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**AIIMS**  
**New Delhi**

List of publications of AIIMS, New Delhi  
for the month of JUNE, 2019  
[Source: [www.pubmed.com](http://www.pubmed.com)].

1: Abraham RA, Agrawal PK, Acharya R, Sarna A, Ramesh S, Johnston R, de Wagt A, Khan N, Porwal A, Kurundkar SB, Pandey A, Pullakhandam R, Nair KM, Kumar GT, Sachdev HPS, Kapil U, Saxena R, Deb S, Khera A, Ramakrishnan L. Effect of temperature and time delay in centrifugation on stability of select biomarkers of nutrition and non-communicable diseases in blood samples. *Biochem Med (Zagreb)*. 2019 Jun 15;29(2):020708. doi: 10.11613/BM.2019.020708. PubMed PMID: 31223262; PubMed Central PMCID: PMC6559620.

**Introduction:** Preanalytical conditions are critical for blood sample integrity and poses challenge in surveys involving biochemical measurements. A cross sectional study was conducted to assess the stability of select biomarkers at conditions that mimic field situations in surveys.

**Material and methods:** Blood from 420 volunteers was exposed to 2 - 8 °C, room temperature (RT), 22 - 30 °C and > 30 °C for 30 min, 6 hours, 12 hours and 24 hours prior to centrifugation. After different exposures, whole blood (N = 35) was used to assess stability of haemoglobin, HbA1c and erythrocyte folate; serum (N = 35) for assessing stability of ferritin, C-reactive protein (CRP), vitamins B12, A and D, zinc, soluble transferrin receptor (sTfR), total cholesterol, high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), triglycerides, albumin, total protein and creatinine; and plasma (N = 35) was used for glucose. The mean % deviation of the analytes was compared with the total change limit (TCL), computed from analytical and intra-individual imprecision. Values that were within the TCL were deemed to be stable.

**Result:** Creatinine (mean % deviation 14.6, TCL 5.9), haemoglobin (16.4%, TCL 4.4) and folate (33.6%, TCL 22.6) were unstable after 12 hours at 22-30°C, a temperature at which other analytes were stable. Creatinine was unstable even at RT for 12 hours (mean % deviation: 10.4). Albumin, CRP, glucose, cholesterol, LDL, triglycerides, vitamins B12 and A, sTfR and HbA1c were stable at all studied conditions.

**Conclusion:** All analytes other than creatinine, folate and haemoglobin can be reliably estimated in blood samples exposed to 22-30°C for 12 hours in community-based studies.

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PMCID: PMC6559620

PMID: 31223262

2: Agarwal A, Gupta S, Yadav AK, Nema RK, Ansari K, Biswas D. Molecular and phylogenetic analysis of Chikungunya virus in Central India during 2016 and 2017 outbreaks reveal high similarity with recent New Delhi and Bangladesh strains. *Infect Genet Evol*. 2019 Jun 24;75:103940. doi: 10.1016/j.meegid.2019.103940. [Epub ahead of print] PubMed PMID: 31247338.

Central India witnessed Chikungunya virus (CHIKV) outbreaks in 2016 and 2017. The present report is a hospital based cross-sectional study on the serological and molecular epidemiology of the outbreak. Mutational and phylogenetic analysis was conducted to ascertain the genetic relatedness of the central Indian strains with other Indian and global strains. Chikungunya infection was confirmed in the clinically suspected patients by the detection of anti-CHIKV IgM antibody by ELISA and viral RNA by RT-PCR. A representative set of the RT-PCR positive samples were sequenced for E1 gene and analyzed to identify the emerging mutations and establish their phylogenetic relationship, particularly with other contemporary strains. Phylogenetic analysis revealed the present strains to be of East Central South African (ECSA) genotype. Emergence of a variant strain was observed in the year 2016, which became the predominant strain in this region in 2017. The strains showed significant identity with recent New Delhi strains of 2015 and 2016 and Bangladesh strains of 2017. The epidemic mutation A226V which emerged in 2006 outbreaks of India and Indian Ocean Islands was found to be absent in the current strains. Among the important mutations viz. K211E, M269V, D284E, I317V & V322A observed in the recent strains. I317V is a novel mutation which has emerged very recently as it was found only in central Indian (2016, 2017), New Delhi strains (2015, 2016) and Bangladesh strains (2017). This study

has identified a unique mutation E1:I317V in the Central Indian strains, which is present only in recent New Delhi and Bangladesh strains till date. This study highlights the need for continuous molecular surveillance of circulating CHIKV strains in order to facilitate the prompt identification of novel strains of this virus and enable the elucidation of their clinical correlates.

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PMID: 31247338

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

**PURPOSE:** Fat embolism syndrome (FES) is systemic manifestation of fat emboli in the circulation seen mostly after long bone fractures. FES is considered a lethal complication of trauma. There are various case reports and series describing FES. Here we describe the clinical characteristics, management in ICU and outcome of these patients in level I trauma center in a span of 6 months.

**METHODS:** In this prospective study, analysis of all the patients with FES admitted in our polytrauma intensive care unit (ICU) of level I trauma center over a period of 6 months (from August 2017 to January 2018) was done.

Demographic data, clinical features, management in ICU and outcome were analyzed.

**RESULTS:** We admitted 10 cases of FES. The mean age of patients was 31.2 years. The mean duration from time of injury to onset of symptoms was 56 h. All patients presented with hypoxemia and petechiae but central nervous system symptoms were present in 70% of patients. The mean duration of mechanical ventilation was 11.7 days and the mean length of ICU stay was 14.7 days. There was excellent recovery among patients with no neurological deficit.

**CONCLUSION:** FES is considered a lethal complication of trauma but timely management can result in favorable outcome. FES can occur even after fixation of the fracture. Hypoxia is the most common and earliest feature of FES followed by CNS manifestations. Any patient presenting with such symptoms should raise the suspicion of FES and mandate early ICU referral.

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PMCID: PMC6543189

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4: Agrawal A, Mahey R, Kachhawa G, Khadgawat R, Vanamail P, Kriplani A. Comparison of metformin plus myoinositol vs metformin alone in PCOS women undergoing ovulation induction cycles: randomized controlled trial. *Gynecol Endocrinol*. 2019 Jun;35(6):511-514. doi: 10.1080/09513590.2018.1549656. Epub 2019 Jan 7. PubMed PMID: 30614289.

The present study was planned to evaluate the benefit of synergetic effect of Metformin plus Myo-inositol versus Metformin alone in infertile polycystic ovarian syndrome (PCOS) women undergoing ovulation induction. One hundred and twenty infertile PCOS women were randomized: Group I (n=60) received Metformin (500mg) plus Myoinositol(600mg) three times a day; Group II received Metformin 500mg three times a day. Subjects were advised to try for spontaneous conception. Those who did not conceive after 3months, were given three cycles of ovulation induction+intrauterine insemination. Hormonal and biochemical profile parameters were done at baseline and after 3months of therapy. Primary outcome measure was live birth rate. Secondary outcomes were improvement in menstrual

cycle, hormonal and biochemical parameters, spontaneous conception, abortions, multiple pregnancy, and ovarian hyperstimulation syndrome. Baseline demographic, hormonal and biochemical parameters were comparable in two groups. There was a significant improvement in menstrual cycles (cycle length and bleeding days) in Group I as compared to Group II. The improvement in biochemical and hormonal parameters were comparable in the two groups after 3 months. Live birth rate was significantly higher in the Group I as compared to Group II [55% (33/60); 26.67% (16/60);  $p=.002$ ]. The study concluded significantly higher live birth rate in women receiving the combination as compared to metformin alone.

DOI: 10.1080/09513590.2018.1549656

PMID: 30614289

5: Anjali VR, Srivastava A, Kakkar A, Mallick S. Extremely Aggressive Behavior of a Completely Resected Case of Gallbladder Undifferentiated Carcinoma, Giant Cell Type: a Rare Case with Breast, Neck Nodes, and Subcutaneous Scalp Nodules Metastasis. *J Gastrointest Cancer*. 2019 Jun 3. doi: 10.1007/s12029-019-00262-5. [Epub ahead of print] PubMed PMID: 31155696.

6: Ayyalusamy A, Vellaiyan S, Subramanian S, Ilamurugu A, Satpathy S, Nauman M, Katta G, Madineni A. Auto-segmentation of head and neck organs at risk in radiotherapy and its dependence on anatomic similarity. *Radiat Oncol J*. 2019 Jun;37(2):134-142. doi: 10.3857/roj.2019.00038. Epub 2019 Jun 30. PubMed PMID: 31266293; PubMed Central PMCID: PMC6610007.

**PURPOSE:** The aim is to study the dependence of deformable based auto-segmentation of head and neck organs-at-risks (OAR) on anatomy matching for a single atlas based system and generate an acceptable set of contours.

**METHODS:** A sample of ten patients in neutral neck position and three atlas sets consisting of ten patients each in different head and neck positions were utilized to generate three scenarios representing poor, average and perfect anatomy matching respectively and auto-segmentation was carried out for each scenario. Brainstem, larynx, mandible, cervical oesophagus, oral cavity, pharyngeal muscles, parotids, spinal cord, and trachea were the structures selected for the study. Automatic and oncologist reference contours were compared using the dice similarity index (DSI), Hausdroff distance and variation in the centre of mass (COM).

**RESULTS:** The mean DSI scores for brainstem was good irrespective of the anatomy matching scenarios. The scores for mandible, oral cavity, larynx, parotids, spinal cord, and trachea were unacceptable with poor matching but improved with enhanced bony matching whereas cervical oesophagus and pharyngeal muscles had less than acceptable scores for even perfect matching scenario. HD value and variation in COM decreased with better matching for all the structures.

**CONCLUSION:** Improved anatomy matching resulted in better segmentation. At least a similar setup can help generate an acceptable set of automatic contours in systems employing single atlas method. Automatic contours from average matching scenario were acceptable for most structures. Importance should be given to head and neck position during atlas generation for a single atlas based system.

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PMCID: PMC6610007

PMID: 31266293

7: Babu AN, Niehaus E, Shah S, Unnithan C, Ramkumar PS, Shah J, Binoy VV, Soman B, Arunan MC, Jose CP. Smartphone geospatial apps for dengue control, prevention, prediction, and education: MOSapp, DISapp, and the mosquito perception index (MPI). *Environ Monit Assess*. 2019 Jun 28;191(Suppl 2):393. doi: 10.1007/s10661-019-7425-0. PubMed PMID: 31254076.

India has the largest number of dengue cases in the world, contributing approximately 34% of the global burden. The framework for a geospatially enabled early warning and adaptive response system (EWARS) was first proposed in 2008. It

was meant to be a decision support system for enhancing traditional surveillance methods for preventing mosquito-borne diseases in India by utilizing remote sensing data and fuzzy logic-based mathematical predictive modeling. This conceptual paper presents a significant evolution of EWARS such that it synthesizes inputs from not only traditional surveillance and reporting systems for dengue but also from the public via participatory disease surveillance. Two smartphone-based applications have been developed to support EWARS. The first-MOSapp-allows field health workers to upload surveillance data and collect key data on environmental parameters by both direct observation and via portable microclimate stations. The second-DISapp-collects relevant information directly from the community to support participatory disease surveillance. It also gives the user a real-time estimate of the risk of exposure to dengue in proximity to their home and has an educational component that provides information on relevant preventive measures. Both applications utilize a new mosquito abundance measure-the mosquito perception index (MPI)-as reported by the user. These data streams will feed into the EWARS model to generate dynamic risk maps that can guide resource optimization and strengthen disease surveillance, prevention, and response. It is anticipated that such an approach can assist in addressing gaps in the current system of dengue surveillance and control in India.

DOI: 10.1007/s10661-019-7425-0

PMID: 31254076

8: Bagri NK. Cyclosporine for Systemic Onset Juvenile Idiopathic Arthritis: Current Stand and Future Directions. *Indian J Pediatr.* 2019 Jul;86(7):576-577. doi: 10.1007/s12098-019-02985-6. Epub 2019 Jun 1. Review. PubMed PMID: 31154576.

9: Baitha U, Ranjan P, Sarkar S, Arora C, Kumari A, Dwivedi SN, Patil A, Jamshed N. Development of self-assessment tool of residents doctors' communication skills of in India. *J Educ Eval Health Prof.* 2019;16:17. doi: 10.3352/jeehp.2019.16.17. Epub 2019 Jun 24. PubMed PMID: 31230429.

**PURPOSE:** Effective communication skills are critical for physicians in order to provide optimum patient care. This study aimed to develop and validate a questionnaire for the self assessment of residents' communication skills in India.

**METHODS:** This was a mixed methods study conducted in two phases. The first phase consisted of questionnaire development including identification of relevant literature, focused group discussions with residents and experts from clinical specialities and pre-testing of the questionnaire. The second phase involved the questionnaire survey to 95 residents from Departments of Medicine, Emergency Medicine, Paediatrics, and Surgery at All India Institute of Medical Sciences, New Delhi, India in April 2019. Internal consistency was tested and factor structure for construct validity test was analyzed.

**RESULTS:** The questionnaire consisted of 3 sections: (A) 4 items on doctor-patient conflicts and role of communication skills to avoid these conflicts, (B) 29 items on self-assessment of communication skills in different settings, and (C) 8 items covering the barriers in practicing good communication skills. Sections B and C had good internal consistencies (Cronbach's alpha 0.005 and 0.771 respectively). Section C had a two-factor solution and could classify the barriers into 'training' and 'infrastructure' factors.

**CONCLUSION:** This appears to be a valid assessment tool of resident doctors' communication skills, which has potential utility for identifying gaps in communication skills and developing communication skills modules.

DOI: 10.3352/jeehp.2019.16.17

PMID: 31230429

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

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

DOI: 10.1038/s10038-019-0591-7

PMID: 30911093

11: Banerjee S, Niyas VKM, Soneja M, Shibeesh AP, Basheer M, Sadanandan R, Wig N, Biswas A. First experience of ribavirin postexposure prophylaxis for Nipah virus, tried during the 2018 outbreak in Kerala, India. *J Infect.* 2019 Jun;78(6):491-503. doi: 10.1016/j.jinf.2019.03.005. Epub 2019 Mar 6. PubMed PMID: 30851290.

12: Basu P, Muwonge R, Bhatla N, Nene BM, Joshi S, Esmey PO, Poli URR, Joshi G, Verma Y, Zomawia E, Shastri SS, Pimple S, Anantharaman D, Prabhu PR, Hingmire S, Sauvaget C, Lucas E, Pawlita M, Gheit T, Jayant K, Malvi SG, Siddiqi M, Michel A, Butt J, Sankaran S, Rameshwari Ammal Kannan TP, Varghese R, Divate U, Willhauck-Fleckenstein M, Waterboer T, Müller M, Sehr P, Vashist S, Mishra G, Jadhav R, Thorat R, Tommasino M, Pillai MR, Sankaranarayanan R; Indian HPV vaccine study group. Two-dose recommendation for Human Papillomavirus vaccine can be extended up to 18 years - updated evidence from Indian follow-up cohort study. *Papillomavirus Res.* 2019 Jun;7:75-81. doi: 10.1016/j.pvr.2019.01.004. Epub 2019 Jan 31. PubMed PMID: 30711698; PubMed Central PMCID: PMC6378832.

