixation required.

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85: Malhotra R, Gautam D. Cup-Cage Construct Using Porous Cup with Burch-Schneider Cage in the Management of Complex Acetabular Fractures. *Hip Pelvis.* 2019 Jun;31(2):87-94. doi: 10.5371/hp.2019.31.2.87. Epub 2019 May 30.

PubMed PMID: 31198775; PubMed Central PMCID: PMC6546672.

Purpose: Cup-cage construct technique was developed to address the massive acetabular defects during revision hip arthroplasty. Indications have extended to complex acetabular fractures with pelvic discontinuity necessitating acute total hip arthroplasty. However, its use is constrained in low socioeconomic countries due to non-availability of the original cages from Trabecular Metal Acetabular Revision System and high cost. We used a novel technique using the less expensive Burch-Schneider (BS) cage and Trabecular Metal Revision Shell (TMRS) to address the problem.

Materials and Methods: We reviewed a consecutive series of 8 cases of acetabular fractures reconstructed using a 'cup-cage construct' technique using a BS cage along with a TMRS. The mean age of the patients was 61.4 years. Patients were followed up for a mean period of 50.5 months (24 to 72 months). The patients were assessed clinically with Harris Hip Score and radiologically with serial X-rays.

Results: All the patients were available at the latest follow up. The mean Harris Hip Score was 87.2. There was no radiological evidence of failure. One patient had dislocation two months following the surgery, which was treated by closed reduction and hip abduction brace. One patient developed an infection at 3 weeks necessitating debridement. The same patient had sciatic nerve palsy that recovered after 4 months.

Conclusion: This novel technique of the cup-cage construct seems to provide a stable construct at short to midterm follow-up. However, a long-term follow up would be required.

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PMCID: PMC6546672

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OBJECTIVES: To describe the sonoelastographic characteristics of the normal endometrium, myometrium, and cervix and to assess their variability with age and different menstrual phases.

METHODS: A total of 56 women were enrolled in this prospective study, who underwent transvaginal ultrasound examinations, including B-mode imaging and shear wave elastography. The elasticity parameters (in kilopascals) of the normal endometrium, myometrium, and cervix were studied. The variability of the mean elasticity value of the endometrium in different menstrual phases and age groups was analyzed. The variability of the mean elasticity of the cervix across different age groups was also studied.

RESULTS: The mean age of the participants was 40 years (range, 25-69 years). The normal mean elasticity values \pm SDs were 25.54 ± 8.56 kPa for the endometrium, 40.24 ± 8.59 kPa for the myometrium, and 18.90 ± 4.22 kPa for the cervix. A mean endometrial-to-myometrial elasticity ratio was calculated, which was found to be 0.65 ± 0.22 . There was no significant difference in the mean endometrial elasticity values for women in different menstrual phases ($P = .176$) or in different age groups ($P = .376$). There was no significant difference in the mean cervical elasticity with age ($P = .192$).

CONCLUSIONS: Shear wave elastography is a promising adjunct to ultrasound for the evaluation of the uterus, and the results from this study may provide normal data, which may further help in diagnosing various uterine diseases.

DOI: 10.1002/jum.15019

PMID: 31077426

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Background: Complex clubfoot does not respond to ponseti method. In 2006 Ponseti et al published the results of treatment of such complex club foot by modified ponseti technique, since then it has become standard method of treatment for complex clubfoot. There has been only few published result of this method and hence, here we are evaluating our experience with 16 patients (27 clubfeet) with complex clubfeet treated at our center by modified ponseti method.

Method: Parents of patient fulfilling the criteria for complex clubfoot were consented and registered under the study. Pirani score at presentation, at prescription of foot abduction brace and at final follow up was noted. total number of casts required for desired correction, number of cast before and after tenotomy, need of tendoachilles tenotomy, relapse and complications were documented.

Result: Average follow up duration was 14.762 months (Range 6 month to 22 months). Of the total 16 patients 11 had bilateral complex clubfoot and 5 had unilateral complex clubfoot, the mean pirani score at the time of presentation was 5.5741 (range 4.5-6), Mean pirani score at latest follow up was 0.0556. Average no. of casts required for the complete correction with modified ponseti method was 7.44 (ranging from 6 to 10 casts). All 27 feet (100%) required tendo achillies tenotomy. Percutaneous tenotomy was done in 19 feet while 8 feet required Mini-Open tenotomy (due to thick pad of fat tendon was not palpable). Relapse rate was 11.11% (3 feet) [all had relapse of equinus, fore foot adduction treated by remanipulation by modified ponseti technique, retenotomy and casting]. An excellent result was achieved with at final follow-up in all 27 feet.

Conclusion: In our experience modified ponseti technique for treatment of complex clubfoot is a successful method of treatment if aided with tendoachilles tenotomy, also it has reduced the requirement of surgical intervention in such patients. Level of Evidence - Level IV.

DOI: 10.1016/j.jcot.2018.05.017

PMCID: PMC6492221 [Available on 2020-05-01]

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Background Polycystic ovary syndrome (PCOS) is frequently associated with infertility, obesity, hypertension, and diabetes mellitus. Cardiac autonomic dysfunction is well documented in long-term patients of PCOS, with impairment being proportionate to disease duration. However, there is paucity of literature on cardiac autonomic tone in the "lean" phenotype of PCOS. We used exercise challenge to probe for autonomic dysfunction, as assessed by heart rate variability (HRV), an index of cardiac autonomic tone. Methods Our study

population consisted of 27 newly diagnosed PCOS patients and 25 healthy females matched by age and body mass index. Short-term HRV was assessed using time and frequency domain indices. Moderate, isotonic exercise was used as an interventional tool. Indices of both groups were compared in three bins - at baseline, immediate, and late postexercise stages. Results The groups had comparable HRV indices at baseline. However, low-frequency (LF) power was significantly reduced in PCOS patients during immediate and late postexercise phases when compared with controls ($p = 0.03$ and 0.03 , respectively). Time domain indices also exhibited a fall postexercise, although not statistically significant. Conclusions Although "lean" phenotype PCOS patients had comparable HRV parameters as controls at baseline, the administration of exercise challenge led to reduced sympathetic drive, evident by reduced LF power in patient group. This may be due to latent autonomic dysfunction in "lean" PCOS, which is unmasked on exposure to exercise challenge. We propose that the evaluation of HRV response to exercise may serve as a sensitive screening tool to detect early cardiovascular dysfunction in newly diagnosed lean PCOS patients.

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A 23-year-old man presented to the emergency department with a history of recurrent episodes of subacute intestinal obstruction. Palpation revealed a firm, non-tender, mobile, non-pulsatile mass of size 8-10cm with indistinct margins and smooth surface in the hypogastrium. Contrast-enhanced CT scan of the abdomen showed clumping of the small bowel loops within a well-defined membrane-like structure without dilatation or thickening of bowel loops. The patient underwent a laparotomy with incision of the membrane and separation of all the small bowel loops inside the cocoon. Abdominal cocoon is the idiopathic variety of sclerosing encapsulating peritonitis and is an unusual cause of acute or subacute intestinal obstruction. Clinical diagnosis is difficult because of non-specific symptoms. CT has facilitated accurate preoperative diagnosis, long before the patient presents with full-fledged symptoms of acute intestinal obstruction. CT scan plays a significant role in excluding the secondary causes and helps in patient management.

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DOI: 10.1136/bcr-2019-229983

PMID: 31154350

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

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

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Oxidative stress (OS) is associated with retinal aging and age-related macular degeneration (AMD). In both cases there are reports for the presence of markers of lipid peroxidation in retinal cells. We investigated if nitrosative stress also occurs in the human retina with aging. We examined the cellular localization of nitro-tyrosine, a biomarker of protein tyrosine nitration, in human donor retina (17-91 years; N=15) by immunohistochemistry. Immunoreactivity (IR) to nitro-tyrosine was present in ten retinas and absent in five retinas. It was predominant in photoreceptor inner segments, cell bodies and axons. In six retinas, IR was present in abnormal, swollen axons of macular and peripheral cones. In the inner retina, weak immunoreactivity was detected in the outer and inner plexiform layer. Transmission electron microscopy revealed a variable degree of microtubule disorganization, abnormal outgrowth from the swollen macular axons (as the fibers of Henle) and few dead axons. The present study adds further evidence to the presence of aberrant photoreceptor axonal changes in the human retina and that nitro-tyrosine immunoreactivity is associated with the photoreceptor cells in select human retina.

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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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Chest is the commonest site of involvement by tuberculosis (TB) in children; lungs being the most frequently affected region, followed by nodes, pleura and chest wall. It is difficult to diagnose TB in children due to lack of overt symptoms and difficulty in obtaining samples for microbiological confirmation. Hence various imaging modalities play an important role in diagnostic algorithm as well as in follow-up after treatment. Standardization of chest radiograph reporting in context of clinically suspected TB is the need of the hour so as to suggest a proper diagnosis and avoid over-diagnosis. This article aims to discuss the imaging features of chest tuberculosis according to the site of involvement on various imaging modalities in the pediatric population.

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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.

DOI: 10.1007/s11548-019-01991-5

PMID: 31062266

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SCOPE: Cause-effect relationship between vitamin D deficiency and cardiometabolic abnormalities remains undefined. The aim is to investigate the role of vitamin D deficiency in cardiac failure, through possible involvement in myocardial insulin signaling.

METHODS AND RESULTS: Male SD rats (n = 6) are fed a normal diet (Con), vitamin D-deficient diet [Con(-)], or high-fat, high fructose diet (HFHFrD) for 20 weeks. Cardiac hypertrophy and fetal gene program are confirmed in Con(-) group. Cardiac dysfunction is assessed by echocardiography. Elevated renin, TGF- β and collagen-1 α mRNAs, p-ERK1/2, and perivascular fibrosis indicate cardiac remodeling in Con(-) group. Increased serum insulin, triglycerides, and blood pressure, and decreased glucose tolerance and HDL cholesterol are observed in Con(-) rats. Decreased p-Akt/Akt, GLUT4, SOD2, and catalase, and increased NF- κ B, TNF- α , and IL-6 are observed in Con(-) hearts. In H9c2 cells, calcitriol attenuates palmitate-induced insulin resistance. VDR-silenced H9c2 cells show reduced Akt phosphorylation, GLUT4 translocation, and 2-NBDG uptake. Findings in Con(-) and HFHFrD groups are comparable.

CONCLUSION: Vitamin D deficiency in rats mimic high-fat-, high-fructose-induced metabolic syndrome and cardiac dysfunction. This study demonstrates that vitamin D deficiency is an independent risk factor for heart failure, at least in part, through induction of myocardial insulin resistance.

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103: 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 RW; 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. *Intest Res*. 2019 May 31. doi: 10.5217/ir.2019.00026. [Epub ahead of print] Review. PubMed PMID: 31146509.

The Asia-Pacific Working Group on inflammatory bowel disease (IBD) was established in Cebu, Philippines, under the auspices of the Asian Pacific Association of Gastroenterology with the goal of improving IBD 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 the conjunction with conventional treatments for ulcerative colitis (UC) and Crohn's disease (CD) in Asia. These statements also address how pharmacogenetics influence the treatments of UC and CD and provide 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 IBD 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: 10.5217/ir.2019.00026

PMID: 31146509

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Anomalies of origin of coronary arteries are an uncommon occurrence and found in approximately 1-2% of the general population. While a large proportion of these anomalies are clinically silent, a few might be hemodynamically significant and may even result in sudden cardiac death. Comprehensive knowledge of the normal as well as variant anatomies of the coronary artery origin and familiarity with imaging appearances and clinical significance of these anomalies is imperative for precise diagnosis and subsequent planning of treatment, whenever required. Multidetector computed tomography angiography, on account of its non-invasiveness, faster scan times and multiplanar reconstruction capabilities, is increasingly being utilized for characterization of coronary artery origin anomalies and their three-dimensional spatial relations. It shows a superior rate of detection of these anomalies compared to conventional angiography, providing more accurate delineation of the ostium as well as course. With the advent of newer generation CT scanners and use of advanced dose reduction techniques, images can be obtained rapidly having excellent spatial resolution and with minimal radiation dose. In this review article, we present the multidetector CT angiography imaging findings of the spectrum of anomalous coronary artery origin, using a third-generation dual-source CT scanner.

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BACKGROUND: Tourette syndrome (TS) and other chronic tic disorders are clinically heterogeneous and cause physical discomfort, social difficulties, and emotional distress. In addition to tics, TS patients have a variety of behavioral comorbidities, including obsessive-compulsive disorders and attention-deficit hyperactivity disorders. TS treatment is multidisciplinary, involving behavioral therapy, oral medications, and botulinum toxin injections.

METHODS: Relevant studies on pharmacological and surgical treatment options for TS and other chronic tic disorders, their limitations and current recommendations were reviewed using the PubMed search till April 2, 2018. Besides, the reference lists of the retrieved publications were manually searched to explore other relevant studies. This review aims to discuss the progress in pharmacological and surgical treatment options for TS and other chronic tic disorders.

RESULTS AND CONCLUSIONS: Both typical and atypical antipsychotic agents are mainstays of pharmacological treatment of TS and other chronic tic disorder patients; however, their use is limited by serious side effects considering their potential of dopamine blockade. Because of the phenotypic variability, no medication has proven effective for all persons with TS and other chronic tic disorders. Botulinum toxin has emerged as a good therapeutic option, especially for focal and dystonic tics. But, their uses are limited by lack of sufficient

evidence and high cost. Surgical treatment is considered in medically refractory and severely disabled tics patients. Deep brain stimulation has replaced lesional surgeries; however, there is uncertainty regarding the selection of patients and target of stimulation.

DOI: 10.1097/NRL.0000000000000218
PMID: 31045720 [Indexed for MEDLINE]

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AIM: The purpose of this study was to examine treatment-related neurochemical changes in 28 unmedicated obsessive-compulsive disorder (OCD) patients using 1 H-magnetic resonance spectroscopy (1 H-MRS).

METHODS: We included subjects diagnosed with OCD (n =28), each with a total duration of illness of less than 5 years, as a study group and age- and sex-matched healthy controls (n =26). The inclusion criteria for the OCD group were right-handed individuals aged 18 years or older who had not been on any specific treatment for OCD for the last at least 8 weeks and who had no other psychiatric comorbidity. A pre-post and case-control design was employed in which OCD patients underwent 1 H-MRS at baseline and 12 weeks after treatment with escitalopram (n =21). Clinical assessment was carried out using a semi-structured pro forma Yale-Brown Obsessive Compulsive Scale and the World Health Organization Disability Assessment Scale 2.0 before and after treatment. Volume-localized 1 H-MRS was carried out with a 3-Tesla Philips MR scanner.

RESULTS: Our data suggested higher levels of myoinositol (mI), total choline (tCho), and glutamate+glutamine (Glx) in the medial thalamus at pre-assessment in OCD subjects as compared to healthy controls and a significant reduction in tCho and Glx after treatment in OCD subjects. The mI levels in the caudate nucleus and Glx levels in the anterior cingulate cortex were significantly correlated with disease severity on the Yale-Brown Obsessive Compulsive Scale.

CONCLUSION: Our study supports the hypothesis of a hyper-glutamergic state (as suggested by increased Glx levels) and neurodegeneration (as suggested by increased tCho and mI in the thalamus) in cortico-striato-thalamocortical circuitry in OCD patients as suggested by previous studies using MRS as well as other functional imaging studies.

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PMID: 30973183

109: Parmar A, Kumar Dubey D, Singh Balhara YP, Kumar Mishra A. Do Addiction Science Journals Endorse Unbiased Reporting of Research? A Systematic Evaluation of Instructions for Authors. *Subst Use Misuse*. 2019;54(10):1734-1742. doi: 10.1080/10826084.2019.1610444. Epub 2019 May 13. PubMed PMID: 31081457.

Introduction: Well-structured instructions for authors in journals help researchers in reporting unbiased results, which subsequently facilitates the review process. There have been reports of systematic evaluations of instructions for authors from journals in various medical specialties. However, precise information on the nature and extent of these instructions for authors in addiction science is lacking. Hence, this study systematically evaluated the instructions for authors for journals in addiction science. Methods: A total of 1139 journal titles were retrieved across multiple databases. Finally, 88 exclusive titles fulfilling the eligibility criteria were considered in this study. The four domains evaluated were journal characteristics, reporting, statistical reporting, and ethical requirements. Results: More than half of the journals were published by academic institutions or professional societies. Less than one-fourth of the journals endorsed adherence to various reporting

guidelines and endorsed the Consolidated Statements on Randomized Controlled Trials guidelines to the maximum level (14.8%). Approximately, half (48.9%) of the journals had a separate section on "statistical analysis." The various parameters of statistical reporting were suboptimally endorsed.

Conclusion/Importance: The instructions for authors in addiction science journals provide insufficient information in various domains. There is an urgent need to improve the author instructions segment of addiction science journals so that the process of research dissemination can occur more effectively. A higher rate of endorsement of various reporting guidelines and statistical reporting may help to minimize reporting bias as well as prevent unnecessary delays in the publication of important research findings.

DOI: 10.1080/10826084.2019.1610444

PMID: 31081457

110: Phulware RH, Gahlot GPS, Malik R, Gupta SD, Das P. Microvillous Inclusion Disease as a Cause of Protracted Diarrhea. *Indian J Pediatr.* 2019 May 2. doi: 10.1007/s12098-019-02963-y. [Epub ahead of print] PubMed PMID: 31049800.

Microvillous inclusion disease (MVID), also known as congenital microvillus atrophy, was first described by Davidson et al. in 1978. Till date, only a handful of cases with MVID have been described in English literature. It is an autosomal recessive disorder with no sex predisposition and more commonly noted in countries with prevalent consanguineous marriages. These patients usually present with intractable secretory diarrhea in early days of life. The pathognomonic findings of MVID are villous atrophy along with the formation of intracellular microvillous inclusions on electron microscopy. Till date, no curative therapy exists, and prognosis mainly depends upon parenteral nutrition. Small bowel transplantation is one of the treatment options. Clinician and pathologist should consider the possibility of MVID in the differential diagnosis of chronic intractable diarrhea in an infant. Herein, authors are describing a case of intractable diarrhea with MVID phenotype diagnosed in a 3-mo-old male child who presented with intractable diarrhea in an outside hospital, and the diagnostic workup was performed by the authors on endoscopic biopsy sample.

DOI: 10.1007/s12098-019-02963-y

PMID: 31049800

111: Phulware RH, Guleria P, Iyer VK, Bakhshi S, Seth R, Mridha AR, Jain D, Mallick S, Arava SK, Agarwal S, Kaushal S, Yadav R, Mathur SR. Cytological diagnosis of Langerhans cell histiocytosis: A series of 47 cases. *Cytopathology.* 2019 Jul;30(4):413-418. doi: 10.1111/cyt.12709. Epub 2019 May 23. PubMed PMID: 31017324.

OBJECTIVE: Langerhans cell histiocytosis (LCH) is a rare disease affecting predominantly children and young adults but can be found in any age group. Diagnosis of LCH is often difficult and can be delayed because of its rarity. The present study highlights the cytomorphological features in a large cohort of cases. An accurate cytological diagnosis may avoid unnecessary biopsy and guide appropriate management.