Earlier publication from the ongoing multi-centric study of the International Agency for Research on Cancer to evaluate less than three doses of the quadrivalent Human Papillomavirus (HPV) vaccine in India amongst unmarried girls demonstrated non-inferior total antibody titres, neutralizing antibody titres and antibody avidity in 2-dose recipients compared to 3-dose recipients at 15-18 years of age (Bhatla et al., 2018) [7]. The number of participants recruited at 15-18 years of age was 1515 and 1795 in the 3-dose and the 2-dose groups respectively. At a median follow-up of 7 years, incident HPV 16/18 infections were detected in 1.6% women receiving two doses and 0.8% women receiving three doses at 15-18 years. Frequency of incident infection was 7.0% in the age- and site-matched unvaccinated women (N=1484). No persistent infection from HPV 16 was observed in the 2- or 3-dose recipients and one (0.2%) persistent HPV 18 infection was documented, each in the 3-dose and 2-dose cohorts. Among the unvaccinated women, the frequency of HPV 16/18 persistent infection was 1.7%. The protection offered by two doses of quadrivalent HPV vaccine against incident and persistent infections in recipients at 15-18 years is comparable to that seen in

3-dose recipients at 15-18 years.

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PMCID: PMC6378832

PMID: 30711698

13: Behera C, Rautji R, Pratap Anuragi R, Niwas Yadav R. Suicide note written on the forearm using a sharp pointed object. *Med Leg J.* 2019 Jun;87(2):92-94. doi: 10.1177/0025817219845234. PubMed PMID: 31244405.

Suicide notes are generally written on readily available materials, such as paper, notebook, wall or mirror by means of pen, pencil, marker or chalk. They can also be communicated by telephone, text messages, internet and digital media. A case has been reported where a note was written with henna. Suicide notes written on one's body are uncommon, and notes engraved on the body with a sharp metallic object are extremely rare. We present two cases where a sharp pointed metallic object was used to write suicide notes on the body.

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PMID: 31244405

14: Bharath G, Mishra PR, Aggarwal P. Tranexamic Acid: Emerging Therapies in Hemoptysis. *Chest.* 2019 Jun;155(6):1303-1304. doi: 10.1016/j.chest.2019.02.018. PubMed PMID: 31174644.

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

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

DOI: 10.1007/s12098-019-02909-4

PMID: 30835073

16: Bhatwalkar SB, Gound SS, Mondal R, Srivastava RK, Anupam R. Anti-biofilm and Antibacterial Activity of *Allium sativum* Against Drug Resistant Shiga-Toxin Producing *Escherichia coli* (STEC) Isolates from Patient Samples and Food Sources. *Indian J Microbiol.* 2019 Jun;59(2):171-179. doi: 10.1007/s12088-019-00784-3. Epub 2019 Feb 18. PubMed PMID: 31031431; PubMed Central PMCID: PMC6458215.

*Escherichia coli* (*E. coli*) colonizes human intestinal tract and is usually harmless to the host. However, several strains of *E. coli* have acquired virulent genes and could cause enteric diseases, urinary tract and even brain infections. Shiga toxin producing *Escherichia coli* (STEC) is an enterohaemorrhagic *E. coli* (EHEC) which can result in bloody diarrhoea and could potentially lead to deadly haemolytic uremic syndrome (HUS). STEC is one of the important food borne

pathogens that causes food poisoning leading to diarrhoea and number of STEC outbreaks have occurred across the world. The use of standard antibiotics to treat STEC infection is not recommended as it increases the production of shiga toxin which could lead to HUS. Therefore, use of alternative approaches which include use of plant products to treat STEC infections have been gaining attention. The objective of this study was to evaluate the antibacterial and anti-biofilm activity of garlic (*Allium sativum*) against STEC strains isolated from various patient and food samples using in vitro assays. The microbiological isolation of STEC from various patient and food samples resulted in eight STEC isolates of which seven strains were multidrug resistant. Antibacterial assay results indicated that all the strains exhibited dose dependent sensitivity towards garlic with zone of inhibition diameters ranging from 7 to 24 mm with 15 µl of fresh garlic extract (FGE). Minimum inhibitory concentration (MIC) of FGE for isolates ranged from 30 to 140 µl/ml. Interestingly, the biofilm formation of all isolates in presence of 4% of FGE decreased by 35 to 59%. FTIR analysis indicated that treatment with 1% FGE results in compositional and content changes in the biofilm. In addition, the total carbohydrate content of biofilm was reduced by 40% upon 1% FGE treatment. The results of the present study report for the first time the antibacterial and anti-biofilm activity of garlic against STEC. The findings will enable development of novel garlic organosulfide based drugs for the prevention and treatment of STEC infections.

DOI: 10.1007/s12088-019-00784-3  
 PMCID: PMC6458215 [Available on 2020-06-01]  
 PMID: 31031431

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

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

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

18: Bindra A, Pathak S, Sikka K. Split Larynx. *Anesthesiology.* 2019 Jun 24. doi: 10.1097/ALN.0000000000002867. [Epub ahead of print] PubMed PMID: 31246601.

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 Jun;15(2):205-210. doi: 10.1007/s11302-019-09660-7. Epub 2019 May 31. 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, Kumar P, Tansir G, Biswas A. Case Report: Cardiac Tamponade in Dengue Hemorrhagic Fever: An Unusual Manifestation of a Common Disease. *Am J Trop Med Hyg.* 2019 Jun 3. doi: 10.4269/ajtmh.19-0153. [Epub ahead of print] PubMed PMID: 31162011.

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

DOI: 10.4269/ajtmh.19-0153

PMID: 31162011

21: Biswas S, Goel A, Ray Y, Sethi P, Kumar A, Nischal N, Sinha S, Wig N. Human trichinosis and febrile myositis. *QJM.* 2019 Jun 1;112(6):449-450. doi: 10.1093/qjmed/hcz081. PubMed PMID: 30968127.

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Guidelines for laparoscopic treatment of ventral and incisional abdominal wall hernias (International Endohernia Society (IEHS))-Part A. *Surg Endosc.* 2019 Jun 27. doi: 10.1007/s00464-019-06907-7. [Epub ahead of print] Erratum in: *Surg Endosc.* 2019 Jul 12;:. PubMed PMID: 31250243.

In 2014, the International Endohernia Society (IEHS) published the first international "Guidelines for laparoscopic treatment of ventral and incisional abdominal wall hernias." Guidelines reflect the currently best available evidence in diagnostics and therapy and give recommendations to help surgeons to standardize their techniques and to improve their results. However, science is a dynamic field which is continuously developing. Therefore, guidelines require regular updates to keep pace with the evolving literature. **METHODS:** For the development of the original guidelines, all relevant literature published up to year 2012 was analyzed using the ranking of the Oxford Centre for Evidence-Based Medicine. For the present update, all of the previous authors were asked to evaluate the literature published during the recent years from 2012 to 2017 and revise their statements and recommendations given in the initial guidelines accordingly. In two Consensus Conferences (October 2017 Beijing, March 2018 Cologne), the updates were presented, discussed, and confirmed. To avoid redundancy, only new statements or recommendations are included in this paper. Therefore, for full understanding both of the guidelines, the original and the current, must be read. In addition, the new developments in repair of abdominal wall hernias like surgical techniques within the abdominal wall, release operations (transversus muscle release, component separation), Botox application, and robot-assisted repair methods were included.

**RESULTS:** Due to an increase of the number of patients and further development of surgical techniques, repair of primary and secondary abdominal wall hernias attracts increasing interests of many surgeons. Whereas up to three decades ago hernia-related publications did not exceed 20 per year, currently this number is about 10-fold higher. Recent years are characterized by the advent of new techniques-minimal invasive techniques using robotics and laparoscopy, totally extraperitoneal repairs, novel myofascial release techniques for optimal closure of large defects, and Botox for relaxing the abdominal wall. Furthermore, a concomitant rectus diastasis was recognized as a significant risk factor for recurrence. Despite insufficient evidence with respect to these new techniques, it seemed to us necessary to include them in the update to stimulate surgeons to do research in these fields.

**CONCLUSION:** Guidelines are recommendations based on best available evidence intended to help the surgeon to improve the quality of his daily work. However, science is a continuously evolving process, and as such guidelines should be updated about every 3 years. For a comprehensive reference, however, it is suggested to read both the initial guidelines published in 2014 together with the update. Moreover, the presented update includes also techniques which were not known 3 years before.

DOI: 10.1007/s00464-019-06907-7

PMID: 31250243

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This case is of a suicide victim who purchased various drugs online using forged prescriptions after detailed research about the drugs to commit suicide. He left a suicide note giving details of his suicide methods and the reasons for it. He also denied any treatment and asked for euthanasia if he survived and remained in a vegetative state.

DOI: 10.1177/0025817218789826

PMID: 30489203

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A preterm infant with zone 1 aggressive posterior retinopathy of prematurity developed infectious endophthalmitis after intravitreal injection of ranibizumab. Urgent empirical intravitreal therapy with vancomycin, ceftazidime, and dexamethasone along with intravenous therapy with amikacin and meropenem helped in early resolution. Vascularization/activity of disease subsided on follow-up, media cleared, and laser photocoagulation was completed. Later the disease reactivated, developed vitreous membranes and central retinal traction, for which 25-gauge lens-sparing vitrectomy was performed. Emergent treatment helped in salvaging the eye from both aggressive ROP disease and devastating endophthalmitis. Rationale approach to such a case is being discussed.

DOI: 10.4103/ijo.IJO\_884\_17  
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PMID: 31124535

26: Chandra P, Salunkhe N, Kumar V, Kumawat D, Tewari R. Retinopathy of prematurity in oculocutaneous albinism. *Indian J Ophthalmol.* 2019 Jun;67(6):960-962. doi: 10.4103/ijo.IJO\_931\_17. PubMed PMID: 31124532; PubMed Central PMCID: PMC6552616.

We report a case of retinopathy of prematurity (ROP) in an infant with oculocutaneous albinism (OCA), with the challenges faced in diagnosis, and subsequent management. Poor fundus contrast and blanching of retinal vessels on indentation caused significant visualization problems in detection of ridge and extraretinal vessel proliferation. Careful examination revealed zone 2 Stage 3 ROP with preplus disease in both eyes. Laser photocoagulation was attempted, but laser uptake was poor. The disease regressed over 3-week close follow-up. ROP along with OCA is a rare finding. There is a need for high index of suspicion and caution while screening and managing such babies.

DOI: 10.4103/ijo.IJO\_931\_17  
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27: Chandra P, Kumawat D, Tewari R. Hybrid clear corneal micro-incision surgical technique for stage 5 retinopathy of prematurity. *Indian J Ophthalmol.* 2019 Jun;67(6):936-938. doi: 10.4103/ijo.IJO\_420\_19. PubMed PMID: 31124519; PubMed Central PMCID: PMC6552579.

A safe technique for entry incisions and closure in stage 5 retinopathy of prematurity (ROP) surgery is being described. Three 23G clear corneal incisions are made which allow for safe and snug entry of 25G calibrated infusion and 25G instruments for performing lensectomy, membrane removal and vitrectomy. At the end of surgery, air is injected and corneal entries are hydrated for sutureless closure. The technique was performed in 50 eyes of 36 children with stage 5 ROP. The hybrid technique ensured safe entry and exit with stable anterior chamber during surgery. None of the cases developed retinal breaks during surgical entry

nor had any complications such as hypotony, flat anterior chamber, hyphaema or corneal edema in post operative period. Clear corneal entry using 23G incisions for 25G instrument access is a safe and effective technique for performing lensectomy and vitrectomy with sutureless closure in cases with stage 5 ROP.

DOI: 10.4103/ijo.IJO\_420\_19

PMCID: PMC6552579

PMID: 31124519

28: Chandra P, Tewari R, Salunkhe N, Kumawat D, Chaurasia AK, Gupta V. Short-term incidence and management of glaucoma after successful surgery for stage 4 retinopathy of prematurity. *Indian J Ophthalmol.* 2019 Jun;67(6):917-921. doi: 10.4103/ijo.IJO\_33\_18. PubMed PMID: 31124515; PubMed Central PMCID: PMC6552587.

Purpose: The purpose of this study is to describe the short-term incidence, clinical features, and management of glaucoma in children after successful surgery for stage 4 retinopathy of prematurity (ROP).

Methods: The retrospective study included all eyes undergoing successful surgery for stage 4 ROP with good outcomes at a tertiary eye care center between June 2014 and June 2016. Cases developing postoperative glaucoma underwent examination under anesthesia for measurement of intraocular pressures (IOP), corneal diameters, Retcam-assisted fundus imaging, and gonioscopy. Outcomes of glaucoma management were evaluated.

Results: Hundred eyes of 70 babies underwent successful surgery for stage 4 ROP (with postoperative attached retina, and minimal sequelae) with minimum follow-up of 15 months. Six eyes (6%) developed postoperative glaucoma. Of these, four eyes had undergone lens-sparing vitrectomy and two were managed with lensectomy and vitrectomy (LV). Median time duration for development of glaucoma after primary vitreous surgery was 17.5 weeks. Two cases could be managed with topical IOP-lowering agents alone, whereas four required filtering surgeries (trabeculotomy with trabeculectomy and 0.04% mitomycin C [MMC] application). Average IOP decreased from  $25 \pm 2.36$  to  $12.2 \pm 2.05$  mmHg at 12 months from glaucoma diagnosis.

Conclusion: Glaucoma is a potential adverse event following successful vitreous surgery for stage 4 ROP. A combined trabeculotomy-trabeculectomy along with MMC gives favorable outcome.

DOI: 10.4103/ijo.IJO\_33\_18

PMCID: PMC6552587

PMID: 31124515

29: Chandra P, Kumawat D, Tewari R, Sinha R. Surgical outcomes of immediate sequential bilateral vitreoretinal surgery for advancing retinopathy of prematurity. *Indian J Ophthalmol.* 2019 Jun;67(6):903-907. doi: 10.4103/ijo.IJO\_741\_18. PubMed PMID: 31124512; PubMed Central PMCID: PMC6552586.

Purpose: Bilateral eye surgery in the same session may be required for advancing stage 4 retinopathy of prematurity (ROP). The purpose of this study was to evaluate the outcomes of immediate sequential bilateral vitreoretinal surgery (ISBVS) in stage 4 ROP.

Methods: In a retrospective interventional study at a tertiary care center, 60 eyes of 30 infants who underwent ISBVS for stage 4 ROP between December 2015 and May 2017 were studied. In cases with clear retrolental access, 25G or 27G lens sparing vitrectomy (LSV) was performed and in the rest 25G lensectomy with vitrectomy (LV) was performed through clear corneal entries. The final anatomical outcome measures were the status of tractional retinal detachment (TRD) and macular status.

Results: The mean gestational age was  $28.4 \pm 2.0$  weeks and birth weight was  $1214.5 \pm 329.7$ gms. The mean postconceptional age at surgery was  $40.8 \pm 2.2$  weeks. Stages 4a and 4b were present in 86.7% and 13.3% eyes respectively. LSV was performed in 95% eyes whereas LV was performed in the rest. None of the eyes developed lens touch, choroidal hemorrhage, postoperative hypotony, corneal decompensation, or endophthalmitis. At last follow-up (mean 45 weeks, range 20-68

weeks), macula was attached in 90% eyes with the TRD resolved completely in 61.7% eyes and significantly decreased in another 25% eyes. Sequelae included macular drag, epiretinal membrane, and progression to fibrotic stage 5 disease. Conclusion: ISBVS is safe and effective for bilateral stage 4 ROP and should be recommended in rapidly progressive cases.