METHOD: Fourty seven (47) cases of LCH diagnosed on cytological material & fine-needle aspiration (FNA) over a period of 14 years (2003-2016) were retrieved from the archives. The cytological smears were evaluated and microscopic findings collected by semi-quantitative assessment done by two different pathologists

RESULT: The age at the diagnosis of the patients ranged from 9 months to 28 years. The majority of cases were in the age group of 0-5 years. The most common site was head and neck region, which included cervical lymphadenopathy and scalp swelling. Two cases were diagnosed each from inguinal lymph node and bronchio-alveolar lavage (BAL). Cytological smears in the majority of the cases were moderate to highly cellular (58%) and showing abundant Langerhans cell in (72%) of cases. Areas of necrosis were seen in 38%, while 78% of cases showed giant cells. The majority of cases showed mild eosinophilia (61%), sparse lymphocytosis (83%) and mild neutrophilic infiltration (64%). There were 1-2 mitoses per 10 high power field in 12 cases (25.5%). No abnormal mitoses were

identified.

CONCLUSION: The presence of cells with features of Langerhans cells associated with the expression of selected immunohistochemical markers allow the diagnosis of LCH on cytological samples, sparing more invasive procedure as a biopsy.

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DOI: 10.1111/cyt.12709

PMID: 31017324

112: Porubsky S, Rudolph B, Rückert JC, Küffer S, Ströbel P, Roden AC, Jain D, Tousseyn T, Van Veer H, Huang J, Antonicelli A, Kuo TT, Rosai J, Marx A; International Thymic Malignancy Interest Group (ITMIG). EWSR1-translocation in primary hyalinising clear cell carcinoma of the thymus. *Histopathology*. 2019 May 3. doi: 10.1111/his.13890. [Epub ahead of print] PubMed PMID: 31050844.

AIMS: In thymic carcinomas, focal clear cell change represents a frequent finding. In addition to a prominent, diffuse clear cell morphology, some of these carcinomas show an exuberant hyalinised extracellular matrix and therefore likely represent a separate entity. However, a characteristic genomic alteration remains elusive. We hypothesized that analogous to hyalinising clear cell carcinomas of the salivary gland, hyalinising clear cell carcinomas of the thymus might also harbour EWSR1-translocations.

METHODS AND RESULTS: We identified 9 archived cases of thymic carcinomas with focal clear cell features and 2 cases that showed remarkable hyalinised stroma and prominent, diffuse clear cell morphology. These 2 cases expressed p40 and were negative for Pax8, CD5 and CD117. Tumour positivity for PD-L1 was highly positive in one case (70%), negative in the other one. EWSR1-translocation was identified in both cases of hyalinising clear cell carcinomas and was absent in all 9 carcinomas that showed clear cell features without substantial hyalinisation. In one of the EWSR1-translocated cases, a fusion between exon 13 and exon 6 of EWSR1 and ATF1, respectively could be identified by next generation sequencing.

CONCLUSIONS: These findings suggest that the EWSR1-translocation and possibly the EWSR1-ATF1-fusion might be a unifying genomic alteration for thymic clear cell carcinomas with prominent hyalinised stroma for which we propose the term "hyalinising clear cell carcinoma of the thymus". Because the immunophenotype is unspecific, testing for the EWSR1-translocation might be helpful in discerning this entity from other thymic neoplasms or metastases, in particular, those with clear cell change. This article is protected by copyright. All rights reserved.

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DOI: 10.1111/his.13890

PMID: 31050844

113: Pramanik R, Sharma A, Sharma A, Gogia A, Sahoo RK, Malik PS, Padma MV, Cyriac SL, Kumar L. POEMS Syndrome: Indian Experience From a Tertiary-Care Institute. *Clin Lymphoma Myeloma Leuk*. 2019 May 29. pii: S2152-2650(19)30062-X. doi: 10.1016/j.clml.2019.05.018. [Epub ahead of print] PubMed PMID: 31262669.

INTRODUCTION: POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes) syndrome is a rare multisystem paraneoplastic syndrome characterized by peripheral neuropathy and monoclonal plasmacytosis.

Retrospective institutional experiences from the Mayo Clinic as well as Chinese, European, and Japanese series have provided important insights into the characteristics and treatment of this disease, but Indian data are extremely limited. We retrospectively analyzed 49 cases from our institute including 10 patients who underwent autologous stem-cell transplantation (ASCT).

PATIENTS AND METHODS: We analyzed clinical and laboratory characteristics, treatment details and outcome of all patients diagnosed with POEMS syndrome between 1993 and 2017.

RESULTS: Complete medical records were available for 49 patients with a median age of 44 years. Male/female ratio was 38:11. Twenty patients (40.8%) had Eastern

Cooperative Oncology Group performance status of 4. Before 2012, melphalan/prednisolone was the most common regimen provided, while bortezomib/dexamethasone and lenalidomide/dexamethasone were used later. Hematologic response was available for 40 patients, 15 (37.5%) of whom experienced complete response, 13 (32.5%) partial response, and 11 (27.5%) stable disease. The median modified Rankin score at baseline was 4 (range, 1-5), which improved to 3 (range, 1-5). Ten patients underwent consolidation ASCT after a median of 4 cycles of induction. Median melphalan dose was 140 mg/m². Engraftment syndrome was observed in 4. After ASCT, all 10 patients experienced hematologic complete response and clinical improvement.

CONCLUSION: This retrospective analysis provides important information on the clinical characteristics of POEMS syndrome in Indian patients, which will help the clinician's decision-making process.

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DOI: 10.1016/j.clml.2019.05.018

PMID: 31262669

114: Pujari A, Selvan H, Goel S, Dada T. Direct Smartphone Disc Video Documentation for Paediatric Glaucomas During Evaluation Under Anaesthesia. *J Glaucoma*. 2019 May 31. doi: 10.1097/IJG.0000000000001294. [Epub ahead of print] PubMed PMID: 31162176.

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

OBJECTIVE: The relation of absolute lymphocyte count (ALC) with minimal residual disease (MRD) in T cell - acute lymphoblastic leukemia (T-ALL) is not known. The objective of the study was to correlate ALC with MRD, steroid-response and complete remission (CR).

METHODS: De-novo T- ALL patients (age 1-18 y) recruited prospectively; 52 enrolled, 9 excluded, and 43 analyzed. 39 achieved CR and MRD was available for 28 patients; 23 were MRD negative.

RESULTS: ALC did not correlate with steroid response and CR. Median (range) ALC at the end of induction was significantly higher in patients who were MRD negative compared to MRD positive [1.24 (0.12, 6.69) vs 0.62 (0.15, 0.87); P=0.03], respectively. Patients having ALC $\geq 700 \times 10^9 /L$ were significantly more likely to be MRD negative than those with lower values (P= 0.028).

CONCLUSION: Our study suggests that ALC is a favorable factor, and may act as surrogate marker for MRD.

PMID: 30898988

116: Pushpam D, Rajput N, Chopra A, Vishnubhatla S, Kumari M, Kumar R, Bakhshi S. Association of absolute lymphocyte count and peripheral blood lymphocyte subsets percentage with minimal residual disease at the end of induction in pediatric B cell acute lymphoblastic leukemia. *Pediatr Hematol Oncol*. 2019 Apr;36(3):138-150. doi: 10.1080/08880018.2019.1594469. Epub 2019 May 3. PubMed PMID: 31046540.

Absolute lymphocyte count (ALC) has been associated with overall survival (OS) and event-free survival, but we do not know if ALC is associated with minimal residual disease (MRD) at the end of induction (EOI) and whether it can be used as surrogate marker in resource limited settings. Immunological differences between MRD-positive and MRD-negative B ALL patients at the EOI are not known at present. This prospective study evaluated the association of ALC and peripheral blood lymphocyte subset percentage at the EOI with MRD. ALC was done at baseline, day 8, and day 15 and at EOI. Assessment for MRD and peripheral blood lymphocyte subset was done at EOI. In 2-year study duration, 197 B cell acute lymphoblastic leukemia (ALL) patients were recruited out of which 150 were analyzed. Peripheral

lymphocyte subset percentage was available for 58 patients. We found that ALC at baseline, day 8, day 15, and EOI was not associated with MRD. Day 8 ALC was significantly higher in poor steroid responders (day 8 blasts $>1 \times 10^9$ cells/l) ($p < 0.0001$). At the EOI, CD4-CD8+ cell percentage in peripheral blood were significantly higher in MRD-positive patients than MRD-negative patients ($p = 0.01$). Our study suggests that ALC at any point is not a surrogate marker for MRD. Immunologically MRD-positive and MRD-negative patients differ in CD4-CD8+ cells. The role of CD8+T and TCR $\alpha\beta$ CD3+T cells in eliminating residual leukemic cells need to be studied further by functional assays.

DOI: 10.1080/08880018.2019.1594469
PMID: 31046540

117: Raina R, Lam S, Raheja H, Krishnappa V, Hothi D, Davenport A, Chand D, Kapur G, Schaefer F, Sethi SK, McCulloch M, Bagga A, Bunchman T, Warady BA. Pediatric intradialytic hypotension: recommendations from the Pediatric Continuous Renal Replacement Therapy (PCRRT) Workgroup. *Pediatr Nephrol.* 2019 May;34(5):925-941. doi: 10.1007/s00467-018-4190-1. Epub 2019 Feb 8. PubMed PMID: 30734850.

Intradialytic hypotension (IDH) is a common adverse event resulting in premature interruption of hemodialysis, and consequently, inadequate fluid and solute removal. IDH occurs in response to the reduction in blood volume during ultrafiltration and subsequent poor compensatory mechanisms due to abnormal cardiac function or autonomic or baroreceptor failure. Pediatric patients are inherently at risk for IDH due to the added difficulty of determining and attaining an accurate dry weight. While frequent blood pressure monitoring, dialysate sodium profiling, ultrafiltration-guided blood volume monitoring, dialysate cooling, hemodiafiltration, and intradialytic mannitol and midodrine have been used to prevent IDH, they have not been extensively studied in pediatric population. Lack of large-scale studies on IDH in children makes it difficult to develop evidence-based management guidelines. Here, we aim to review IDH preventative strategies in the pediatric population and outlay recommendations from the Pediatric Continuous Renal Replacement Therapy (PCRRT) Workgroup. Without strong evidence in the literature, our recommendations from the expert panel reflect expert opinion and serve as a valuable guide.