DOI: 10.4103/ijo.IJO\_741\_18  
 PMCID: PMC6552586  
 PMID: 31124512

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The outcome of single-bundle anterior cruciate ligament (ACL) reconstruction depends largely on the anatomic placement of bone tunnel. The lateral intercondylar ridge (LIR) and bifurcate ridge (BR) are useful bony landmarks for femoral tunnel placement. The purpose of our study was to compare the bony landmarks of ACL footprint on femur by three-dimensional computed tomography (3D CT) scan and arthroscopy in chronic ACL-deficient knees. Fifty patients above 18 years of age who were diagnosed of having ACL tear were selected for the study. All the cases were more than 6 months old since the injury. Preoperative 3D CT scan of the affected knee was obtained for each of them. They underwent single-bundle anatomic ACL reconstruction. Measurements were done on the preoperative 3D CT and arthroscopy to quantify the position of the LIR and BR. The proximodistal distance of lateral femoral condyle was 21.41±2.5 mm on CT scan and 22.02±2.02mm on arthroscopy. On preoperative 3D CT scan, the midpoint of the LIR was found to be located at a mean distance of 11.17±2.11mm from the proximal margin of the lateral femoral condyle. On arthroscopy, it was at 10.18±1.52mm from the proximal margin the lateral femoral condyle. The "bifurcate ridge"(BR) was not visible in any of the cases during arthroscopy or CT scan. We concluded that LIR is an easily identifiable bony landmark on arthroscopy in all cases. It can also be identified on CT scans. BR is not identified both on arthroscopy and CT scans in chronic ACL tears. The arthroscopic measurements of bony landmarks are quite close to those of CT scan. Midpoint of LIR is at 52.185% of the proximodistal distance on CT scan evaluation and it is at 46.21% on arthroscopic evaluation.

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DOI: 10.1055/s-0038-1660515  
 PMID: 29898471

31: Das D, Suresan V, Jnaneswar A, Khurana C, Bhadauria US, Saha D. Oral health status and treatment needs among the Juang tribe-a particularly vulnerable tribal group residing in Northern Odisha, India: A cross-sectional study. *Health Soc Care Community.* 2019 Jun 24. doi: 10.1111/hsc.12788. [Epub ahead of print] PubMed PMID: 31231942.

The study was aimed to assess the oral health status and treatment needs of Juang tribe residing in Bansapal taluk of Northern Odisha. A cross-sectional survey was carried out among 1,412 Juangs using a cluster random sampling procedure. Bansapal taluk is subdivided into six Gram Panchayat's (GP) with each GP considered as a cluster. From each of the six GP's, equal number of villages was chosen randomly using lottery method in order to get uniform representation. A total of 16 villages were chosen using this method. From each selected village, every alternate household on each side of the street was included and all the people in that household were surveyed through a door-to-door survey. Data were collected using the WHO Oral Health Assessment Form, 1997. All the examinations were carried out by a single examiner assisted by a trained recording assistant who was sitting close enough to the examiner so that instructions and codes could

be easily heard. The periodontal health status as recorded by Community Periodontal Index indicated that majority of the subjects (75.6%) had calculus. Assessment of loss of attachment showed that majority of the subjects (64.5%) had an attachment loss of 0-3 mm. Caries experience in primary dentition was 34.2% and in permanent dentition was 83.4%. The study population was characterised by high prevalence of periodontal disease, dental caries and high treatment needs. The results from this study could be used as a baseline information for health authorities and dental professionals for planning strategies for oral health promotion, prevention and treatment among the Juang population.

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PMID: 31231942

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**PURPOSE:** To evaluate the role of amide proton transfer-weighted (APT-w) magnetic resonance imaging (MRI) in differentiating neoplastic and infective mass lesions using different contrast normalizations, region of interest (ROI) selection, and histogram analysis.

**PROCEDURES:** Retrospective study included 32 treatment-naive patients having intracranial mass lesions (ICMLs): low-grade glioma (LGG)=14, high-grade glioma (HGG) =10, and infective mass lesions=8. APT-w MRI images were acquired along with conventional MRI images at 3 T. APT-w contrast, corrected for B<sub>0</sub>-field inhomogeneity, was computed and optimized with respect to different types of normalizations. Different ROIs on lesion region were selected followed by ROI analysis and histogram analysis. Statistical analysis was performed using Shapiro-Wilk's test, t tests, ANOVA with Tukey's post hoc test, and receiver operation characteristic (ROC) analysis.

**RESULTS:** ICMLs showed significantly ( $p < 0.01$ ) higher APT-w contrast in lesion compared with contralateral side. There was a substantial overlap between mean APT-w contrast of neoplastic and infective mass lesions as well as among different groups of ICMLs irrespective of ROI selection and normalizations. APT-w contrast (using type 4 normalization: normalized with reference signal at negative offset frequency and APT-w contrast in normal-appearing white matter) reduced variability of APT-w contrast across different subjects, and overlap was less compared with other types of normalizations. There was a significant difference ( $p < 0.05$ ) between neoplastic and infective mass lesions using t test for different histogram parameters of type 4 normalized APT-w contrast. ANOVA with post hoc showed significant difference ( $p < 0.05$ ) for different histogram parameters of APT-w contrast (Type 4 normalization) between LGG and HGG, LGG, and infective mass lesion. Histogram parameters such as standard deviation, mean of top percentiles, and median provided improved differentiation between neoplastic and infective mass lesions compared with mean APT-w contrast. A greater number of histogram parameters of type 4 normalized APT-w contrast corresponding to active lesion region can significantly differentiate between ICMLs than other types of normalizations and ROIs.

**CONCLUSIONS:** APT-w contrast using type 4 normalization and active lesion region (ROI-2) should be used for studying APT. APT-MRI should be combined with other MRI techniques to further improve the differential diagnosis of ICMLs.

DOI: 10.1007/s11307-019-01382-x

PMID: 31228076

34: Gautam H, Singla M, Jain R, Lodha R, Kabra SK, Singh UB. Point-of-care urine lipoarabinomannan antigen detection for diagnosis of tuberculosis in children. *Int J Tuberc Lung Dis*. 2019 Jun 1;23(6):714-719. doi: 10.5588/ijtld.18.0364. PubMed PMID: 31315704.

<sec> <title>BACKGROUND</title> Diagnosis of tuberculosis (TB) in children remains challenging due to the paucibacillary nature of the disease. Detection of TB using urine lipoarabinomannan (LAM) antigen was evaluated in children with presumed TB. </sec> <sec> <title>MATERIAL and METHODS</title> Children with presumed intrathoracic tuberculosis (ITTB) and lymph node TB (LNTB) were enrolled. Expecterated or induced sputum or gastric aspirates from ITTB patients and fine-needle cytological aspirates from LNTB patients were subjected to Ziehl-Neelsen staining, MGIT™960™ culture and Xpert® MTB/RIF testing. Urine samples were tested to detect LAM, and the sensitivity and specificity calculated. </sec> <sec> <title>RESULTS</title> Of 280 children with presumed ITTB and 101 with presumed LNTB, respectively 71 (25.3%) and 25 (24.7%) were categorised as 'confirmed TB', 70 (25%) and 33 (32.7%) as 'unconfirmed TB', and 139 (49.6%) and 43 (42.5%) as 'unlikely TB'. Respectively 8 (2.8%) children with ITTB and 3 (2.9%) with LNTB were positive on smear, 56 (20.0%) and 23 (22.7%) on Xpert, and 50 (17.8%) and 9 (8.9%) on culture. LAM assay sensitivity was 73.2% in confirmed ITTB cases, and 76% in confirmed LNTB cases; LAM assay specificity in children with ITTB and those with LNTB initiated on anti-tuberculosis treatment was respectively 92% and 93%. Detection of TB using the LAM assay was significantly better than detection using Xpert (P < 0.05 vs. P < 0.002). </sec> <sec> <title>CONCLUSION</title> Urinary LAM testing showed high specificity and sensitivity, was detected in more cases initiated on treatment than reference tests, and improved disease detection by 38.5% in ITTB patients and by 41.6% in LNTB patients. </sec>.

DOI: 10.5588/ijtld.18.0364

PMID: 31315704

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**BACKGROUND:** Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound with an echobronchoscope-guided fine needle aspiration (EUS-B-FNA) are useful modalities in the evaluation of mediastinal pathologies in adults. However, sparse data are available in children.

**OBJECTIVE:** To describe the utility and safety of EBUS-TBNA and EUS-B-FNA in children with mediastinal pathologies of unknown etiology.

**DESIGN:** Chart review.

**SETTING:** Pediatric Chest and Tuberculosis Clinics, Department of Pediatrics, AIIMS, New Delhi from May 2015 to March 2018.

**PATIENTS:** Children <18 years of age with mediastinal pathologies of undefined etiology.

**METHODS:** Case records of children who underwent EBUS-TBNA and EUS-B-FNA were

reviewed. Data on demographic profile, clinical features, laboratory investigations, the technique of EBUS-TBNA/ EUS -B- FNA, complications, and findings were collected.

**RESULTS:** Thirty children (19 males) with mean (SD) age of 9.6 ( $\pm 3.5$ ) years underwent endobronchial procedures. Median (IQR) weight(kg) and height(cm) were 29 (19.5, 35) and 134 (125, 150) respectively. Tuberculosis was the most common preprocedure clinical diagnosis (73.3%), followed by lymphoma (13.3%). Presenting features were fever (80%), cough (53.3%), hepatomegaly (13%), peripheral lymphadenopathy (21.7%), and positive tuberculin skin test (63.3%). Approximately one fourth were on antitubercular therapy without definite evidence of TB.

Conscious sedation was used for the procedures: midazolam and fentanyl (n=22), propofol (n=8). Transesophageal, transtracheal, and both routes were used in 20 (66.6%), 7 (23.3%), and 3 (10.1%), respectively. Lymph-nodes were sampled in 24 children (subcarinal in 16, right paratracheal in 4 and both in 4). Mean (SD) size of lymph node (in cm) on EBUS was 1.93( $\pm 0.5$ ) and median (IQR) number of FNAC needle passes per node were 2 (2, 4). The diagnosis was confirmed in 11 (36.6%, tuberculosis in 10 by GeneXpert/ MGIT/ cytopath and lymphoma in one) patients. Only 3.3% had a minor complication.

**CONCLUSION:** EBUS-TBNA and EUS-B-FNA are helpful in children with undiagnosed mediastinal pathology with fair diagnostic yield and excellent patient safety profile.

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PMID: 30891940

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Phosphopantetheine adenylyltransferase (PPAT, EC. 2.7.7.3) catalyzes an essential step in the reaction that transfers an adenylyl group from adenosine triphosphate (ATP) to 4'-phosphopantetheine (pPant) yielding 3'- dephospho-coenzyme A (dPCoA) and pyrophosphate (PP) in the coenzyme A (CoA) biosynthesis pathway. The enzyme PPAT from *Acinetobacter baumannii* (AbPPAT) was cloned, expressed and purified. The binding studies of AbPPAT were carried out with two compounds, tri-sodium citrate (TSC) and l-ascorbic acid (LAA, vitamin-C) using fluorescence spectroscopic (FS) and surface Plasmon resonance (SPR) methods. Both methods provided similar values of dissociation constants for TSC and LAA which were of the order of 10<sup>-8</sup>M and 10<sup>-5</sup>M respectively. The computer aided docking studies indicated fewer interactions of LAA with AbPPAT as compared to those of TSC. The freshly purified samples of AbPPAT were crystallized. The crystals of AbPPAT were soaked in the solutions containing TSC and LAA. However, the crystals of the complex of AbPPAT with LAA did not diffract well and hence the structure of the complex of AbPPAT with LAA could not be determined. On the other hand, the crystals of the complex of AbPPAT with TSC diffracted well and the structure was determined at 1.76Å resolution. It showed that TSC bound to AbPPAT at the ATP binding site and formed several intermolecular contacts including 12 hydrogen bonds. The results of binding studies for both TSC and LAA and the structure of the complex of AbPPAT with TSC clearly indicated a potential role of TSC and LAA as antibacterial agents.

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PMID: 30885618

40: Gupta D, Thakral D, Kumar P, Kabra SK, Lodha R, Kumari R, Mohanty SK, Chakraborty S, Bagri N, Mitra DK. Primary Immunodeficiency Disorders Among North Indian Children. *Indian J Pediatr.* 2019 Jun 8. doi: 10.1007/s12098-019-02971-y. [Epub ahead of print] PubMed PMID: 31177511.

**OBJECTIVES:** To report the distribution pattern of various categories of primary immunodeficiency disorders (PIDs) in children from North India, frequency of warning signs and critical parameters for evaluation.

**METHODS:** In this retrospective study, 528 children below 18 y of age after clinical assessment and presentation suggestive of PID were further screened by immunophenotyping for immune cell markers by flow cytometry.

**RESULTS:** A total of 120 (23%) children were diagnosed with PID with median age at diagnosis being 2.5 y in males and 3.5 y in females and an average delay in diagnosis from onset of symptoms being approximately 5 y. Chronic lower respiratory tract infections, gastrointestinal symptoms like persistent diarrhea and failure to thrive were amongst the most common warning signs in these patients. PIDs were classified according to the International Union of Immunological Societies' (IUIS) criteria. The diagnosis of index study subjects included combined humoral and cellular immunodeficiency (29%), phagocytic defects (29%), followed by predominantly antibody deficiency (18%), innate immunity and dysregulation (17%) and other well-defined syndromes (7%). A family history of PID (23%), consanguineous marriage (8%) and previous sibling death (23%) were observed as major clinical predictors/clues for underlying PID. All children received prophylactic antibiotics and/or antifungals in addition to specific therapy for underlying immune deficiency.

**CONCLUSIONS:** The field of PIDs in India remains largely unexplored and we are faced with various challenges in the diagnosis of PIDs due to lack of awareness as well as absence of equipped immunological laboratory support. The authors propose a methodical step-wise laboratory diagnostic approach that can facilitate early diagnosis and timely intervention of these mis/underdiagnosed disorders.

DOI: 10.1007/s12098-019-02971-y  
PMID: 31177511

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**PURPOSE:** Multiple myeloma (MM) is a hematological malignancy marked by uncontrolled proliferation and accumulation of plasma cells in bone marrow. Despite presence of numerous diagnostic markers for MM, their invasive and non-specific nature demands identification of some effective biomarker. Small non-coding RNAs, i.e., microRNAs being secreted out in circulation could depict the change in homeostasis. Earlier, we reported diagnostic potential of a proteoglycan, Versican (VCAN) in MM, hence, VCAN linked cell-free microRNAs have been explored to study their diagnostic involvement in MM.

**METHODS:** Biopsy proven MM patients and controls were recruited. The relative microRNA expression of VCAN linked microRNAs (miR-143, miR-144, miR-199, and miR-203) along with levels of VCAN have been investigated in bone marrow supernatant fluid (BMSF) and blood serum and their correlation were done with clinico-pathological parameters. The diagnostic potential was assessed using ROC curve.

**RESULTS:** Relative microRNA expression of all microRNAs was found significantly lower in MM patients in both BMSF and serum while VCAN levels were substantially higher in patients. VCAN levels showed positive trend while microRNAs expression showed negative trend with severity of disease. miR-203 showed significant correlation with myeloma-associated parameters and also showed optimum

sensitivity and specificity for diagnosis of MM in serum.

CONCLUSIONS: Downregulation of cell-free microRNAs illustrates their importance in MM. The negative trend of microRNAs with disease progression suggests their diagnostic significance. Correlation of miR-203 with myeloma clinical parameters along with optimum sensitivity and specificity affirms its non-invasive diagnostic potential in MM which could further be validated in larger patient cohort.

DOI: 10.1007/s00432-019-02896-1

PMID: 30891618 [Indexed for MEDLINE]

42: Gupta R, Abraham RA, Kondal D, Dhatwalia S, Jeemon P, Reddy KS, Prabhakaran D, Ramakrishnan L. Association of trans fatty acids with lipids and other cardiovascular risk factors in an Indian industrial population. *BMC Res Notes*. 2019 Jun 17;12(1):342. doi: 10.1186/s13104-019-4352-7. PubMed PMID: 31208468; PubMed Central PMCID: PMC6580624.

OBJECTIVE: Trans-fat, an invariable component of industrial fat is considered as one of the major dietary factors associated with CVD. Although the use of trans-fat is completely banned in some of the high-income countries where the CVD epidemic is declining, it is widely used in LMIC. We aimed to investigate the association of trans fatty acid in serum with risk markers of CVD in an industrial population in India. Participants were randomly selected from a study conducted in an industrial setting among employees and their family members. Information related to their demographic profile, anthropometric measurements, oil intake were recorded. Fasting samples were collected and stored at  $-80^{\circ}\text{C}$  for analysis. Their lipid profile and hs CRP were measured and fatty acids analyzed using gas chromatography (GC) with flame ionization detector (FID). RESULTS: Complete data was available for 176 participants. Among trans fatty acids, mono trans fatty acid was significant predictor of serum triglycerides [Unadjusted  $\beta$  (95% CI) 22.9 (2.6, 43.2); Adjusted  $\beta$  (95% CI) 20.4 (3.5, 37.3)]. None of the other trans fatty acids either individually or in group correlated with any of the biochemical markers studied.

DOI: 10.1186/s13104-019-4352-7

PMCID: PMC6580624

PMID: 31208468

43: Gupta S, Shiny H, Bhukya RK, Jain S, Kumar V. Myelinated retinal nerve fibers and persistent hyperplastic primary vitreous. *Indian J Ophthalmol*. 2019 Jun;67(6):952. doi: 10.4103/ijo.IJO\_1518\_18. PubMed PMID: 31124528; PubMed Central PMCID: PMC6552573.

44: Gupta S, Selvan H, Khokhar S. Hook and flip technique: for phacoemulsification in non-rotating nuclei and posterior polar cataracts. *Int Ophthalmol*. 2019 Jun;39(6):1219-1223. doi: 10.1007/s10792-018-0928-9. Epub 2018 Apr 27. PubMed PMID: 29704132.

PURPOSE: We put forward a physical levitation method to hook and flip the chopped nuclear fragments that could not be solely drawn by vacuum during phacoemulsification, due to various reasons such as a non-rotating nuclei or posterior polar cataracts where hydrodissection was unsuccessful or contra-indicated, respectively.

METHOD: A Sinsky hook is insinuated through the crack of the divided nuclei into a plane behind the nuclear pie to 'hook and flip' the chopped piece, heading it towards the phacoemulsification probe. This simple step disassembles the nuclear chunk, thereby creating space to facilitate the dismantling of the rest of the fragments. The remnant epinuclear cushion guards the posterior capsule, mitigating the chances of serious intra-operative complications.

RESULT: We have employed this technique in 17 eyes during similar situations. No specific intra-operative complications were observed; all surgeries were uneventful. A Sinsky hook utilised for this step ensures safety and familiarity,

none encountered posterior capsular rent. This technique not only eases the surgery, but also decreases the anticipated intra-operative and post-operative complications.

CONCLUSION: 'Hook and flip technique' thus proves useful whenever dismantling difficulties are encountered during phacoemulsification.

DOI: 10.1007/s10792-018-0928-9

PMID: 29704132 [Indexed for MEDLINE]

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46: Jain S, Padhan R, Bopanna S, Jain SK, Dhingra R, Dash NR, Madhusudan KS, Gamanagatti SR, Sahni P, Garg PK. Percutaneous Endoscopic Step-Up Therapy Is an Effective Minimally Invasive Approach for Infected Necrotizing Pancreatitis. *Dig Dis Sci.* 2019 Jun 11. doi: 10.1007/s10620-019-05696-2. [Epub ahead of print] PubMed PMID: 31187325.

BACKGROUND: Infected pancreatic necrosis (IPN) is a major complication of acute pancreatitis (AP), which may require necrosectomy. Minimally invasive surgical step-up therapy is preferred for IPN.

AIM: To assess the effectiveness of percutaneous endoscopic step-up therapy in patients with IPN and identify predictors of its success.

METHODS: Consecutive patients with AP hospitalized to our tertiary care academic center were studied prospectively. Patients with IPN formed the study group. The treatment protocol for IPN was percutaneous endoscopic step-up approach starting with antibiotics and percutaneous catheter drainage, and if required necrosectomy. Percutaneous endoscopic necrosectomy (PEN) was performed using a flexible endoscope through the percutaneous tract under conscious sedation. Control of sepsis with resolution of collection(s) was the primary outcome measure.

RESULTS: A total of 415 patients with AP were included. Of them, 272 patients had necrotizing pancreatitis and 177 (65%) developed IPN. Of these 177 patients, 27 were treated conservatively with antibiotics alone, 56 underwent percutaneous drainage alone, 53 required underwent PEN as a step-up therapy, 1 per-oral endoscopic necrosectomy, and 52 required surgery. Of the 53 patients in the PEN group, 42 (79.2%) were treated successfully-34 after PEN alone and 8 after additional surgery. Eleven of 53 patients died due to organ failure-7 after PEN and 4 after surgery. Independent predictors of mortality were >50% necrosis and early organ failure.

CONCLUSION: Percutaneous endoscopic step-up therapy is an effective strategy for IPN. Organ failure and extensive pancreatic necrosis predicted a suboptimal outcome in patients with infected necrotizing pancreatitis.

DOI: 10.1007/s10620-019-05696-2

PMID: 31187325

47: Jose A, Nagori SA, Arya S, Roychoudhury A. Hyoid bone syndrome masquerading as temporomandibular joint dysfunction. *Br J Oral Maxillofac Surg.* 2019 Jun;57(5):477-478. doi: 10.1016/j.bjoms.2019.01.022. Epub 2019 May 1. PubMed PMID: 31054794.

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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48: Kakkar A, Nandy SB, Gupta S, Bharagava B, Airan B, Mohanty S. Adipose tissue derived mesenchymal stem cells are better respondents to TGF $\beta$ 1 for in vitro generation of cardiomyocyte-like cells. *Mol Cell Biochem.* 2019 Jun 21. doi: 10.1007/s11010-019-03570-3. [Epub ahead of print] PubMed PMID: 31227975.

Mesenchymal stem cells (MSCs) are multipotent cells which hold immense potential in translational research as a novel treatment modality. In recent years, MSCs isolated from various tissues have been used in several clinical trials for the treatment of cardiac injury caused by permanent myocardial loss. However, a better MSCs source and an optimum inducer for in vitro cardiac differentiation are still far reaching and unexplored. The aim of the study was to compare the ability and efficiency of differentiation of MSCs isolated from bone marrow (BM-MSCs) and adipose tissue (ADSC) into cardiomyocyte-like cells to aid translational research. To fulfill this aim, freshly isolated BM-MSCs and ADSCs were differentiated into cardiomyocytes using 5-Azacytidine (6  $\mu$ M) and TGF- $\beta$ 1 (25 ng/ml). These two differentiation protocols were compared on the basis of morphological, transcriptional, translational and functionality analysis. Both tissue specific MSCs, ADSCs and BM-MSCs, have similar surface marker profile and population doubling time. In both the treatment regimes, BM-MSCs and ADSCs showed morphological changes like flattening of cells and myotube formation in concurrence with structure and multinucleation, with early sign of differentiation in ADSCs. Further, the expression of cardiac specific markers including myosin light chain-2v (Mlc-2v), cardiac troponin I (cTnI), and sarco/endoplasmic reticulum Ca<sup>2+</sup>-ATPase (SerCa2) were higher in AD-TGF $\beta$ 1 group, both at transcriptional and translational level. During functionality analysis by KCl stimulation, increased intracellular calcium fluorescence was observed in AD-TGF $\beta$ 1 group as compared to others. Thus, ADSCs proved to be a better choice for stem cell therapy in cardiovascular diseases when induced with TGF- $\beta$ 1.

DOI: 10.1007/s11010-019-03570-3  
PMID: 31227975

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In the present study, we have evaluated the nephroprotective effect of hydroalcoholic extract of Terminalia chebula in cisplatin-induced nephrotoxicity model. Standardised extract was orally administered to Wistar rats for 10 days at different doses. On day 7, 8 mg/kg of cisplatin was administered intra-peritoneally to rats in all groups. T. chebula, in a dose-dependent manner significantly inhibited the elevation of serum creatinine, blood urea nitrogen and oxidant stress markers. The immunohistochemical analysis revealed the increased levels of apoptotic markers and cytokines in cisplatin group were significantly lowered by T. chebula extract. The cisplatin-treated rats kidney showed diffused tubular necrosis and infiltration of inflammatory cells which was reversed in the treatment group. Chemical characterisation of extract by HPLC

revealed the presence of corilagin, chebulinic, chebulagic, chebulic, gallic and ellagic acid. The findings of this study discovered that *T. chebula* ameliorated oxidative and histological damage caused by cisplatin.

DOI: 10.1080/14786419.2018.1425843  
PMID: 29343091

51: Kant S, Kumar R, Malhotra S, Kaur R, Haldar P. Prevalence and Determinants of Anemia among Adult Males in a Rural Area of Haryana, India. *J Epidemiol Glob Health*. 2019 Jun;9(2):128-134. doi: 10.2991/jegh.k.190513.001. PubMed PMID: 31241871.

Anemia is an under-recognized morbidity among adult males causing significant productivity loss. A study was done among adult males ( $\geq 18$  years) in a rural area of Haryana, India to estimate the prevalence and determinants of anemia and to explore their attitude and beliefs about anemia. Mixed methods approach was adopted. A total of 1219 participants were selected by multi-stage simple random sampling for the cross-sectional study and were administered a questionnaire followed by hemoglobin measurement using HemoCue method. Six focus group discussions were conducted. Age adjusted prevalence of anemia was 27.9% [95% confidence interval (95% CI): 27.4-28.4%]. Anemia was found to be positively associated with age more than 50 years (OR: 2.7 (95% CI: 1.7-4.2) in age group 50-59 years and 3.6 (95% CI: 2.3-5.6) in age group  $\geq 60$  years as compared with age group 18-24 years) and presence of chronic co-morbidity (OR: 2.0; 95% CI: 1.2-3.2). There were misconceptions among study participants about the role of specific dietary factors in causation of anemia. Poor purchasing capacity was cited as main reason for not consuming iron rich diet. Anemia was a common morbidity in this study population.

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DOI: 10.2991/jegh.k.190513.001  
PMID: 31241871

52: Kapil U, Kapil R, Gupta A. Prevention and Control of Anemia Amongst Children and Adolescents: Theory and Practice in India. *Indian J Pediatr*. 2019 Jun;86(6):523-531. doi: 10.1007/s12098-019-02932-5. Epub 2019 May 11. PubMed PMID: 31079321.

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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54: Kathpalia P, Nag TC, Chattopadhyay P, Sharma A, Bhat MA, Roy TS, Wadhwa S. In ovo Sound Stimulation Mediated Regulation of BDNF in the Auditory Cortex and Hippocampus of Neonatal Chicks. *Neuroscience*. 2019 Jun 1;408:293-307. doi: 10.1016/j.neuroscience.2019.04.014. Epub 2019 Apr 24. PubMed PMID: 31026564.

Brain-derived neurotrophic factor (BDNF) is known to mediate activity-dependent changes in the developing auditory system. Its expression in the brainstem auditory nuclei, auditory cortex and hippocampus of neonatal chicks (*Gallus*

*gallus domesticus*) in response to in ovo high intensity sound exposure at 110 dB (arrhythmic sound: recorded traffic noise, 30-3000Hz with peak at 2700Hz, rhythmic sound: sitar music, 100-4000Hz) was examined to understand the previously reported altered volume and neuronal number in these regions. In the brainstem auditory nuclei, no mature BDNF, but proBDNF at the protein level was detected, and no change in its levels was observed after in ovo sound stimulation (music and noise). Increased ProBDNF protein levels were found in the auditory cortex in response to arrhythmic sound, along with decreased levels of one of the BDNF mRNA transcripts, in response to both rhythmic and arrhythmic sound stimulation. In the hippocampus, increased levels of mature BDNF were found in response to music. Expression microarray analysis was performed to understand changes in gene expression in the hippocampus in response to music and noise, followed by gene ontology analysis showing enrichment of probable signaling pathways. Differentially expressed genes like CAMK1 and STAT1 were found to be involved in downstream signaling on comparing music versus noise-exposed chicks. In conclusion, we report that BDNF is differentially regulated in the auditory cortex at the transcriptional and post-translational level, and in the hippocampus at the post-translational level in response to in ovo sound stimulation.

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56: Khandelwal P, Thomas CC, Rathi BS, Hari P, Tiwari AN, Sinha A, Bagga A. Membrane-filtration based plasma exchanges for atypical hemolytic uremic syndrome: Audit of efficacy and safety. *J Clin Apher.* 2019 Jun 7. doi: 10.1002/jca.21711. [Epub ahead of print] PubMed PMID: 31173399.

**BACKGROUND:** While complement blockade with eculizumab is recommended as first-line therapy of atypical hemolytic uremic syndrome (aHUS), plasma exchanges (PEX) remain the chief option for anti-factor H (FH) antibody associated disease and when access to eculizumab is limited.

**METHODS:** We reviewed adverse events (AEs) and adverse outcomes (eGFR <30mL/min/1.73m<sup>2</sup> or death), in all patients with aHUS managed with membrane-filtration based PEX at one tertiary care center over 5.5 years.

**RESULTS:** During January 2013 to June 2018, 109 patients with aHUS (74 with antibodies to FH), aged median (range) 7.6 (0.5-18) year weighing 22.1 (6-90) kg, underwent 2024 sessions of PEX. AE, in 12.1% patients, were usually self-limiting and included chills (5.5%), vomiting/abdominal pain (3.3%), hypotension (1.6%), urticaria (1.5%), seizures (0.2%), hypocalcemia (0.2%), and hemorrhage (0.1%); plasma hypersensitivity and severe reactions were rare. Rate of catheter-related infections was 1.45/1000 catheter-days. Filter reuse (OR 1.69; 95% CI 1.26-2.26; P<.001) and >20 sessions of PEX/patient (OR 1.99; 95% CI 1.27-3.10; P = .002) were independently associated with adverse events; infusion of IV calcium gluconate during PEX was protective (OR 0.26; 95% CI 0.16-0.43; P<.001). Hematological remission was achieved in 96.3% patients after 6 (5-8) PEX sessions; 80.8% and 89.6% patients were dialysis independent by one and 3 months, respectively.