DOI: 10.1007/s00467-018-4190-1
PMID: 30734850

118: Rajagopal R, Garg PK, Khera PS, Sharma S. "Double-lumen" aortic arch with "double-lumen" brachiocephalic artery. *Ann Pediatr Cardiol.* 2019 May-Aug;12(2):141-143. doi: 10.4103/apc.APC_106_18. PubMed PMID: 31143041; PubMed Central PMCID: PMC6521648.

Persistence of the embryological fifth aortic arch in postnatal life has been a subject of debate for over more than a century. We describe a patient with congenital kyphoscoliosis and variant anatomy in the aortic arch and brachiocephalic trunk which could be possibly explained by the persistence of bilateral fifth aortic arches, a pattern which has never been previously reported in literature.

DOI: 10.4103/apc.APC_106_18
PMCID: PMC6521648
PMID: 31143041

119: Ronsard L, Sood V, Yousif AS, Ramesh J, Shankar V, Das J, Sumi N, Rai T, Mohankumar K, Sridharan S, Dorschel A, Ramachandran VG, Banerjea AC. Genetic Polymorphisms in the Open Reading Frame of the CCR5 gene From HIV-1 Seronegative and Seropositive Individuals From National Capital Regions of India. *Sci Rep.* 2019 May 20;9(1):7594. doi: 10.1038/s41598-019-44136-z. PubMed PMID: 31110236; PubMed Central PMCID: PMC6527560.

C-C chemokine receptor type 5 (CCR5) serves as a co-receptor for Human immunodeficiency virus (HIV), enabling the virus to enter human CD4 T cells and

macrophages. In the absence of CCR5, HIV strains that require CCR5 (R5 or M-tropic HIV) fail to successfully initiate infection. Various natural mutations of the CCR5 gene have been reported to interfere with the HIV-CCR5 interaction, which influences the rate of AIDS progression. Genetic characterization of the CCR5 gene in individuals from the National Capital Regions (NCRs) of India revealed several natural point mutations in HIV seropositive/negative individuals. Furthermore, we identified novel frame-shifts mutations in the CCR5 gene in HIV seronegative individuals, as well as the well reported CCR5 Δ 32 mutation. Additionally, we observed a number of mutations present only in HIV seropositive individuals. This is the first report to describe the genetic variations of CCR5 in individuals from the NCRs of India and demonstrates the utility of investigating understudied populations to identify novel CCR5 polymorphisms.

DOI: 10.1038/s41598-019-44136-z

PMCID: PMC6527560

PMID: 31110236

120: Roy K, Satapathy AK, Houhton JAL, Flanagan SE, Radha V, Mohan V, Sharma R, Jain V. Congenital Hyperinsulinemic Hypoglycemia and Hyperammonemia due to Pathogenic Variants in GLUD1. Indian J Pediatr. 2019 May 22. doi: 10.1007/s12098-019-02980-x. [Epub ahead of print] PubMed PMID: 31119523.

Congenital hyperinsulinism (CHI) is a clinically and genetically heterogeneous disorder, characterized by dysregulated insulin secretion. Pathogenic variants in at least twelve different genes (ABCC8, KCNJ11, GLUD1, GCK, HADH, SLC16A1, HNF4A, HNF1A, UCP2, TRMT10A HK1, and PGM1) are known to cause CHI. Pathogenic variants in the GLUD1 gene, which encodes the enzyme glutamate dehydrogenase (GDH), account for 5% of the cases of congenital hyperinsulinemic hypoglycemia. Pathogenic variants in GLUD1 typically present in late infancy, are diet and/or diazoxide-responsive and cause protein-induced hyperinsulinemic hypoglycemia as insulin secretion is triggered by allosteric activation of GDH by leucine. The authors are presenting three unrelated Indian children, who manifested with fasting as well as dietary protein induced hypoglycemia in late infancy, and were diagnosed to have hyperinsulinemic hyperammonemic hypoglycemia due to pathogenic variants in GLUD1. Although the hypoglycemia responded to diazoxide, delayed diagnosis and irregular treatment had resulted in neurological problems in two of the three children. Early identification, appropriate dietary modifications and regular treatment with diazoxide can prevent adverse neurological outcome.

DOI: 10.1007/s12098-019-02980-x

PMID: 31119523

121: Sahay P, Maharana PK, Mandal S, Sinha R, Agarwal T, Sharma N, Titiyal JS. Cataract surgery outcomes in eyes with chorioretinal coloboma. J Cataract Refract Surg. 2019 May;45(5):630-638. doi: 10.1016/j.jcrs.2019.01.016. PubMed PMID: 31030778.

PURPOSE: To evaluate the outcomes of cataract surgery in patients with chorioretinal coloboma.

SETTING: Tertiary eyecare center, New Delhi, India.

DESIGN: Retrospective case series.

METHODS: Medical records of patients with chorioretinal coloboma having cataract surgery between January 2016 and May 2018 were reviewed. The corrected distance visual acuity (CDVA), grade of cataract, type of chorioretinal coloboma, type of surgery, postoperative CDVA, and complications were recorded.

RESULTS: Thirty-eight patients with a mean age at surgery of 36.7 years were included. The mean CDVA at presentation was 1.83 logarithm of the minimum angle of resolution [logMAR] \pm 0.31 (SD). Advanced nuclear sclerosis occurred in 61.4% of cases and lens subluxation in 10.2% of cases. Phacoemulsification (56.4%) was the most commonly performed cataract surgery followed by lens aspiration (12.8%) and extracapsular cataract surgery (12.8%). Uneventful cataract surgery with intraocular lens (IOL) implantation was performed in 69.2% of cases.

Intraoperative complications included 7 cases of bag dialyses, 3 of posterior

capsule ruptures, and 1 of capsulorhexis extension. The mean postoperative CDVA at 6 weeks and 1 year was 1.64 ± 0.51 logMAR and 1.51 ± 0.58 logMAR, respectively. Postoperative complications included 11 cases each of raised intraocular pressure and corneal edema; 2 cases each of IOL decentration, capsule phimosis, and corneal edema; and 1 case of posterior capsule opacification. A second intervention was required in 4 cases (2 endothelial keratoplasties, 1 IOL explantation, 1 neodymium:YAG capsulotomy).

CONCLUSIONS: Cataracts in patients with chorioretinal coloboma are usually advanced compared with age-matched patients with senile cataract. Delayed surgery results in suboptimum outcomes; thus, surgery should be scheduled as soon as possible after the cataract is documented.

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DOI: 10.1016/j.jcrs.2019.01.016

PMID: 31030778

122: Sankar J, Ismail J, Das R, Dev N, Chitkara A, Sankar MJ. Effect of Severe Vitamin D Deficiency at Admission on Shock Reversal in Children With Septic Shock: A Prospective Observational Study. *J Intensive Care Med.* 2019 May;34(5):397-403. doi: 10.1177/0885066617699802. Epub 2017 Mar 24. PubMed PMID: 28335672.

OBJECTIVES:: To evaluate the association of severe vitamin D deficiency with clinically important outcomes in children with septic shock.

METHODS:: We enrolled children ≤ 17 years with septic shock prospectively over a period of 6 months. We estimated 25-hydroxyvitamin D [25 (OH) D] levels at admission and 72 hours. Severe deficiency was defined as serum 25 (OH) < 10 ng/mL. We performed univariate and multivariate analysis to evaluate association with clinically important outcomes.

RESULTS:: Forty-three children were enrolled in the study. The prevalence of severe vitamin D deficiency was 72% and 69% at admission and 72 hours, respectively. On univariate analysis, severe vitamin D deficiency at admission was associated with lower rates of shock reversal, 74% (23) versus 25% (3); relative risk (95% confidence interval [CI]): 2.9 (1.09-8.08), at 24 hours and greater need for fluid boluses (75 vs 59 mL/kg). On multivariate analysis, nonresolution of shock at 24 hours was significantly associated with severe vitamin D deficiency after adjusting for other key baseline and clinical variables, adjusted odds ratio (95% CI): 12 (2.01-87.01); 0.01.

CONCLUSION:: The prevalence of severe vitamin D deficiency is high in children with septic shock admitted to pediatric intensive care unit. Severe vitamin D deficiency at admission seems to be associated with lower rates of shock reversal at 24 hours of ICU stay. Our study provides preliminary data for planning interventional studies in children with septic shock and severe vitamin D deficiency.

DOI: 10.1177/0885066617699802

PMID: 28335672

123: Sankhyan LK, Chowdhury UK, Diplomate NB, Bansal N, Hasiya S, Jagia P. Left Bidirectional Cavopulmonary Connection in Raghiv's Defect: Report of 5 Cases and Review of Literature. *World J Pediatr Congenit Heart Surg.* 2019 May 22;2150135118822699. doi: 10.1177/2150135118822699. [Epub ahead of print] PubMed PMID: 31117879.

We report five male patients aged 3, 6, 8, 10, and 15 years, respectively, undergoing left bidirectional cavopulmonary connection and concomitant Dacron patch closure of the atrial septal defect for Raghiv's defect with persistent left superior vena cava. The circulation was successfully corrected. This extracardiac procedure uses only autogenous tissues having growth potential, reduces myocardial ischemia, and avoids later baffle deterioration with pulmonary venous obstruction associated with intra-atrial baffling procedures. A wider appreciation and application of this management modality is warranted.