**CONCLUSIONS:** PEX is safe and associated with satisfactory short-term outcomes in children with aHUS. Prolonged PEX and filter-reuse are associated with complications.

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DOI: 10.1002/jca.21711  
PMID: 31173399

57: Khurana S, Mathur P, Malhotra R. *Staphylococcus aureus* at an Indian tertiary hospital: Antimicrobial susceptibility and minimum inhibitory concentration (MIC) creep of antimicrobial agents. *J Glob Antimicrob Resist.* 2019 Jun;17:98-102. doi:

10.1016/j.jgar.2018.10.021. Epub 2018 Oct 30. PubMed PMID: 30389637.

**OBJECTIVES:** Staphylococcus aureus causes a variety of symptoms and diseases and has been associated with high morbidity and mortality. A global population drift in clinical S. aureus isolates towards reduced antimicrobial susceptibility is being reported. In this study, the antimicrobial susceptibility profile and minimum inhibitory concentration (MIC) creep of vancomycin, linezolid, teicoplanin and rifampicin against clinical S. aureus isolates at an Indian tertiary centre from January 2012 to December 2016 were investigated.

**METHODS:** All consecutive, non-duplicate S. aureus isolates (n=1466) recovered from hospitalised patients identified by VITEK®2 were included in the study. Clinical isolates were tested against 20 antibiotics and were evaluated according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Statistical significance of the MIC creeps of four antimicrobials (vancomycin, linezolid, teicoplanin and rifampicin) was ascertained.

**RESULTS:** S. aureus isolates recovered from all clinical samples demonstrated high resistance to ampicillin, ciprofloxacin and penicillin (75-100%) and low resistance to amikacin, linezolid, netilmicin, nitrofurantoin, teicoplanin and vancomycin (0-13%). The MIC90 values (MIC required to inhibit 90% of the isolates) for vancomycin, linezolid and rifampicin decreased, whereas the MIC90 for teicoplanin increased. The change in the geometric mean MIC of rifampicin was found to be statistically significant. A statistically significant and progressive MIC creep was observed for teicoplanin and rifampicin.

**CONCLUSION:** Despite remaining susceptible, S. aureus is not inert to antibiotic pressure. Implementation of preventive measures in healthcare settings is required worldwide to combat the increasing number of infections by this pathogen.

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DOI: 10.1016/j.jgar.2018.10.021  
PMID: 30389637

58: Kriplani A, Sehgal R, Konar H, Vivekanand A, Vanamail P, Purandare CN. A 1-year comparison of TCu380Ag versus TCu380A intrauterine contraceptive devices in India. Int J Gynaecol Obstet. 2019 Jun;145(3):268-277. doi: 10.1002/ijgo.12809. Epub 2019 Apr 11. PubMed PMID: 30919459.

**OBJECTIVE:** To compare TCu380Ag and TCu380A intrauterine contraceptive devices after 1 year of use.

**METHODS:** A prospective randomized controlled trial was conducted among healthy married women aged 20-35 years who attended the family planning clinics of three tertiary centers in India between August 1, 2015, to March 31, 2018. The TCu380Ag group (n=300) received one of three sizes of this device depending on uterocervical length: maxi (8.0-9.0 cm), normal (7.0-8.5 cm), or mini (6.0-7.5 cm). The remaining 300 participants received TCu380A. Follow-up was conducted at 3-monthly intervals to assess continuation rate, acceptability, efficacy, adverse effects, and complications.

**RESULTS:** The TCu380Ag group had a higher continuation rate than the TCu380A group at 1 year (84.0% vs 75.8%; P=0.01), with an efficacy of 99.6% versus 100.0% (P>0.05). Overall estimated continuation rates were 94.5% (95% confidence interval [CI] 91.7%-96.4%) and 88.4% (95% CI 83.2%-91.5%), respectively (P=0.026). Use of TCu380Ag was associated with fewer adverse effects (heavy menstrual bleeding, abdominal pain, or expulsion) when compared with TCu380A (P>0.05 for all comparisons). Discontinuation rates owing to adverse effects were 6.59% for TCu380Ag versus 13.26% for TCu380A (P=0.01).

**CONCLUSIONS:** Varying sizes of TCu380Ag could provide an alternative to TCu380A.

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59: Krishnan A, Kumar R, Broor S, Gopal G, Saha S, Amarchand R, Choudekar A, Purkayastha DR, Whitaker B, Pandey B, Narayan VV, Kabra SK, Sreenivas V, Widdowson MA, Lindstrom S, Lafond KE, Jain S. Epidemiology of viral acute lower respiratory infections in a community-based cohort of rural north Indian children. *J Glob Health*. 2019 Jun;9(1):010433. doi: 10.7189/jogh.09.010433. PubMed PMID: 31131104; PubMed Central PMCID: PMC6513504.

**Background:** In India, community-based acute lower respiratory infections (ALRI) burden studies are limited, hampering development of prevention and control strategies.

**Methods:** We surveyed children <10 years old at home weekly from August 2012-August 2014, for cough, sore throat, rhinorrhoea, ear discharge, and shortness of breath. Symptomatic children were assessed for ALRI using World Health Organization definitions. Nasal and throat swabs were obtained from all ALRI cases and asymptomatic controls and tested using polymerase chain reaction for respiratory syncytial virus (RSV), human metapneumovirus (hMPV), parainfluenza viruses (PIV), and influenza viruses (IV). We estimated adjusted odds ratios (aOR) using logistic regression to calculate etiologic fractions (EF). We multiplied agent-specific ALRI incidence rates by EF to calculate the adjusted incidence as episodes per child-year.

**Results:** ALRI incidence was 0.19 (95% confidence interval (CI)=0.18-0.20) episode per child-year. Association between virus and ALRI was strongest for RSV (aOR=15.9; 95% CI=7.3-34.7; EF=94%) and least for IV (aOR=4.6; 95% CI=2.0-10.6; EF=78%). Adjusted agent-specific ALRI incidences were RSV (0.03, 95% CI=0.02-0.03), hMPV (0.02, 95% CI=0.01-0.02), PIV (0.02, 95% CI=0.01-0.02), and IV (0.01, 95% CI=0.01-0.01) episode per child-year.

**Conclusions:** ALRI among children in rural India was high; RSV was a significant contributor.

DOI: 10.7189/jogh.09.010433

PMCID: PMC6513504

PMID: 31131104 [Indexed for MEDLINE]

60: Kumar A, Agarwal D, Chawla R. Commentary: Coats disease: Our experience in India. *Indian J Ophthalmol*. 2019 Jun;67(6):783-784. doi: 10.4103/ijo.IJO\_823\_19. PubMed PMID: 31124486; PubMed Central PMCID: PMC6552633.

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

**BACKGROUND:** The caregivers of patients with first episode psychosis (FEP) experience significant distress. It is important to understand their needs to plan adequate interventions for them.

**AIM:** The aim of this study was to explore the needs of caregivers of young patients with FEP in India, using a qualitative approach.

**METHODS:** The study was conducted in two phases. In phase I, a script for conducting focus group discussions (FGDs) with caregivers was developed, based on literature search and expert opinion generated from FGD with mental health professionals. In phase II, five FGDs were conducted with 30 caregivers of young patients with FEP having minimal of 6 participants in each FGD. Data was analyzed using principles of grounded theory.

**RESULTS:** Seven broad themes and subthemes of the needs of caregivers emerged from the FGDs. The final themes, which highlighted the needs of caregivers of young patients with FEP, were (in order of ranking) as follows: information regarding treatment, information regarding illness, services provided by the government, optimum quality of care from treatment facility, management of psychosocial issues related to patient's illness, availability and accessibility of treatment, and identification and recognition of mental health and physical problems in

family members.

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

DOI: 10.1177/0020764019852650

PMID: 31190603

62: Kumar P, Sharma YR, Chandra P, Azad R, Meshram GG. Comparison of the Safety and Efficacy of Intravitreal Ranibizumab with or without Laser Photocoagulation Versus Dexamethasone Intravitreal Implant with or without Laser Photocoagulation for Macular Edema Secondary to Branch Retinal Vein Occlusion. *Folia Med (Plovdiv)*. 2019 Jun 1;61(2):240-248. doi: 10.2478/foimed-2018-0081. PubMed PMID: 31301668.

BACKGROUND: There is an ambiguity regarding the therapy of choice for patients with macular edema following branch retinal vein occlusion (BRVO).

AIM: The purpose of the study was to compare the efficacy and safety of ranibizumab (3 injections 0.5 mg) versus ranibizumab (1 injection 0.5 mg) with laser photocoagulation (LP) versus dexamethasone intravitreal (IVT) implant (0.7 mg) with or without LP in patients with macular edema following BRVO.

MATERIALS AND METHODS: 60 eyes of 60 patients were divided into 4 groups. Group 1 received IVT ranibizumab (3 injections 0.5 mg), Group 2 received IVT ranibizumab (1 injection 0.5 mg) + LP, Group 3 received dexamethasone IVT implant (0.7 mg), and Group 4 received dexamethasone IVT implant (0.7 mg) + LP. The endpoints were the difference in mean changes in best corrected visual acuity (BCVA), central macular thickness (CMT), and inter-group differences in contrast sensitivity (CS), retinal sensitivity (RS), and intraocular pressure (IOP).

RESULTS: BCVA gains in Group 1 (18.00±8.51) patients were significantly ( $p < 0.05$ ) higher than patients in Groups 2 (10.00±10.26), 3 (9.50±9.60), and 4 (10.50±10.97), after 6 months of therapy. No significant inter-group variation was found in the CMT, CS, and RS.

CONCLUSIONS: Ranibizumab (3 injections 0.5 mg) showed significantly higher BCVA gains at 6 months post-therapy. Improvements in the BCVA, CMT, CS, and RS were comparable initially in all the therapies.

DOI: 10.2478/foimed-2018-0081

PMID: 31301668

63: Kumar P, Bal C, Damle NA, Ballal S, Dwivedi SN, Agarwala S. Lesion-Wise Comparison of Pre-Therapy and Post-Therapy Effective Half-Life of Iodine-131 in Pediatric and Young Adult Patients with Differentiated Thyroid Cancer Undergoing Radioiodine Therapy. *Nucl Med Mol Imaging*. 2019 Jun;53(3):199-207. doi: 10.1007/s13139-019-00592-z. Epub 2019 Apr 23. PubMed PMID: 31231440; PubMed Central PMCID: PMC6554380.

Purpose: The effective half-life of radioiodine is an important parameter for dosimetry in differentiated thyroid cancer patients, particularly in children. We determined the pre-therapy and post-therapy effective half-life in different types of lesions, i.e., remnant, node, or lung metastases.

Methods: Of 84 patients recruited, 27 were <18 years (group 1) and the remaining 57 were between 18 and 21 years (group 2). A total of 114 studies were conducted and 253 lesions were analyzed. Serial whole-body scans were acquired at 24, 48, and ≥72 h after administration of iodine-131. Region of interests was drawn over lesions to determine counts in the lesion. Time versus counts graphs were plotted and mono-exponentially fitted to determine effective half-life.

Results: The post-therapy effective half-life was found to be lesser than pre-therapy effective half-life in all types of lesions and in all groups. Median effective half-life was found maximum in intact lobe, minimum in the lung, and intermediate in remnant and nodes. In the assessment of all lesions together, pre- and post-therapy median and interquartile range (IQR) effective half-life were 59.8 (37-112) h and 48.6 (35.2-70.8) h ( $p < 0.0001$ ) in group 1, 73.9 (46.2-112.7) h and 60 (57.4-85.9) h ( $p < 0.0001$ ) in group 2, and 68.6

(41.53-112.36) h and 54.7 (36-80.6) h ( $p < 0.0001$ ) in combined group, respectively. Importantly, the pre- and post-therapy median effective half-life serially dropped after each successive cycles of iodine-131. Conclusions: There was a significant difference in pre-therapy and post-therapy effective half-life in all types of lesions. These results may have implications in calculating the correct therapeutic dose in children and in young adults.

DOI: 10.1007/s13139-019-00592-z  
PMCID: PMC6554380 [Available on 2020-06-01]  
PMID: 31231440

64: Kumar R, Parray HA, Shrivastava T, Sinha S, Luthra K. Phage display antibody libraries: A robust approach for generation of recombinant human monoclonal antibodies. *Int J Biol Macromol*. 2019 Aug 15;135:907-918. doi: 10.1016/j.ijbiomac.2019.06.006. Epub 2019 Jun 3. Review. PubMed PMID: 31170490.

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

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DOI: 10.1016/j.ijbiomac.2019.06.006  
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65: Kumar V, Deorari V, Swaroop S, Biswas A. Panophthalmitis in a patient with dengue fever. *BMJ Case Rep*. 2019 Jun 3;12(6). pii: e229588. doi: 10.1136/bcr-2019-229588. PubMed PMID: 31164382.

Dengue fever is known for its life-threatening complications of bleeding and capillary leak syndrome. We report an unusual complication of dengue fever causing panophthalmitis, leading to rapidly progressive painful visual loss within days. Later on, the patient developed secondary bacterial infection of the eyeball and developed multiple brain abscesses due to spread of infection from the eyeball. Culture from pus swab of the right eye grew *Staphylococcus epidermidis*. The patient was promptly treated with broad spectrum antibiotics and after stabilisation, evisceration of the affected eye was done. Supportive therapy in the form of mechanical ventilation in view of poor sensorium, platelet transfusions for thrombocytopenia and guided fluid therapy was also provided. After multiple challenges in the management of the patient, fortunately, the patient survived but we failed to save his right eye. Therefore, it is necessary to carefully examine all vital organs at an early stage to prevent unfortunate outcome.

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**INTRODUCTION:** BK polyomavirus is ubiquitous and remains dormant in the urothelial tract, reactivating and replicating in the immunocompromised state especially in the setting of post-renal transplantation where it is believed to be directly oncogenic based on recent reports. Its oncogenic role in the immunocompetent host is controversial. This study aimed to investigate the association of BK polyomavirus in Urothelial Carcinoma.

**MATERIAL AND METHODS:** Patients with suspected urothelial carcinoma (UC) admitted under Department of Urology over a period of one year were recruited and transurethral bladder tumor (TURBT) resection was performed, along with sampling of cystoscopically normal-appearing urothelium away from the tumor. In addition, cystectomy specimens with UC were included, with sampling of grossly normal-appearing urothelium away from the tumor. Immunohistochemistry (IHC) for SV40 T-Antigen and chromogenic in situ hybridization (CISH) using BK polyomavirus specific probe was performed on the paired samples (tumor and normal).

**RESULTS:** Twenty-three TURBT and 14 cystectomy specimens were assessed. None of the cases showed evidence of BK polyomavirus infection in tumor or in surrounding mucosa by IHC. CISH performed in ten cases were also found to be negative. In comparison, one post-renal transplant urothelial carcinoma in our experience showed diffuse SV40 staining.

**CONCLUSIONS:** This study suggests that BK polyomavirus infection is not associated with urothelial malignancy in the immunocompetent setting unlike in the immunocompromised setting where it should always be investigated for.

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**Purpose:** To evaluate the characteristics and morbidity due to ocular auto-stimulation (OAS) in stage 5 Retinopathy of Prematurity (ROP).

**Methods:** Stage 5 ROP cases presenting to ROP clinic of a tertiary care centre from January 2017 to December 2017 were recruited. Eye-pressing was elicited on history from parents and categorized as infrequent (performed <50% of waking time) or frequent (≥50% of time). B-scan ultrasonography was performed for configuration of retinal detachment (open or closed funnel). Keratometry was performed in eyes undergoing vitrectomy under general anaesthesia using automated hand-held keratometer. The outcome measures were the presence and characteristics of OAS, enophthalmos, corneal opacity and keratometry values.

**Results:** Out of 93 eyes of 49 babies, 78.5% (n = 73) had OAS. Gestational age, birth weight, sex, retinal funnel configuration, and visual function did not significantly affect OAS. However, post-conceptual age was significantly greater in eyes with OAS (95% CI: 63.1 to 69.9 weeks) than those without OAS (95% CI: 52.4 to 63.4 weeks) (P = 0.018). OAS occurred frequently in 32.8% (n = 24/73) eyes, more commonly in eyes with light followability. Keratometry did not differ significantly with the presence of OAS (P = 0.88). Enophthalmos, corneal opacity, posterior synechiae were noted in 79.5% (58/73), 21.9% (16/73), and 28.8% (21/73) eyes with OAS, respectively. Enophthalmos occurred significantly in eyes with OAS (P = 0.001), while corneal opacity and posterior synechiae did not (P = 0.071 and 0.91, respectively).

**Conclusion:** OAS and its resultant morbidity are common occurrences in stage 5 ROP. The post-conceptual age and residual visual function may govern the

characteristics of OAS.

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PMCID: PMC6552578

PMID: 31124514

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The poor often experience illness and the treatment costs are high and even catastrophic for the poor. This paper reports the extent of illness, treatment-seeking behaviour and out of pocket healthcare expenditures and the determinants of treatment-seeking behaviour and healthcare expenditures among the urban poor living in Delhi. A total of 2,998 households participated in the study. Socio-demographic details, illness experiences (episodic illness in the past 3 months, hospitalisation in the past 1 year and any chronic illness), treatment seeking and healthcare expenditures were collected for all household members through a pretested, interviewer-administered questionnaire. Logistic regressions were carried out for factors associated with treatment-seeking choices. Multiple linear regressions were carried out for factors associated with out of pocket expenditures (OOPE). Of the total 15,218 household members (of the 2,998 households), 4,052 (26.6%) experienced episodic illness (mainly fever, respiratory illnesses, food- and waterborne diseases and eye infections) in the past 3 months, 230 (1.5%) were hospitalised and 976 (6.4%) have chronic illness (mainly hypertension, diabetes, arthritis and respiratory problems). Of the 2,998 households, 2,225 (74.2%) households reported at least one event of illness. Unqualified practitioners were the main source of care for episodic illnesses. Perceived seriousness of the illness, having Employees State Insurance Scheme (ESIS) benefit, higher educational status of the head of the household, higher monthly household incomes, belonging other backward castes and settled-migrant status led to seeking formal care. Dengue was the main reason for hospitalisation. Government including ESIS hospitals were mainly utilised for hospitalisation. Healthcare expenditures were higher for private healthcare. Possession of mandatory health insurance was protective against OOPEs. OOPEs were more for the men/boys and for the young. Improving access to government healthcare services is important. Extending the ESIS to the unorganised workers including urban poor migrants should be considered so as to bring them under mandatory social protection.

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BACKGROUND/AIMS: Uncomplicated crown fracture is the most common traumatic dental injury. The International Association of Dental Traumatology has recommended

fragment reattachment as the best method for restoring uncomplicated crown fractures of permanent teeth. Dehydration can affect fracture resistance after reattachment. However, a standard protocol for rehydration is still lacking. Hence, the aim of this study was to design a humidification chamber and assess its efficacy for improving the rehydration of tooth fragments and increasing fracture resistance after reattachment.

**MATERIALS AND METHODS:** Sixty mandibular bovine incisors with similar dimensions and free of any structural deformities were fractured and randomized into five groups: Group I, Control Group (sound teeth); Group II (dehydrated for 24 hours); Group III (rehydrated in distilled water for 15 minutes); Group IV (rehydrated in a humidification chamber for 15 minutes); and Group V (restored with composite). A humidification chamber was designed and used for rehydration for 15 minutes in Group IV. Fragments in Group III were immersed in distilled water for 15 minutes. Reattachment procedures and materials remained the same in all groups. Fracture resistance was tested in a universal testing machine, and statistical analysis was done by Stata-14.

**RESULTS:** The Control Group with sound teeth (Group I) exhibited a maximum value of  $282 \pm 10.32$  N, while Group II (fragment reattached without rehydration) had the least fracture resistance,  $49.75 \pm 5.2$  N. Rehydration by means of the humidification chamber protocol (Group IV) resulted in significantly higher fracture resistance ( $150.54 \pm 6.49$  N) than in Group III (rehydration by means of immersion).

**CONCLUSIONS:** Fracture resistance after fragment reattachment was significantly affected by the rehydration of fragments for 15 minutes in the humidification chamber. Fragment reattachment after rehydration showed better fracture resistance than the composite restorations.

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

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**Context:** Pathogenesis of idiopathic hypoparathyroidism (IH) is under investigation. Abnormalities in central immune tolerance have yet not been investigated in this condition. T-cell receptor excision circles (TRECs) and kappa-deleting recombination excision circles (KRECs), formed during receptor gene rearrangements, are tools to assess central T- and B-cell output. **Objective:** We assessed the number of circulating TRECs and KRECs in patients with IH, autoimmune type 1 diabetes (T1D), and autoimmune thyroiditis (ATs) and healthy controls (HCs). **Design:** Comparative case-control at tertiary care center. **Subjects and Methods:** Absolute and relative TRECs and KRECs were measured in DNA extracted from whole blood of patients with IH (n = 181, 22 of whom were reassessed after a decade of follow-up) and T1D (n = 133), AT (n = 53), and HC (n = 135) using a quantitative real-time PCR/TaqMan® probe technique. **Results:** Absolute and relative means of TRECs and KRECs in IH were comparable to HCs, and no differences were found between IH with and without calcium-sensing receptor antibodies or class I HLA-A\*26:01 association. TRECs and KRECs did not change after a decade of follow-up. T1D had significantly higher absolute TRECs than IH, AT, and HCs, whereas AT patients showed lower TRECs and the highest KRECs; these levels showed no noteworthy correlation with thyroid dysfunctions. **Conclusion:** Patients with IH showed TRECs and KRECs comparable to HCs, indicating an intact mechanism of T- and B-cell central immune tolerance. Interestingly, absolute TRECs were significantly higher in T1D than HCs, suggesting impaired central immune tolerance in T1D.

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**OBJECTIVE:** To investigate the effect of number and combination of b values used on the accuracy of estimated Intravoxel Incoherent Motion (IVIM) parameters using simulation and clinical data.

**MATERIALS AND METHODS:** Simulations with seven combinations of b values were performed for 4, 6, 8, and 13 numbers of b values with six different values of D, D\*, and f parameters. Two methodologies were implemented for IVIM analysis: standard biexponential model (BE) and biexponential model with total variation penalty function (BE+TV). Clinical data set of six patients with prostate cancer was retrospectively analyzed using 4, 8, and 13 b values.

**RESULTS:** BE+TV method showed lesser error and lower variability in simulation and clinical data, respectively. 8 and 13 b values showed good agreement in the values of parameters estimated with high correlation coefficient ( $\rho=0.83-0.93$ ). Clinical data showed high spurious noise with lower b values [4 b values leading to high coefficient of variation (CV); however, substantially, lower CV was observed with 8 and 13 b values].

**DISCUSSION:** BE model with TV penalty function is robust to combination of b values used for IVIM analysis. Combination of 8 b values provided a reasonably good accuracy in IVIM parameters.

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**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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Recently, cell membrane-derived nanoparticles, particularly of RBCs, have been explored for delivery of hydrophilic solutes of varied size and complexities. So far, these naturally derived nanoparticles show a significant overlap with liposomes in terms of stability, solute encapsulation, and release. Unlike hydrophilic molecules, which are loaded inside the aqueous core, hydrophobic moieties largely partition inside the lipophilic shell, hence fate of these nanocarriers may be different. Since vesicles have more complex membrane architecture (due to natural lipids and additional proteins and glycoproteins), ease of loading hydrophobic drug, its release pattern, and overall particle stability cannot be compared to those of synthetic lipid-based carriers. Therefore, we derived nanovesicles (NVEs) from RBC membrane, loaded with hydrophobic drug camptothecin (CPT) and labeled noncovalently with amphiphilic fluorophore (CM-DiI). Although both CPT and CM-DiI are known to partition inside the membrane, the overall stability of NVEs and composition of membrane proteins, particularly CD47, "marker of self", did not change. Additionally, the developed NVEs were found to be nonphagocytic even in the presence of serum and showed minimal stimulation of macrophages to release cytokines. Further, this system showed slow release but strong retention of CPT and CM-DiI, respectively, over 24 h, hence appropriate for theranostic applications. Also, NVEs were internalized by lung carcinoma cells and possessed slightly higher toxicity than free CPT. When injected intravenously in balb/c mice, these nanovesicles showed higher retention in blood over 48 h and insignificant accumulation in vital organs like heart and kidneys, thus suggesting its potential for in vivo application. We believe that this system has superior stealth and comparable physicochemical properties to synthetic lipid-based nanocarriers; hence, it can be further developed as personalized medicine.

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PMID: 31148443

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**BACKGROUND:** Malignant tumors of the trachea (MTT) account for 0.01-0.4% of all cancer cases. The rarity of the tumor along with different histologies makes it is a great challenge on how to optimally treat tracheal tumors and most of the available data is from small retrospective data series. We performed a systematic review and individual patient data analysis to evaluate the patterns of care and survival outcomes in patient with MTT.

**METHODOLOGY:** A comprehensive search in Pub Med and Google scholar was done to find all possible publications related to malignant tumors of the trachea. The data on patient demography, treatment, survival and recurrence pattern of individual patient was collected from the published data and was entered in a predesigned proforma. Progression free survival [PFS] and overall survival [OS] was calculated from the date of diagnosis to the date of documented progression and death respectively. Kaplan- Meier method was used for survival analysis and uni-variate analysis was performed using log rank test. SPSS v16 was used for all statistical analysis.

**RESULTS:** 733 patients were included in this analysis. The most common histology was adenoid cystic carcinoma (ACC) followed by squamous cell carcinoma (SCC). The gender ratio was 4.43: 1[male: female] in patients with SCC while it was 0.85:1[male: female] in ACC. Smoking and age >50 years were associated with worse OS. The estimated median overall survival for entire cohort was 96 months. Survival was significantly better in patients with ACC than in patients with SCC [165 vs. 14 months,  $p < 0.001$ ]. The use of definitive surgery was associated with a significantly better survival of 180 months when compared to 48 months with radiation as local therapy, [ $p < 0.001$ ]. The radiation dose used also affected survival in patients with SCC with a better median OS of 24 months in patients who recieved more than 60Gy vs 6 months in whom the dose was less than 60Gy although not statistically significant ( $p = 0.011$ ).

**CONCLUSION:** ACC and SCC are the most common MTT. ACC has better prognosis compared to SCC. Surgery seems to provide better outcomes than radiation for ACC and sarcoma. Role of definitive radiotherapy versus surgery in SCC needs to be further studied.

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**PURPOSE:** To evaluate the utility of Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) in assessing treatment response in patients of intestinal tuberculosis (ITB).

**METHOD AND MATERIALS:** MR Enterography (MRE) was done for patients with suspicion of ITB and 19 patients with pre- and post-treatment imaging were included in the

analysis. MRE included T1W, T2W, post-contrast T1W, and DWI sequences. DWI was done using b values-0, 400 and 800 s/mm<sup>2</sup>, and ADC maps were generated. The trace DW images and ADC values were compared before and after therapy. Composite gold standard (clinical, colonoscopic criteria, and biopsy) was used to assess treatment response and to classify into no response, partial response, and complete response.

**RESULTS:** Thirty-one bowel segments were evaluated at baseline and after treatment in 19 patients. Prior to therapy, restricted diffusion was seen in 29/31 (93.5%) segments. After treatment, patients with either complete or partial response (27/31 segments, 15 patients) showed significant rise in mean ADC values from  $1.1 \pm 0.37 \times 10^{-3}$  to  $2.1 \pm 0.64 \times 10^{-3}$  mm<sup>2</sup>/s (p value < 0.05), whereas no significant change was found in mean ADC values of non-responders (4/29 segments in 4 patients) which increased from  $1.0 \pm 0.1 \times 10^{-3}$  mm<sup>2</sup>/s on baseline scan to  $1.32 \pm 0.2 \times 10^{-3}$  mm<sup>2</sup>/s on post-treatment scan (p value = 0.318). An increase in ADC value was found to be a reliable and objective marker of improvement with response to therapy.

**CONCLUSION:** ADC values show good correlation with treatment response in ITB and can be used for objectively quantifying it.

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PMID: 31175381

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CD38 on CD8+T cells is considered a reliable marker of HIV disease progression. *Withania somnifer*, a traditional ayurvedic medicine, has Th1 immunomodulatory properties. PBMCs from 38 HIV patients were exposed to *Withania somnifer* root extract at standardized concentration. An overall decline in the percentage of CD38 expressing CD8+T lymphocytes was observed, though the statistical significance was varied with different categories of HIV patients. *Withania somnifer* could have promising impact on HIV disease and therefore warrants a further study on larger parameters.

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**OBJECTIVE:** To prospectively assess the growth parameters in a cohort of children with classical 21-hydroxylase deficiency congenital adrenal hyperplasia, comprehensively profile their clinical data and evaluate the prevalence of testicular adrenal rest tumors among affected boys.

**METHODS:** Children with congenital adrenal hyperplasia aged 0-18 y were prospectively followed up for six mo to 2 y (mean follow-up:  $17 \pm 6$  mo). Baseline data were obtained by interviewing parents and from clinic records. Anthropometry, biochemical parameters, X-ray for bone age, and ultrasound scrotum (in boys >5 y) for testicular adrenal rest tumors were performed.

**RESULTS:** Among the 81 children (32 boys, 49 girls), two-thirds (57) had salt-wasting and the remaining had simple virilizing type and the mean age at enrolment was  $6.2 \pm 4.9$  y. The overall height standard deviation score was -0.6 (-2.0 to 0.8) with a greater compromise in children in the age groups 0-2 y and >10 y and those with salt-wasting type. Overall, 25 (31%) children had short stature and 45 (55.6%) had growth velocity below the reference range. Bone age

advancement beyond 2 standard deviation score was seen in 46% of children assessed. Testicular adrenal rest tumors were detected in 5 out of 21 boys (23.8%).

**CONCLUSIONS:** The auxological pattern observed in this homogenously-managed Indian pediatric cohort with congenital adrenal hyperplasia highlights that infancy and peri-pubertal age groups are the most vulnerable, reiterating the importance of diligent growth monitoring. The high prevalence of testicular adrenal rest tumors merits the incorporation of annual ultrasound in the follow-up protocol of these patients.