DOI: 10.1177/2150135118822699
PMID: 31117879

124: Sarkar L, Biswas S, Ray A, Sinha S. Hydropneumothorax following diagnostic bronchoalveolar lavage: A rarest of rare complication. *Lung India*. 2019 May-Jun;36(3):270-271. doi: 10.4103/lungindia.lungindia_423_18. PubMed PMID: 31031359; PubMed Central PMCID: PMC6503703.

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

126: Selvan H, Sharma A, Dada T. Inferior Bitot's spot in a case of Crouzon syndrome: The environmental theory reaffirmed. *BMJ Case Rep*. 2019 May 27;12(5). pii: e229853. doi: 10.1136/bcr-2019-229853. PubMed PMID: 31138597.

127: Selvan H, Angmo D, Sharma A. The Missing Mesenchyme Captured-Axenfeld-Rieger Anomaly. *JAMA Ophthalmol*. 2019 May 1;137(5):e184507. doi: 10.1001/jamaophthalmol.2018.4507. Epub 2019 May 9. PubMed PMID: 31070683.

128: 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.

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

129: Sharma S, Kumari P, Vashist A, Kumar C, Nandi M, Tyagi JS. Cognate sensor kinase-independent activation of Mycobacterium tuberculosis response regulator DevR (DosR) by acetyl phosphate: implications in anti-mycobacterial drug design. *Mol Microbiol*. 2019 May;111(5):1182-1194. doi: 10.1111/mmi.14196. Epub 2019 Jan 31. PubMed PMID: 30589958.

The DevRS/DosT two-component system is essential for mycobacterial survival under hypoxia, a prevailing stress within granulomas. DevR (also known as DosR) is activated by an inducing stimulus, such as hypoxia, through conventional phosphorylation by its cognate sensor kinases, DevS (also known as DosS) and DosT. Here, we show that the DevR regulon is activated by acetyl phosphate under

'non-inducing' aerobic conditions when *Mycobacterium tuberculosis* devS and dosT double deletion strain is cultured on acetate. Overexpression of phosphotransacetylase caused a perturbation of the acetate kinase-phosphotransacetylase pathway, a decrease in the concentration of acetyl phosphate and dampened the aerobic induction response in acetate-grown bacteria. The operation of two pathways of DevR activation, one through sensor kinases and the other by acetyl phosphate, was established by an analysis of wild-type DevS and phosphorylation-defective DevSH395Q mutant strains under conditions partially mimicking a granulomatous-like environment of acetate and hypoxia. Our findings reveal that DevR can be phosphorylated in vivo by acetyl phosphate. Importantly, we demonstrate that acetyl phosphate-dependent phosphorylation can occur in the absence of DevR's cognate kinases. Based on our findings, we conclude that anti-mycobacterial therapy should be targeted to DevR itself and not to DevS/DosT kinases.

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DOI: 10.1111/mmi.14196

PMID: 30589958

130: Sharma U, Agarwal K, Hari S, Mathur SR, Seenu V, Parshad R, Jagannathan NR. Role of diffusion weighted imaging and magnetic resonance spectroscopy in breast cancer patients with indeterminate dynamic contrast enhanced magnetic resonance imaging findings. *Magn Reson Imaging*. 2019 May 22;61:66-72. doi: 10.1016/j.mri.2019.05.032. [Epub ahead of print] PubMed PMID: 31128225.

PURPOSE: Dynamic contrast enhanced MRI (DCEMRI), diffusion weighted imaging (DWI) and in vivo proton (¹H) magnetic resonance spectroscopy (MRS) provides functional and molecular nature of breast cancer. This study evaluates the potential of the combination of three MR parameters [curve kinetics, apparent diffusion coefficient (ADC) and total choline (tCho) concentration] determined from these techniques in increasing the sensitivity of breast cancer detection.

METHODS: MR investigations were carried out at 1.5T on 56 patients with cytologically/histologically confirmed breast carcinoma. Single-voxel MRS was used to determine the tCho concentration. 3D FLASH was used for DCEMRI while single shot EPI based DWI was used for ADC determination.

RESULTS: On DCEMRI, one patient showed type I curve, while 8 showed type II and 47 showed type III curve thus giving a sensitivity of 83.9% as detection rate of malignancy. tCho concentration was above cut-off value (2.54mmol/kg) for 50/56 cases giving a sensitivity of 89.3%. Among 9 indeterminate DCEMRI cases, tCho showed malignancy in 6 cases with type II curve. DWI detected malignancy in 54/56 cases that included 9 cases that were false negative on DCEMRI, yielding a sensitivity of 96.4%. A total of 54 cases showed malignancy when any two of the three MR parameters was positive for malignancy yielding a sensitivity of 96.4% while it increased to 100% when any one parameters showed positive result.

CONCLUSION: DWI showed highest sensitivity of detection compared to DCEMRI and MRS. Multi-parametric approach yielded 96.4% and 100% sensitivity when any two or one of the three parameters was taken as positive for malignancy, respectively. Also the results demonstrated that addition of DWI and MRS play a significant role in establishing the final diagnosis of malignancy, especially in cases where DCEMRI is indeterminate.

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DOI: 10.1016/j.mri.2019.05.032

PMID: 31128225

131: Shaw M, Khurana R, Kumar S, Ojha V. Imaging Depiction of Large Pericardial Metastasis From Osteosarcoma of Tibia. *Ann Thorac Surg*. 2019 May;107(5):e355. doi: 10.1016/j.athoracsur.2018.12.005. Epub 2019 Jan 2. PubMed PMID: 30610850.

132: Shin SS, Carpenter CL, Ekstrand ML, Wang Q, Grover S, Zetola NM, Yadav K, Sinha S, Nyamathi AM. Cervical cancer awareness and presence of abnormal cytology

among HIV-infected women on antiretroviral therapy in rural Andhra Pradesh, India. *Int J STD AIDS*. 2019 May;30(6):586-595. doi: 10.1177/0956462419825950. Epub 2019 Feb 27. PubMed PMID: 30813859; PubMed Central PMCID: PMC6510620.

Cervical cancer is a leading cause of death among women in low- and middle-income countries, and women living with HIV are at high risk for cervical cancer. The objective of this study was to estimate the prevalence and correlates of cervical cancer and pre-cancer lesions and to examine cervical cancer knowledge among women living with HIV receiving antiretroviral therapy in rural Andhra Pradesh, India. We conducted cytology-based screening and administered a standardized questionnaire among 598 HIV-infected women. We found 5 (0.8%), 39 (6.5%), 29 (4.9%), and 4 (0.7%) had atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), and squamous cervical carcinoma (SCC), respectively. In multivariable logistic regression analysis, ASCUS/LSIL was independently associated with age >16 years old at first sexual encounter and smokeless tobacco use. We found no factors associated with HSIL/SCC. In total, 101 women (16.9%) had heard of cervical cancer and 28 (27.7%) of them correctly identified HIV infection as a risk factor. In light of the high prevalence of pre-cancer lesions and low level of cervical cancer knowledge in our study population, focused interventions are needed to improve cervical cancer literacy and prevention among rural women living with HIV.

DOI: 10.1177/0956462419825950
PMCID: PMC6510620 [Available on 2020-05-01]
PMID: 30813859

133: Sihota R, Sen S, Mohanty S, Ahmad M, Ravi A, Gupta V, Bhatla N. Effect of intracameral human cord blood-derived stem cells on lasered rabbit trabecular meshwork. *Int Ophthalmol*. 2019 May 28. doi: 10.1007/s10792-019-01120-w. [Epub ahead of print] PubMed PMID: 31140023.

BACKGROUND: This study aimed to investigate the effect of intracameral human cord blood stem cells on lasered rabbit trabecular meshwork.
METHODS: Immediately following diode laser application to the trabecular meshwork, human cord blood stem cells were injected intracamerally, in one eye of 12 albino rabbits. The other eye of ten rabbits was lasered controls and two eyes were normal controls. Rabbits were killed after 4, 8 and 12 weeks.
RESULTS: Lasered control rabbit eyes showed significant disruption of trabecular architecture, loss and pleomorphism of trabecular endothelial cells and progressive narrowing of trabecular spaces till 12 weeks. In contrast, lasered eyes, concurrently injected with human cord blood stem cells, showed relatively preserved endothelial cellularity and structure of the trabecular meshwork, at all time points. Human CD34- and CD44-positive cells were identified in 7/8 eyes treated with stem cells, at 4 and 8 weeks, and 2 of 3 at 12 weeks. Many PKH26-labeled human cord blood cells were visible throughout the trabecular area at 4 weeks. They gradually decreased in number by 8 weeks, and at 12 weeks, they appeared to be oriented along trabecular beams.
CONCLUSIONS: There was a relative preservation of cellularity and architecture of the trabecular meshwork in eyes injected with human cord blood stem cells, as compared to lasered control eyes up to 12 weeks, without significant inflammation. This suggests a probable role for such stem cells in eyes with glaucoma, having trabecular dysfunction.

DOI: 10.1007/s10792-019-01120-w
PMID: 31140023

134: Sikidar A, Kalyanasundaram D. An open-source plugin for OpenSim(®) to model the non-linear behaviour of dense connective tissues of the human knee at variable strain rates. *Comput Biol Med*. 2019 Jul;110:186-195. doi: 10.1016/j.combiomed.2019.05.021. Epub 2019 May 31. PubMed PMID: 31173942.