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PMID: 30697677

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Several attempts have been made to engineer a viable three-dimensional (3D) bone tissue equivalent using conventional tissue engineering strategies, but with limited clinical success. Using 3D bioprinting technology, scientists have developed functional prototypes of clinically relevant and mechanically robust bone with a functional bone marrow. Although the field is in its infancy, it has shown immense potential in the field of bone tissue engineering by re-establishing the 3D dynamic micro-environment of the native bone. In spite of their in vitro success, maintaining the viability and differentiation potential of such cell-laden constructs overtime, and their subsequent preclinical testing in terms of stability, mechanical loading, immune responses, and osseointegrative potential still needs to be explored. Progress is slow due to several challenges such as but not limited to the choice of ink used for cell encapsulation, optimal cell source, bioprinting method suitable for replicating the heterogeneous tissues and organs, and so on. Here, we summarize the recent advancements in bioprinting of bone, their limitations, challenges, and strategies for future improvisations. The generated knowledge will provide deep insights on our current understanding of the cellular interactions with the hydrogel matrices and help to unravel new methodologies for facilitating precisely regulated stem cell behaviour.

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PMID: 30812062

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

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

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Broad and potent neutralizing antibodies (bnAbs) with multiple epitope specificities evolve in HIV-1 infected children. Herein, we studied two antiretroviral naïve chronically HIV-1C infected monozygotic pediatric twins AIIMS\_329 and AIIMS\_330 with potent plasma bnAbs. Elite plasma neutralizing activity was observed since initial sampling at 78 months in AIIMS\_330 and persisted throughout, while in AIIMS\_329 it was seen at 90-months of age after which potency decreased overtime. We evaluated potential viral characteristics associated with varied immune profile by generating single genome amplified pseudoviruses. The AIIMS\_329 viruses generated from 90-month time point were neutralization sensitive to bnAbs and contemporaneous plasma antibodies, while viruses from 112-month and 117-month timepoints were resistant to most bnAbs and contemporaneous plasma. AIIMS\_329 viruses developed resistance to plasma nAbs plausibly by N160-glycan loss, V1- and V4-loop lengthening. The viruses generated from AIIMS\_330 (at 90 and 117-months) showed varied susceptibility to bnAbs and autologous contemporaneous plasma antibodies while the viruses of 112-month timepoint, at which plasma nAb specificities mapped to the V2-glycan, V3-glycan and CD4bs, were resistant to contemporaneous plasma antibodies as well as to most bnAbs. Chimeric viruses were constructed from 90-month time-point PG9 sensitive AIIMS-329 and AIIMS\_330 viruses with swapped V1V2 regions of their respective evolved viruses (at 112 and 117-month), that led to higher resistance to neutralization by PG9 and autologous plasma antibodies. We observed evolution of a viral pool in AIIMS\_330 donor, comprising of plasma antibody neutralization sensitive or resistant diverse autologous viruses that may have contributed to development and maintenance of elite neutralizing activity. IMPORTANCE Herein, we report longitudinal development of bnAbs in a pair of chronically HIV-1C infected monozygotic pediatric twins, AIIMS\_329 and AIIMS\_330, who acquired the infection by vertical transmission. The plasma from both the donors, sharing similar genetic makeup and infecting virus, showed the involvement of bnAbs targeting common epitopes in the V2 and V3 regions of the envelope, suggesting bnAb development in these twins may perhaps be determined by specific sequences in the shared virus that can guide development of immunogens aimed at eliciting V2 and V3 bnAbs. Characterization of the neutralization sensitive and resistant viruses coevolving with bnAbs in the contemporaneous AIIMS\_330 plasma provides information towards understanding the viral alterations that may have contributed to the development of resistance to bnAbs. Further longitudinal studies in more monozygotic and dizygotic twin pairs will help in delineating the role of host and viral factors that may contribute to the development of bnAbs.

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87: Mishra S, Sinha R, Ray BR, Pandey RK, Darlong V, Punj J. Effect of entropy-guided low-flow desflurane anaesthesia on laryngeal mask airway removal time in children undergoing elective ophthalmic surgery - A prospective, randomised, comparative study. *Indian J Anaesth.* 2019 Jun;63(6):485-490. doi: 10.4103/ija.IJA\_237\_19. PubMed PMID: 31263301; PubMed Central PMCID: PMC6573054.

**Background and Aims:** In children, entropy-guided titration of isoflurane and sevoflurane leads to faster recovery after anaesthesia. However, role of entropy in recovery following desflurane anaesthesia is not known. Hence, we compared laryngeal mask airway (LMA) removal time and desflurane consumption with entropy and minimal alveolar concentration-guided titration in children given low-flow desflurane anaesthesia.

**Methods:** After ethics committee approval and parental consent, 80 American Society of Anesthesiologists grade I-II children, age 2-14 years, undergoing elective ophthalmic surgery were randomised into entropy and minimal alveolar concentration-guided groups. After LMA insertion, anaesthesia was maintained using oxygen, air (FiO<sub>2</sub> 0.5) and desflurane using low fresh gas flow of 0.75 L/min. In the entropy-guided group, desflurane was titrated to maintain state entropy between 40 and 60. In the minimal alveolar concentration-guided group, desflurane was titrated to maintain a minimal alveolar concentration between 1 and 1.3. We recorded LMA removal time (from switching off desflurane at the end of surgery till removal of LMA), haemodynamic parameters, uptake and consumption of desflurane between the groups.

**Results:** LMA removal time was significantly decreased in the entropy-guided group in comparison to the minimal alveolar concentration-guided group (4.34 ± 2.03 vs 8.8 ± 2.33 min) (P < 0.0001). Consumption of desflurane was significantly less in the entropy-guided group compared with the minimal alveolar concentration-guided group (18.7 ± 5.07 vs 25.3 ± 8.11 mL) (P < 0.0001).

**Conclusion:** Entropy-guided low-flow desflurane anaesthesia is associated with faster LMA removal and reduced consumption of desflurane in children undergoing ophthalmic surgery.

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PMID: 31263301

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G-quadruplex structure forming motifs are among the most studied evolutionarily conserved drug targets that are present throughout the genome of different organisms and susceptible to influencing various biological processes. Here we report highly conserved potential G-quadruplex motifs (PGQs) in three essential genes (espK, espB, and cyp51) among 160 strains of the Mycobacterium tuberculosis genome. Products of these genes are involved in pathways that are responsible for virulence determination of bacteria inside the host cell and its survival by maintaining membrane fluidity. The espK and espB genes are essential players that prevent the formation of mature phagolysosome and antigen presentation by host macrophages. The cyp51 is another PGQ-possessing gene involved in sterol biosynthesis pathway and membrane formation. In the present study, we revealed the formation of stable intramolecular parallel G-quadruplex structures by Mycobacterium PGQs using a combination of techniques (NMR, circular dichroism [CD], and gel electrophoresis). Next, isothermal titration calorimetry (ITC) and

CD melting analysis demonstrated that a well-known G-quadruplex ligand, TMPyP4, binds to and stabilizes these PGQ motifs. Finally, polymerase inhibition and qRT-PCR assays highlight the biological relevance of PGQ-possessing genes in this pathogen and demonstrate that G-quadruplexes are potential drug targets for the development of effective anti-tuberculosis therapeutics.

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Background: Prevalence of type 2 diabetes (T2D) is increasing worldwide. Identifying and targeting individuals at high risk, is essential for preventing T2D. Several studies point to mobile health initiatives delivered through personal smart devices being a promising approach to diabetes prevention, through weight loss. The aim of the mobile health and diabetes (mDiab) trial was twofold: to achieve 5% weight loss and to look at the association of weight loss with degree of engagement with the mDiab app. Methods: The mDiab randomized control trial was carried out among smartphone users who are at high risk for T2D mellitus in three cities-Chennai, Bengaluru, and New Delhi in India. The intervention was delivered through a mobile phone application along with weekly coach calls for 12 weeks. While individuals in the intervention group individuals received the app, which enabled tracking their weight, physical activity, and diet along with 12 weekly video lessons on T2D prevention and coach calls, the control group received usual care. Results: The intervention group experienced a significant 1kg weight loss while the control group lost 0.3kg ( $P < 0.05$ ). More individuals in the intervention group ( $n=139$ , 15%) met the 5% weight loss target than in the control group ( $n=131$ , 9%). In the intervention group those who viewed the videos experienced greater weight loss (2.4kg) than those who only attended coach calls (0.9kg) ( $P < 0.01$ ). Conclusions: An mHealth intervention helped to achieve moderate weight loss. Future studies should explore the sustainability of this weight loss.

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

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This systematic review and meta-analysis was performed to investigate whether methylprednisolone (MP) administered via any route improves postoperative outcomes (pain, trismus, and oedema) following mandibular third molar surgery. An electronic search of the PubMed, Scopus, Cochrane CENTRAL, and Google Scholar databases was performed to identify studies published in English up until January 2018. A total of 28 studies were included in the review: 25 randomized clinical trials (RCTs) and three controlled clinical trials. Studies were grouped according to the route of administration of MP for qualitative and quantitative analysis. Three studies were of 'high' quality and 22 were of 'medium' quality; three studies had a high risk of bias. Within the purview of the limitations of this review, the results showed that MP administered via any route significantly improves oedema in the early postoperative period, but has no effect on late postoperative oedema. Oral and intra-masseteric MP also seems to reduce pain and trismus in the early postoperative period. The results also indicate that oral MP may reduce late postoperative pain, while intra-masseteric MP may improve the late trismus outcome. More high quality RCTs are required to provide stronger evidence on the use of MP in third molar surgery.

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Ultrafine gold particles (AuPs) can be emerged as a good candidate in the field of drug delivery as well as in imaging applications. However, little attention has been paid to detailed study of nanoparticle's interaction with blood components before systemic use. An investigation into the interaction of ultrafine AuPs with blood components is must for its clinical application. In present study, the interaction of ultrafine sized AuPs ( $2\pm 0.5$  nm,  $5\pm 1$  nm, and  $10\pm 2$  nm) with blood components and its immunogenic property (pro-inflammatory reaction) was investigated. All three sized AuPs did not cause any significant hemolysis. Plasma coagulation study showed significant increase in Prothrombin time (PT) with International Normalized Ratio (INR) value raised to 1.53 with 10 nm AuPs. Maximum prolongation of activated partial thromboplastin time (APTT) (3.2s) was seen with 5 & 10 nm sized AuPs. Maximum thrombin time (TT) prolongation was seen with 2 nm (18.3s) with the difference of 1.4 s as compared

to control. Platelet aggregation was faster in case of 5 & 10 nm sized AuPs. All three sized AuPs exhibited in-vitro C3 complement activation whereas they did not stimulate significant proliferation of peripheral blood mononuclear cells (PBMC). These findings further validate the utility of ultrafine AuPs for in-vivo applications.

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

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It is well known that quality of hearing decreases with increasing age due to changes in the peripheral or central auditory pathway. Along with the decrease in the number of neurons the neurotransmitter profile is also affected in the various parts of the auditory system. Particularly, changes in the inhibitory neurons in the inferior colliculus (IC) are known to affect quality of hearing with aging. To date, there is no information about the status of the inhibitory

neurotransmitter GABA in the human IC during aging. We have collected and processed inferior colliculi of persons aged 11-97 years at the time of death for morphometry and immunohistochemical expression of glutamic acid decarboxylase (GAD67) and parvalbumin. We used unbiased stereology to estimate the number of cresyl-violet and immunostained neurons. Quantitative real-time PCR was used to measure the relative expression of the GAD67 mRNA. We found that the number of total, GABAergic and PV-positive neurons significantly decreased with increasing age ( $p < 0.05$ ). The proportion of GAD67-ir neurons to total number of neurons was also negatively associated with increasing age ( $p = 0.004$ ), but there was no change observed in the proportion of PV-ir neurons relative to GABAergic neurons ( $p = 0.25$ ). Further, the fold change in the levels of GAD67 mRNA was negatively correlated to age ( $p = 0.024$ ). We conclude that the poorer quality of hearing with increasing age may be due to decreased expression of inhibitory neurotransmitters and the decline in the number of inhibitory neurons in the IC.

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Innate immunity plays an important role in pathophysiology of tuberculosis which is influenced by various host factors. One such factor is vitamin D which, along with its associated molecule, can alter the host defense against Mycobacterium Tuberculosis (M.Tb.) via altered production of cathelicidin and nitric oxide, both having bactericidal effect. Therefore, assessment of vitamin D and its associated molecules in tuberculosis patients and household contacts as compared to healthy controls were done and the implication of these findings in susceptibility to tuberculosis (TB) was studied. 80 active TB patients, 75 household contacts and 70 healthy controls were included. Vitamin D receptor (VDR), vitamin D binding protein (VDBP) and inducible nitric oxide synthase (iNOS) mRNA levels were studied using quantitative PCR. Serum VDR, cathelicidin, and iNOS levels were measured using ELISA. Vitamin D and NO levels were measured in serum using chemiluminescence based immunoassay and greiss reaction based colorimetry kit respectively. Decreased serum levels of vitamin D were observed in active TB patients as compared to healthy controls ( $p < 0.001$ ). VDR and iNOS mRNA levels were found to be significantly lower in active TB patients compared to household contacts and healthy controls ( $p < 0.0001$  and  $0.005$  respectively). VDBP mRNA expression was found to be lower in active TB group as compared to household contacts and healthy controls however the difference was not found to be significant ( $p > 0.21$ ). Although, mRNA expression of VDR, VDR protein and iNOS along with vitamin D levels were significantly ( $p < 0.05$ ) higher in household contacts compared to active TB group. However, levels of iNOS, NO and cathelicidin were found to be higher in TB patients as compared to household contacts and healthy controls ( $p < 0.01$ ,  $0.05$  and  $0.01$  respectively). Higher levels of Vitamin D along with VDR and iNOS expression in household contacts as compared to active TB patients suggest vitamin D might have a protective role against TB plausibly decreasing disease susceptibility. Low vitamin D levels in active TB patients warrants further studies to determine the role of vitamin D supplementation in prevention and treatment of TB.

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**BACKGROUND:** There is a lack of clinical predictors for prognosticating lymphoblastic lymphoma (LBL). In view of this lacuna, we evaluated outcomes and prognostic factors for LBL treated with a uniform protocol at our center. **PATIENTS AND METHODS:** This study included consecutive patients of pediatric LBL aged  $\leq 18$  years from January 2003 to January 2017. Patients were staged using the St Jude staging system. All patients were treated with acute lymphoblastic leukemia like BFM90 protocol. The Kaplan-Meier method was used for survival analysis. A statistical model was made using stepwise regression and forward selection of the factors predicting event-free survival (EFS) and overall survival (OS).

**RESULTS:** Sixty-five patients were evaluated with a median age of 12 years (range, 1-18 years) and male:female ratio of 2.25:1. Fifty-four patients presented with mediastinal disease. Median follow-up was 54.57 months (range, 0.6-140.5 months). EFS at 10 years was  $62 \pm 6\%$  (95% confidence interval [CI], 0.49-0.73) and OS  $71 \pm 5\%$  (95% CI, 0.57-0.81). In multivariate analysis, symptom duration  $\leq 30$  days, white blood cell (WBC) count  $>12000/\mu\text{L}$  and serum albumin  $\leq 3.5$  g/dL predicted inferior EFS and OS. A prognostic model with these 3 factors suggested that those without any of these risk factors had an OS of  $92 \pm 5\%$  whereas those with 2 or 3 factors had an OS of  $37 \pm 14\%$ .

**CONCLUSION:** Our outcomes are 15% to 20% lower than in the published literature. Low albumin level, high WBC count at baseline, and symptom duration  $<30$  days emerged as adverse predictors for EFS and OS. These clinical predictors and prognostic model for pediatric LBL should be validated in prospective cohorts.