The force-length characteristics of dense connective tissues (DCTs) vary non-linearly as a function of strain rate. However, there is no class of OpenSim®

available to incorporate the effect of strain rate into the OpenSim® model. In this work, a new plugin for OpenSim® was developed to incorporate the non-linear strain rate behaviour of dense connective tissues (DCTs) of the human knee. Experimental force-length plots from the literature were used to extract the shape factor, scale factor, the coefficient of viscosity and elastic stiffness corresponding to specific strain rates. A new class object termed as NonLinearLigament was formulated using a customized plugin based on a structural constitutive model. A test platform was created to evaluate the force-length patterns at multiple strain rates ranging from 0.0001 s⁻¹ to 100 s⁻¹ for the DCT bundles. Knee kinematics of 25 DCT bundles were subjected to forward simulation at various strain rates. To understand the significance, the force-length characteristics of each of the DCTs were simulated as a function of strain rate for both existing Ligament class of OpenSim® and the proposed NonLinearLigament class. In the proposed ligament class, higher forces were observed with an increase of strain rate in DCTs. Existing Ligament class in OpenSim® was devoid of any changes at different strain rates. In summary, the developed plugin takes into account the short term viscoelastic behaviour of DCTs and hence, would help in accurate modelling of tissue behaviour specifically for dynamic situations.

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DOI: 10.1016/j.compbio.2019.05.021
PMID: 31173942

135: Singal AK, Karthikeyan G. Aspirin for primary prevention: Is this the end of the road? Indian Heart J. 2019 Mar - Apr;71(2):113-117. doi: 10.1016/j.ihj.2019.04.001. Epub 2019 May 2. Review. PubMed PMID: 31280821.

Aspirin is one of the oldest and most commonly used cardiovascular drugs. Despite there being high-quality evidence supporting the use of aspirin for patients with known cardiovascular disease, a definitive consensus regarding its use for patients at risk for cardiovascular disease (and without established cardiovascular disease) has never been reached. Many randomized control trials have produced conflicting results, and consequently, society guidelines have issued differing recommendations. Three major trials were published in 2018, which supplement the existing data on aspirin's role in primary prevention and provide further guidance on this contentious issue. This article reviews the history of aspirin through the last two decades, with special emphasis on these new trials.

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DOI: 10.1016/j.ihj.2019.04.001
PMID: 31280821

136: Singh G, Singh SK, Nalwa A, Singh L, Pradeep I, Barwad A, Sinha A, Hari P, Bagga A, Bagchi S, Agarwal SK, Dinda AK. Glomerular C4d Staining Does Not Exclude a C3 Glomerulopathy. Kidney Int Rep. 2019 Feb 13;4(5):698-709. doi: 10.1016/j.ekir.2019.02.006. eCollection 2019 May. PubMed PMID: 31080925; PubMed Central PMCID: PMC6506704.

Introduction: C4d, an early product in the classical/lectin complement pathway has shown potential in the evaluation of C3 glomerulopathy where its absence would support an alternative pathway abnormality. As autoimmune/genetic complement testing is not readily available to most parts of the world, glomerular C4d staining may serve as a useful additional step toward the diagnosis.

Methods: To test this hypothesis, C4d staining was performed on a large cohort of C3 glomerulopathy. Archival cases from 2011 to 2017 were reviewed and immunohistochemistry for C4d was performed, scored (scale of 0 to 3+), and uncorrelated with the immunofluorescence and ultrastructural findings. Paraffin immunofluorescence was performed in cases of "discordant C4d" to unmask Igs. Results: Twenty-seven cases of dense deposit disease (DDD) and 14 cases of C3

glomerulonephritis (C3GN) were retrieved. C4d demonstrated a range of staining intensities with negative/traces in only 22% of DDD and 64% of C3GN. Lower-intensity C4d staining (1 to 2+) was mostly concordant with similar amounts of Igs/C1q. Discordant 3+ staining was noted in approximately 50% of cases of DDD and 20% of cases of C3GN. Among them, paraffin immunofluorescence unmasked polyclonal Igs in 2 of 5 cases of DDD and 1 of 3 cases of C3GN. Conclusion: This observational study suggests that the presence of glomerular C4d should not exclude a C3 glomerulopathy. In lower intensities, it appears to represent overlying classical/lectin pathway activation with concordant Ig/C1q deposits. A subset of cases, however, displays intense and discordant C4d staining, which raises the possibility of an associated lectin pathway abnormality, a potential future area of study.

DOI: 10.1016/j.ekir.2019.02.006

PMCID: PMC6506704

PMID: 31080925

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Inflammation in uveal melanoma (UM) is linked to a bad prognosis. It is rare type of cancer, of which the metastases are usually fatal within a year. Infiltration with an inflammatory infiltrate increases with disease progression but does not seem to inhibit metastasis. The Canonical NFκB (C-NFκB) pathway is known to play a crucial role in tumor inflammation. We therefore, studied the expression of canonical NFκB proteins and their prognostic relevance in UM. Our study evaluated the expression of C-NFκB proteins (p65, p50, and c-Rel) by using immunohistochemistry on sections from 75 formalin-fixed UM. Activation of the NFκB subunit was determined on fresh tumor specimens by measuring the DNA-binding activity in nuclei using an NFκB ELISA assay. Real-time PCR was performed on frozen material on 58 tumors. The presence of native C-NFκB heterodimers (p65/p50 and c-Rel/p50) was confirmed by co-immunoprecipitation followed by Western blotting. We observed a high nuclear immunoreactivity of p65, p50, and c-Rel proteins in 54, 60 and 41% UM cases, respectively. Expression of C-NFκB proteins significantly correlated with parameters which are related to the inflammatory environment of UM. Nuclear immunoreactivity of p65 and p50 was associated with lower patient survival ($p=0.041$; $p=0.048$) while c-Rel was not. Our finding reveals that C-NFκB proteins expressed are more often in UM with inflammation than those without inflammation. Activation of the canonical NFκB pathway is more frequent in high risk UM patients. These observations might help to understand the behaviour of high risk tumors, with upregulation of C-NFκB proteins contributing to tumor aggressiveness.

DOI: 10.1007/s10585-019-09969-y

PMID: 31069565

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Cognitive deficits in Schizophrenia interfere with everyday functioning and social functioning. Strong familial associations in schizophrenia might serve to establish cognitive impairments as endophenotypic markers. Therefore, visuo-spatial working memory simulating day-to-day activities at high memory load was assessed in patients with schizophrenia, their first-degree relatives and healthy controls to explore pre-trial and pre-response EEG microstates and their intracranial generators. Twenty-eight patients with schizophrenia, first-degree relatives and matched healthy controls participated in the study. Brain activity during visuo-spatial working memory task was recorded using 128-channel electroencephalography. Pre-trial and pre-response microstate maps of correct and error trials were clustered across groups according to their topography. Microstate map parameters and underlying cortical sources were compared among groups. Pre-trial (correct) microstate Map 1 was significantly different between controls and patients which could qualify it as a state marker with its intracranial generator localized to right inferior frontal gyrus (rIFG). Pre-response (correct) microstate map was significantly different between controls and first-degree relatives which could be considered an endophenotypic marker for schizophrenia. No significant differences were observed for error trials between groups. rIFG which is involved in the execution of multi-component behaviour and selective inhibitory control could distinguish patients with schizophrenia from their first-degree relatives and healthy controls. Further, microstate based biomarkers have the potential to facilitate diagnosis of schizophrenia at a preclinical stage resulting in efficient diagnosis and better prognosis.

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DOI: 10.1016/j.bbr.2019.111964
PMID: 31129232

143: Sreenath K, Chaudhry R, Vinayaraj EV, Thakur B. Antibiotic susceptibility of environmental Legionella pneumophila isolated in India. Future Microbiol. 2019 May;14:661-669. doi: 10.2217/fmb-2019-0049. Epub 2019 May 31. PubMed PMID: 31148475.

Aim: Data are limited regarding the antibiotic susceptibility of Legionella pneumophila in India. The aim of this study was to determine the drug susceptibility of environmental L. pneumophila isolates in India for antibiotics commonly used in clinical practice for Legionnaires' disease treatment. Materials & methods: The activities of seven antibiotics against 46 environmental isolates of L. pneumophila were evaluated by using E-test on buffered charcoal yeast extract- α agar. Results: Among the L. pneumophila isolates tested, no tendency toward drug resistance was observed. Rifampicin was the most potent drug followed by levofloxacin, while doxycycline and tetracycline were found to be the less active agents. Conclusion: Susceptibility testing of Legionella environmental isolates could be beneficial to notify resistance to antibiotics in the environment before it becomes evident in clinical strains.

DOI: 10.2217/fmb-2019-0049
PMID: 31148475

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145: Srinivasapura Venkateshmurthy N, Mc Namara K, Koorts H, Mohan S, S Ajay V, Jindal D, Malipeddi BR, Roy A, Tandon N, Prabhakaran D, Worsley T, Maddison R, O'Reilly S. Process evaluation protocol for a cluster randomised trial of a complex, nurse-led intervention to improve hypertension management in India. *BMJ Open.* 2019 May 19;9(5):e027841. doi: 10.1136/bmjopen-2018-027841. PubMed PMID: 31110103; PubMed Central PMCID: PMC6530308.

INTRODUCTION: India has high prevalence of hypertension but low awareness, treatment and control rate. A cluster randomised trial entitled 'm-Power Heart Project' is being implemented to test the effectiveness of a nurse care coordinator (NCC) led complex intervention to address uncontrolled hypertension in the community health centres (CHCs). The trial's process evaluation will assess the fidelity and quality of implementation, clarify the causal mechanisms and identify the contextual factors associated with variation in the outcomes. The trial will use a theory-based mixed-methods process evaluation, guided by the Consolidated Framework for Implementation Research.

METHODS AND ANALYSIS: The process evaluation will be conducted in the CHCs of Visakhapatnam (southern India). The key stakeholders involved in the intervention development and implementation will be included as participants. In-depth interviews will be conducted with intervention developers, doctors, NCCs and health department officials and focus groups with patients and their caregivers. NCC training will be evaluated using Kirkpatrick's model for training evaluation. Key process evaluation indicators (number of patients recruited and retained; concordance between the treatment plans generated by the electronic decision support system and treatment prescribed by the doctor and so on) will be assessed. Fidelity will be assessed using Borrelli et al's framework. Qualitative data will be analysed using the template analysis technique. Quantitative data will be summarised as medians (IQR), means (SD) and proportions as appropriate. Mixed-methods analysis will be conducted to assess if the variation in the mean reduction of systolic blood pressure between the intervention CHCs is influenced by patient satisfaction, training outcome, attitude of doctors, patients and NCCs about the intervention, process indicators etc. **ETHICS AND DISSEMINATION:** Ethical approval for this study was obtained from the ethics committees at Public Health Foundation of India and Deakin University. Findings will be disseminated via peer-reviewed publications, national and international conference presentations. **TRIAL REGISTRATION NUMBER:** NCT03164317; Pre-results.

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DOI: 10.1136/bmjopen-2018-027841
PMCID: PMC6530308
PMID: 31110103

146: Suliankatchi Abdulkader R, Sinha DN, Jeyashree K, Rath R, Gupta PC, Kannan S, Agarwal N, Venugopal D. Trends in tobacco consumption in India 1987-2016: impact of the World Health Organization Framework Convention on Tobacco Control. *Int J Public Health.* 2019 Jul;64(6):841-851. doi: 10.1007/s00038-019-01252-x. Epub 2019 May 28. PubMed PMID: 31134319.

OBJECTIVES: We describe national and subnational trends in tobacco use over three decades in India, assess the impact of the World Health Organization's Framework Convention on Tobacco Control (FCTC) on them and draw inferences for regional tobacco control policy.

METHODS: Data from nine cross-sectional surveys conducted between 1987 and 2016 were analysed. Time trends in gender- and state-wise prevalence were derived for different forms of tobacco. To assess Framework Convention's impact, relative

changes in tobacco prevalence before and after its implementation were estimated. Progress towards global noncommunicable diseases target was also measured. RESULTS: Post-implementation of the FCTC, smoking and smokeless tobacco use declined by 52.9% and 17.6%, respectively. The tobacco product mix (exclusive smokeless/exclusive smoked/dual) underwent a reversal from 37:52:11 in 1987 to 65:22:13 in 2016. Having achieved 20.5% relative reduction since 2009, India is en route to achieving the global noncommunicable diseases target. CONCLUSIONS: Steep declines in tobacco use have followed the implementation of FCTC in India. However, the impact has been unequal on smokeless and smoked forms. Tobacco-control policies in high smokeless burden countries should take cognizance of this pattern and design comprehensive and flexible policies.

DOI: 10.1007/s00038-019-01252-x
PMID: 31134319

147: Suri TM, Esquinas A, Hadda V, Mohan A. HVNI vs NIPPV in the treatment of acute decompensated heart failure: Is acute stabilization enough? *Am J Emerg Med.* 2019 May 7. pii: S0735-6757(19)30330-4. doi: 10.1016/j.ajem.2019.05.019. [Epub ahead of print] PubMed PMID: 31085011.

148: Syed Abuthahir S, NizamMohideen M, Viswanathan V, Abiraman T, Balasubramanian S. The crystal structures and Hirshfeld surface analysis of N',N'''-((1E,1'E)-{methyl-enebis(-oxy)}bis-(6-bromo-3,1-phenyl-ene)}bis-(methan-yl-ylidene))bis-(isonicotinohydrazide) dihydrate and N',N'''-((1E,1'E)-{butane-1,4-diylbis(-oxy)}bis-(2,1-phenyl-ene)}bis-(methan-yl-ylidene))bis-(isonicotino-hydrazide) [+ solvent]. *Acta Crystallogr E Crystallogr Commun.* 2019 Apr 18;75(Pt 5):655-661. doi: 10.1107/S2056989019005048. eCollection 2019 May 1. PubMed PMID: 31110806; PubMed Central PMCID: PMC6505606.

The title compounds, C₂₇H₂₀Br₂N₆O₄·2H₂O, (I), and C₃₀H₂₈N₆O₄·[+ solvent], (II), both crystallize with one half-mol-ecule in the asymmetric unit. The whole mol-ecule of (I) is generated by twofold rotation symmetry, with the twofold rotation axis bis-ecting the C atom of the -O-CH₂-O- bridge. This results in a folded or U-shaped conformation of the mol-ecule. The whole mol-ecule of (II) is generated by inversion symmetry, with the central CH₂-CH₂ bond of the -O-(CH₂)₄-O- bridge being located about a center of inversion. This results in a step-like conformation of the mol-ecule. The central C(=O)N=N=C regions of the isonicotinohydrazide moieties in both compounds are planar and the configuration about the imine C=N bonds is E. In compound (I), the benzene and pyridine rings are inclined to each other by 37.60 (6)°. The two symmetry-related pyridine rings are inclined to each other by 74.24 (6)°, and the two symmetry-related benzene rings by 7.69 (6)°. In compound (II), the benzene and pyridine rings are inclined to each other by 25.56 (11)°. The symmetry-related pyridine rings are parallel, as are the two symmetry-related benzene rings. In the crystal of (I), a pair of water mol-ecules link the organic mol-ecules via Owater-H··O and Owater-H··N hydrogen bonds, forming chains along [001], and enclosing an R 4 2(8) and two R 1 2(5) ring motifs. The chains are linked by N-H··Npyridine hydrogen bonds, forming a supra-molecular framework. There are also a number of C-H··O hydrogen bonds, and C-H··n and offset π-π inter-actions [inter-planar distance = 3.294 (1) Å] present reinforcing the framework. In the crystal of (II), mol-ecules are linked by N-H··Npyridine hydrogen bonds, forming a supra-molecular framework. Here too there are also a number of C-H··O hydrogen bonds present, and a C-H··n inter-action, reinforcing the framework. For compound (II), a region of disordered electron density was corrected for using the SQUEEZE [Spek (2015 ▶)]. *Acta Cryst.* C71, 9-18] routine in PLATON. Their formula mass and unit-cell characteristics were not taken into account during refinement.

DOI: 10.1107/S2056989019005048
PMCID: PMC6505606
PMID: 31110806

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cavopulmonary connection. *J Card Surg.* 2019 May;34(5):236-238. doi: 10.1111/jocs.14037. Epub 2019 Mar 29. PubMed PMID: 30924563.

BACKGROUND: Total Cavopulmonary connection (Fontan) is the final palliation for patients with a functionally univentricular heart. This is commonly accomplished after a prior bidirectional Glenn on cardiopulmonary bypass (CPB) with separate cannulation of the aorta, superior vena cava (SVC), and inferior vena cava. We describe an alternative technique of Fontan completion that eliminates the need for cannulation and dissection of the SVC, and pulmonary artery dissection.

METHODS: Between January and October 2018, 17 patients underwent completion Fontan using an alternate technique at our institute. All operations were conducted on CPB at normothermia without cannulating the SVC **RESULTS:** Mean CPB time was 60±16.8minutes (range, 39-102minutes). There were no early deaths. Mean postoperative Fontan pressures were 15.6±1.2mmHg with no gradient between the SVC and IVC pressures. Mean duration of hospital stay was 15.6±3.6days (range, 10-22days). No patient developed phrenic nerve paresis or palsy.

CONCLUSIONS: Completion without cannulating the SVC is simple, reproducible, and easy to teach. It avoids the disadvantages associated with routine techniques.

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DOI: 10.1111/jocs.14037
PMID: 30924563

150: Taneja N, Gupta S. Apremilast is efficacious in refractory alopecia areata. *J Dermatolog Treat.* 2019 May 6:1-3. doi: 10.1080/09546634.2019.1616046. [Epub ahead of print] PubMed PMID: 31055978.

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Pain sensitivity is a recognized feature of fibromyalgia syndrome (FMS) but the contribution of spinal nociceptive circuitry to this phenomenon is unknown. Therefore, the objectives were to study the changes in spinal nociception i.e. nociceptive flexion reflex (NFR) in patients with FMS and to investigate correlation if any, between NFR threshold, pain duration and tender points in FMS. One hundred and three patients with FMS and 74 healthy volunteers participated in the study. To record NFR, sural nerve was stimulated in the retro malleolar region and the reflex response was recorded from the short head of biceps femoris muscle. NFR was elicited at significantly lower [21.0(18.0-25.0)V] thresholds in FMS group when compared to healthy subjects [30.0(24.75-35.0)V; p=0.001] indicating hyperalgesic response to electrocutaneous stimulation in FMS patients. The latency and other parameters of NFR were comparable in both the groups. No significant correlation was found among NFR threshold and pain duration or tender points. On the basis of results of present study, it may be concluded that the functional deficit of the spinal nociceptive system can contribute to hyperalgesia in FMS. This is first study that correlates a marker of central hyper-excitability (NFR threshold) with clinical symptoms (pain duration and tender points) of FMS.

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PMID: 31080004

152: Tripathi M, Taylor D, Khan SI, Tekwani BL, Ponnann P, Das US, Velpandian T, Rawat DS. Hybridization of Fluoro-amodiaquine (FAQ) with Pyrimidines: Synthesis and Antimalarial Efficacy of FAQ-Pyrimidines. *ACS Med Chem Lett.* 2019 Mar 13;10(5):714-719. doi: 10.1021/acsmchemlett.8b00496. eCollection 2019 May 9. PubMed PMID: 31097988; PubMed Central PMCID: PMC6511959.

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

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PMCID: PMC6511959 [Available on 2020-05-09]
PMID: 31097988

153: Tyagi A, Pramanik R, Bakhshi R, Singh A, Vishnubhatla S, Bakhshi S. Expression of mitochondrial genes predicts survival in pediatric acute myeloid leukemia. *Int J Hematol*. 2019 Aug;110(2):205-212. doi: 10.1007/s12185-019-02666-2. Epub 2019 May 22. PubMed PMID: 31119613.

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
PMID: 31119613

154: U M P, Bhatia R, V S, Singh N, Joseph R, Dash D, Singh RK, Tripathi M, Srivastava MVP, Singh MM, Suri A, Prasad K. Validation of ICH and ICH-GS Scores in an Indian Cohort: Impact of Medical and Surgical Management. *J Stroke Cerebrovasc Dis*. 2019 May 28. pii: S1052-3057(19)30223-X. doi: 10.1016/j.jstrokecerebrovasdis.2019.05.003. [Epub ahead of print] PubMed PMID: 31151837.

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.

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155: Vibha D, Prasad K. Prevailing practices in the treatment of tuberculous meningitis (TBM): a cross-sectional study. *Postgrad Med J.* 2019 Jun;95(1124):348-349. doi: 10.1136/postgradmedj-2019-136486. Epub 2019 May 13. PubMed PMID: 31085623.

156: Vinchure OS, Sharma V, Tabasum S, Ghosh S, Singh RP, Sarkar C, Kulshreshtha R. Polycomb complex mediated epigenetic reprogramming alters TGF- β signaling via a novel EZH2/miR-490/TGIF2 axis thereby inducing migration and EMT potential in glioblastomas. *Int J Cancer.* 2019 Sep 1;145(5):1254-1269. doi: 10.1002/ijc.32360. Epub 2019 May 10. PubMed PMID: 31008529.

Recent advancement in understanding cancer etiology has highlighted epigenetic deregulation as an important phenomenon leading to poor prognosis in glioblastoma (GBM). Polycomb repressive complex 2 (PRC2) is one such important epigenetic modifier reportedly altered in GBM. However, its defined mechanism in tumorigenesis still remains elusive. In present study, we analyzed our in-house ChIPseq data for H3k27me3 modified miRNAs and identified miR-490-3p to be the most common target in GBM with significantly downregulated expression in glioma patients in both TCGA and GBM patient cohort. Our functional analysis delineates for the first time, a central role of PRC2 catalytic unit EZH2 in directly regulating expression of this miRNA and its host gene CHRM2 in GBM. In accordance, cell line treatment with EZH2 siRNA and 5-azacytidine also confirmed its coregulation by CpG and histone methylation based epigenetic mechanisms. Furthermore, induced overexpression of miR-490-3p in GBM cell lines significantly inhibited key hallmarks including cellular proliferation, colony formation and spheroid formation, as well as epithelial-to-mesenchymal transition (EMT), with downregulation of multiple EMT transcription factors and promigratory genes (MMP9, CCL5, PIK3R1, ICAM1, ADAM17 and NOTCH1). We also for the first time report TGFBR1 and TGIF2 as two direct downstream effector targets of miR-490-3p that are also deregulated in GBM. TGIF2, a novel target, was shown to promote migration and EMT that could partially be rescued by miR-490-3p overexpression. Overall, this stands as a first study that provides a direct link between epigenetic modulator EZH2 and oncogenic TGF- β signaling involving novel miR-490-3p/TGIF2/TGFBR1 axis, that being targetable might be promising in developing new therapeutic intervention strategies for GBM.

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157: Walter SD, Macaskill P, Turner R, Guyatt G, Cook R, Prasad K. Comment to the reply letter: Letter to the Editor: Preference option randomized design (PORD) for comparative effectiveness research: Statistical power for testing comparative effect, preference effect, selection effect, intent-to-treat effect, and overall effect (SMMR, Vol. 28, Issue 2, 2019). *Stat Methods Med Res.* 2019 May;28(5):1603. doi: 10.1177/0962280218768107. Epub 2018 Apr 10. PubMed PMID: 29633654.

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Triangular alopecia presents as a unilateral triangular-shaped non-scarring alopecia usually involving the temporal scalp. There are few reports of occipital scalp involvement and bilateral disease. Usually it is seen at 2-3 years of age but occasionally can be present at birth. Here we present a unique case of triangular alopecia involving the eyebrows in a 23-year-old man. He had bilateral symmetrical involvement since birth. Points in favour of triangular alopecia in our case were non-scarring alopecia, oval-to-triangular shape, fringe of terminal hair at superior margin; trichoscopy showing significant decrease in hair diameter diversity with increased number of vellus and intermediate hair and histopathology showing normal hair follicle density and increased vellus and intermediate hair (miniaturisation) with absence of inflammation on histopathology. Other differential diagnoses kept were partial duplication of eyebrows, congenital alopecia areata and mild form of ectodermal dysplasia.

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160: Yadav M, Sinha A, Khandelwal P, Hari P, Bagga A. Efficacy of low-dose daily versus alternate-day prednisolone in frequently relapsing nephrotic syndrome: an open-label randomized controlled trial. *Pediatr Nephrol.* 2019 May;34(5):829-835. doi: 10.1007/s00467-018-4071-7. Epub 2018 Sep 7. PubMed PMID: 30194663.

BACKGROUND: While patients with frequently relapsing nephrotic syndrome (FRNS) are initially treated with long-term alternate-day prednisolone, relapses and adverse effects are common. In an open-label randomized controlled trial, we compared the efficacy of therapy with low-dose daily to standard alternate-day prednisolone in reducing relapse rates over 12-month follow-up.

METHODS: Consecutive patients, aged 2-18 years, with FRNS were included. Following therapy of relapse, prednisolone was tapered to 0.75 mg/kg on alternate days. Stratifying for steroid dependence, patients were randomly assigned to prednisolone at 0.2-0.3 mg/kg daily or 0.5-0.7 mg/kg alternate day for 12 months. Relapses were treated with daily prednisolone, followed by return to intervention. Primary outcome was the incidence of relapses. Proportion with therapy failure (≥ 2 relapses in any 6 months or significant steroid toxicity) and sustained remission, cumulative prednisolone intake and adverse events were evaluated.

RESULTS: Patients receiving daily prednisolone (n=30) showed significantly fewer relapses than those on alternate-day therapy (n=31) (0.55 relapses/person-year versus 1.94 relapses/person-year; incidence rate ratio 0.28; 95% CI 0.15, 0.52). Daily therapy was associated with higher rates of sustained remission at 6 months (73.3 versus 48.4%) and 1 year (60 versus 31.6%; log rank $p=0.013$), lower rates of treatment failure at 6 months (3.3 versus 32.8%) and 1 year (6.7 versus 57.4%; $p<0.0001$), and lower prednisolone use (0.27 ± 0.07 versus 0.39 ± 0.19 mg/kg/day; $p=0.003$). Three and two patients need to receive the study intervention to enable sustained remission and prevent treatment failure, respectively.

CONCLUSIONS: In patients with FRNS, daily administration of low-dose prednisolone is more effective than standard-dose alternate day therapy in lowering relapse

rates, sustaining remission, and enabling steroid sparing.

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Gluten is known to be the main triggering factor for celiac disease (CeD), an immune-mediated disorder. CeD is therefore managed using a strict and lifelong gluten-free diet (GFD), the only effective treatment available currently. However, the GFD is restrictive. Hence, efforts are being made to explore alternative therapies. Based on their mechanisms of action on various molecular targets involved in the pathogenesis of CeD, these therapies may be classified into one of the following five broad approaches. The first approach focuses on decreasing the immunogenic content of gluten, using strategies like genetically modified wheat, intra-intestinal gluten digestion using glutenases, microwave thermal treatment of hydrated wheat kernels, and gluten pretreatment with either bacterial/ fungal derived endopeptidases or microbial transglutaminase. The second approach involves sequestering gluten in the gut lumen before it is digested into immunogenic peptides and absorbed, using binder drugs like polymer p(HEMA-co-SS), single chain fragment variable (scFv), and anti- gluten antibody AGY. The third approach aims to prevent uptake of digested gluten through intestinal epithelial tight junctions, using a zonulin antagonist. The fourth approach involves tissue transglutaminase (tTG) inhibitors to prevent the enhancement of immunogenicity of digested gluten by the intestinal tTG enzyme. The fifth approach seeks to prevent downstream immune activation after uptake of gluten immunogenic peptides through the intestinal mucosal epithelial layer. Examples include HLA-DQ2 blockers that prevent presentation of gluten derived-antigens by dendritic cells to T cells, immune- tolerizing therapies like the vaccine Nexvax2 and TIMP-Glia, cathepsin inhibitors, immunosuppressants like corticosteroids, azathioprine etc., and anti-cytokine agents targeting TNF- α and interleukin-15. Apart from these approaches, research is being done to evaluate the effectiveness of probiotics/prebiotics, helminth therapy using *Necator americanus*, low FODMAP diet, and pancreatic enzyme supplementation in CeD symptom control; however, the mechanisms by which they play a beneficial role in CeD are yet to be clearly established. Overall, although many therapies being explored are still in the pre-clinical phase, some like the zonulin antagonist, immune tolerizing therapies and glutenases have reached phase II/III clinical trials. While these potential options appear exciting, currently they may at best be used to supplement rather than supplant the GFD.

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162: Zhao CW, Singh V, Singh V. Childhood acute lymphoblastic leukaemia relapse with atypical localised presentation mimicking ankle trauma in a 28-year-old man. *BMJ Case Rep.* 2019 May 21;12(5). pii: e228541. doi: 10.1136/bcr-2018-228541. PubMed PMID: 31118175.

Acute lymphoblastic leukaemia (ALL) is a common paediatric cancer with a tendency to relapse, usually within 3 years of remission. Most patients present with hepatomegaly, splenomegaly, pallor, fever and bruising. Localised musculoskeletal presentation is extremely rare. Here, we present a case of leukaemia relapse in the bone marrow of a 28-year-old man 9 years after achieving remission, presenting only with ankle pain and normal routine labs besides mild hypercalcemia, and no signs of disease in common bone marrow biopsy sites. This highly localised presentation is unusual and would hopefully inform clinicians to have a high index of suspicion for relapse in an adult patient who has had childhood ALL.

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