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Mucormycosis due to Mucorales is reported at large numbers in uncontrolled diabetics across India, but systematic multicenter epidemiological study has not been published yet. The present prospective study was conducted at four major tertiary care centers of India (two in north and two in south India) during 2013-2015 to compare the epidemiology, treatment strategies and outcome of mucormycosis between the two regions. Molecular techniques were employed to confirm the identity of the isolates or to identify the agent in biopsy samples. A total of 388 proven/probable mucormycosis cases were reported during the study period with overall mortality at 46.7%. Uncontrolled diabetes (n = 172, 56.8%) and trauma (n = 31, 10.2%) were the common risk factors. Overall, *Rhizopus*

arrhizus (n = 124, 51.9%) was the predominant agent identified, followed by *Rhizopus microsporus* (n = 30, 12.6%), *Apophysomyces variabilis* (n = 22, 9.2%) and *Rhizopus homothallicus* (n = 6, 2.5%). On multivariate analysis, the mortality was significantly associated with gastrointestinal (OR: 18.70, P = .005) and pulmonary infections (OR: 3.03, P = .015). While comparing the two regions, majority (82.7%) cases were recorded from north India; uncontrolled diabetes (n = 157, P = .0001) and post-tubercular mucormycosis (n = 21, P = .006) were significantly associated with north Indian cases. No significant difference was noted among the species of Mucorales identified and treatment strategies between the two regions. The mortality rate was significantly higher in north Indian patients (50.5%) compared to 32.1% in south India (P = .016). The study highlights higher number of mucormycosis cases in uncontrolled diabetics of north India and emergence of *R. microsporus* and *R. homothallicus* across India causing the disease.

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Metronomic chemotherapy transitioned from the bench to bedside in the early 2000s and since then has carved a niche for itself in pediatric oncology. It has been used solely or in combination with other modalities such as radiotherapy, maximum tolerated dose chemotherapy, and targeted agents in adjuvant, palliative, as well as maintenance settings. No wonder, the resulting medical literature is extremely heterogeneous. In this review, the authors review and synthesize the published literature in pediatric metronomics giving a glimpse of its history, varied applications, and evolution of this genre of chemotherapy in pediatric cancers. Limitations, future prospects, and grey areas are also highlighted.

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Background: Atypical hemolytic uremic syndrome (aHUS), an important cause of acute kidney injury (AKI), is characterized by dysregulation of the alternative complement pathway. Autoantibodies to factor H (FH), a chief regulator of this pathway, account for a distinct subgroup. While high anti-FH titers predict relapse, they do not correlate well with disease activity and their functional characterization is required. Methods: Of 781 patients <18-year-old of aHUS in the nationwide database from 2007 to 2018, 436 (55.8%) had anti-FH antibodies. Clinical features and outcome of patients managed in the last 6-year (n = 317)

were compared to before (n = 119). In plasma samples of 44 patients, levels of serial circulating FH immune complexes (CIC), free FH, soluble terminal complement complex (sC5b-9), sheep red blood cell (SRBC) lysis and epitope specificity (n = 8) were examined. Functional renal reserve, ambulatory hypertension, left ventricular hypertrophy (LVH), and proteinuria were evaluated in a subset. Results: Patients presented with markedly elevated anti-FH titers ( $10,633.2 \pm 998.5$  AU/ml). Management varied by center, comprising plasma exchange (PEX; 77.5%) and immunosuppression (73.9%). Patients managed in the last 6-year showed better renal survival at mean  $28.5 \pm 27.3$  months (log rank  $P = 0.022$ ). Mean anti-FH titers stayed 700-1,164 AU/ml during prolonged follow-up, correlating with CIC. Patients with relapse had lower free-FH during remission [Generalized estimating equations (GEE),  $P = 0.001$ ]; anti-FH levels  $\geq 1,330$  AU/ml and free FH  $\leq 440$  mg/l predicted relapse (hazards ratio, HR 6.3;  $P = 0.018$ ). Epitope specificity was similar during onset, remission and relapse. Antibody titer  $\geq 8,000$  AU/ml (HR 2.23;  $P = 0.024$ ), time to PEX  $\geq 14$  days (HR 2.09;  $P = 0.071$ ) and PEX for  $< 14$  days (HR 2.60;  $P = 0.017$ ) predicted adverse renal outcomes. Combined PEX and immunosuppression improved long-term outcomes (HR 0.37;  $P = 0.026$ ); maintenance therapy reduced risk of relapses (HR 0.11;  $P < 0.001$ ). At  $4.4 \pm 2.5$  year, median renal reserve was 15.9%; severe ambulatory, masked and pre-hypertension were found in 38, 30, and 18%, respectively. Proteinuria and LVH occurred in 58 and 28% patients, respectively. Conclusion: Prompt recognition and therapy with PEX and immunosuppression, is associated with satisfactory outcomes. Free-FH predicts early relapses in patients with high anti-FH titers. A significant proportion of impaired functional reserve, ambulatory hypertension, proteinuria and LVH highlight the need for vigilant long-term follow-up.

DOI: 10.3389/fimmu.2019.01282

PMCID: PMC6567923

PMID: 31231391

108: Rashid H, Katyal J, Tripathi M, Sood M, Gupta YK. Validation of the Indian version of Neurological Disorders Depression Inventory for Epilepsy (NDDI-E). *Epilepsy Behav.* 2019 Jun;95:75-78. doi: 10.1016/j.yebeh.2019.03.048. Epub 2019 Apr 24. PubMed PMID: 31026787.

**PURPOSE:** The Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) is an efficient tool for rapid detection of depression, an important comorbid condition in persons with epilepsy (PWE). Since social and cultural differences can potentially affect the cutoff score of NDDI-E, in this study, the reliability and validity of the Indian version of the NDDI-E in PWE was determined.

**METHOD:** After ethical clearance, 217 PWE above 18 years of age, on antiepileptic drugs (AEDs), attending neurology outpatient department (OPD) of All India Institute of Medical Sciences (AIIMS), New Delhi, India, were evaluated for depression using the NDDI-E (Indian version) and Mini International Neuropsychiatric Interview (MINI-Module A, version 6.0.0) as reference standard. Informed consent was taken before recruitment. Receiver operating characteristic (ROC) analysis and Cronbach's  $\alpha$ , a measure of the internal consistency and reliability, were carried out to validate cutoff and questionnaire, respectively.

**RESULTS:** Of the 217 PWE (112 males/105 females), mean age of  $28.6 \pm 9.4$  years, with generalized (69.1%) or focal seizures (30.9%), 41.5% and 10.6% were diagnosed with depression using MINI and NDDI-E Indian version (at cutoff  $> 15$ ), respectively. However, at a cutoff score of  $> 11$ , the Indian version of NDDI-E had a sensitivity of 96.67%, a specificity of 84.25%, a positive predictive value of 81.31%, and a negative predictive value of 97.27%. ROC analysis showed an area under the curve (AUC) of 0.9547 (confidence interval (CI) 95% = 0.929-0.979; standard error (SE): 0.0127). With the Indian version of NDDI-E, the Cronbach's  $\alpha$  value was 0.877.

**CONCLUSION:** A periodic assessment of PWE using a quickly administrable and reliable tool for screening depression is highly desirable given the high incidence. In the Indian population with a cutoff of  $> 11$ , NDDI-E is a reliable and valid instrument to screen depression in PWE.

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DOI: 10.1016/j.yebeh.2019.03.048

PMID: 31026787

109: Remenyi B, Carapetis J, Stirling JW, Ferreira B, Kumar K, Lawrenson J, Marijon E, Mirabel M, Mocumbi AO, Mota C, Paar J, Saxena A, Scheel J, Viali S, Vijayalakshmi IB, Wheaton GR, Zuhlke L, Sidhu K, Dimalapang E, Gentles TL, Wilson NJ. Inter-rater and intra-rater reliability and agreement of echocardiographic diagnosis of rheumatic heart disease using the World Heart Federation evidence-based criteria. *Heart Asia*. 2019 Jun 24;11(2):e011233. doi: 10.1136/heartasia-2019-011233. eCollection 2019. PubMed PMID: 31297166; PubMed Central PMCID: PMC6591009.

**Objective:** Different definitions have been used for screening for rheumatic heart disease (RHD). This led to the development of the 2012 evidence-based World Heart Federation (WHF) echocardiographic criteria. The objective of this study is to determine the intra-rater and inter-rater reliability and agreement in differentiating no RHD from mild RHD using the WHF echocardiographic criteria. **Methods:** A standard set of 200 echocardiograms was collated from prior population-based surveys and uploaded for blinded web-based reporting. Fifteen international cardiologists reported on and categorised each echocardiogram as no RHD, borderline or definite RHD. Intra-rater and inter-rater reliability was calculated using Cohen's and Fleiss' free-marginal multirater kappa ( $\kappa$ ) statistics, respectively. Agreement assessment was expressed as percentages. Subanalyses assessed reproducibility and agreement parameters in detecting individual components of WHF criteria.

**Results:** Sample size from a statistical standpoint was 3000, based on repeated reporting of the 200 studies. The inter-rater and intra-rater reliability of diagnosing definite RHD was substantial with a kappa of 0.65 and 0.69, respectively. The diagnosis of pathological mitral and aortic regurgitation was reliable and almost perfect, kappa of 0.79 and 0.86, respectively. Agreement for morphological changes of RHD was variable ranging from 0.54 to 0.93  $\kappa$ .

**Conclusions:** The WHF echocardiographic criteria enable reproducible categorisation of echocardiograms as definite RHD versus no or borderline RHD and hence it would be a suitable tool for screening and monitoring disease progression. The study highlights the strengths and limitations of the WHF echo criteria and provides a platform for future revisions.

DOI: 10.1136/heartasia-2019-011233

PMCID: PMC6591009

PMID: 31297166

110: Rewari V, Ramachandran R. Continuous wound infiltration of local anaesthetics for acute postoperative pain - A revisit. *Indian J Anaesth*. 2019 Jun;63(6):425-427. doi: 10.4103/ija.IJA\_425\_19. PubMed PMID: 31263292; PubMed Central PMCID: PMC6573056.

111: Reza-Paul S, Lazarus L, Maiya R, Venukumar KT, Lakshmi B, Roy A, Haldar P, Andina M, Lafort Y, Lorway R. Delivering community-led integrated HIV and sexual and reproductive health services for sex workers: A mixed methods evaluation of the DIFFER study in Mysore, South India. *PLoS One*. 2019 Jun 21;14(6):e0218654. doi: 10.1371/journal.pone.0218654. eCollection 2019. PubMed PMID: 31226141; PubMed Central PMCID: PMC6588234.

**INTRODUCTION:** Women in developing countries continue to face barriers to accessing sexual and reproductive health (SRH) services, with marginalized women facing increased challenges to accessing care. The Diagonal Interventions to Fast-Forward Enhanced Reproductive Health (DIFFER) project implemented a package of interventions for female sex workers and women from the general population which integrated horizontal health services for the general population with

existing vertical targeted interventions aimed at sex workers with an aim to improve SRH and HIV services. We present an outcome evaluation of the DIFFER project in terms of uptake rates for SRH services among sex workers in Mysore, India.

**METHODS:** Ashodaya Samithi, a sex worker-led organization, implemented the DIFFER strategy through their community-based clinic and a Well Women Clinic (WWC), established at a partner private hospital that provided SRH services for women living with HIV. Mixed methods were used to evaluate the intervention that included a baseline (2012-13) and end of project (2015-16) cross sectional surveys (CSS), focus group discussions (FGDs), key informant interviews, and analysis of service statistics from 2013-2016.

**RESULTS:** The CSS found that condom use, STI testing, and treatment were high before, and throughout the intervention; cervical cancer screening and treatment increased significantly, from 11.5% to 56% (aOR 9.85,  $p < 0.001$ ) and HIV testing in the last 3 months increased from 26.3% to 73.3% (aOR 7.25,  $p < 0.001$ ). The proportion of sex workers using any SRH service in the past year doubled from 25.7% to 51.4% (aOR 2.91,  $p < 0.001$ ). Service statistics showed similar trends. The FGDs and key informant interviews showed that women and stakeholders held high levels of satisfaction with the strategy, and affirmed potential for scale up.

**CONCLUSION:** The DIFFER strategy demonstrated that SRH service uptake can occur in conjunction with HIV services offered to sex workers. This model of integrated service delivery has been accepted by policy makers and needs further analysis for scaling up.

DOI: 10.1371/journal.pone.0218654

PMCID: PMC6588234

PMID: 31226141

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**OBJECTIVE:** The technique of distraction, compression, extension, and reduction (DCER) is effective to reduce, realign, and relieve cranio-spinal compression through posterior only approach.

**METHODS:** Study included all patients with atlantoaxial dislocation and basilar invagination (BI) with occipitalized C1 arch. Study techniques included Nurick grading, computed tomography scan to study atlanto-dental interval, BI, hyper-lordosis, and neck tilt. Sagittal inclination (SI), coronal inclination (CI), cranio-cervical tilt, presence of pseudo-joints, and anomalous vertebral artery were also noted. Patients underwent DCER with/without joint remodeling or extra-articular distraction (EAD) based on the SI being  $< 100^\circ$ ,  $100^\circ - 160^\circ$ , or  $> 160^\circ$  respectively. In cases with pseudo-joints, joint remodeling was performed in type I and EAD in type II. Customized 'bullet shaped' PSC spacers (n=124) and prototype of the universal craniovertebral junction reducer (UCVJR, n=36) were useful.

RESULTS: A total of 148 patients with average age  $27.25 \pm 17.43$  years, ranging from 3 to 71 years (87 males) were operated. Nurick's grading improved from  $3.14 \pm 1.872$  to  $1.22 \pm 1.17$  ( $p < 0.0001$ ). Fifty-two percent of total joints ( $n = 154/296$  joints) were either type I (19%)/type II (33%) pseudo-joints. All traditional indices such as Chamberlain line, McRae line, atlanto-dental interval, and Ranawat line improved ( $p < \text{at least } 0.001$ ). BI, SI, and CI values correlated with type of pseudo-joints ( $p < 0.0001$ ). Side of neck tilt correlated with the type of pseudo-joint ( $p < 0.0001$ ). Cervical hyperlordosis improved significantly ( $p < 0.0001$ ).

CONCLUSION: Occipito-C2 pseudo-joints are important in determining the severity of BI. Asymmetrical pseudo-joint causes coronal/neck tilt. Type of pseudo-joint can strategize by DCER. Customized instruments and implants make technique safe, effective and easier.

DOI: 10.14245/ns.1938194.097

PMCID: PMC6603831

PMID: 31261462

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117: Satapathy AK, Pandey S, Chaudhary MR, Bagga A, Kabra M, Uwe K, Gupta N. Report of Another Mutation Proven Case of Carbonic Anhydrase II Deficiency. *J Pediatr Genet*. 2019 Jun;8(2):91-94. doi: 10.1055/s-0038-1675781. Epub 2018 Nov 18. PubMed PMID: 31061753; PubMed Central PMCID: PMC6499615.

Carbonic anhydrase (CA) II deficiency results in an uncommon type of autosomal recessive sclerosing bone dysplasia with renal tubular acidosis and intracerebral calcification. We report a classic case of CA II-associated osteopetrosis with a previously reported homozygous frameshift mutation. Child was evaluated for short stature and failure to thrive. He was diagnosed as osteopetrosis in view of the presence of hepatosplenomegaly and increased bone density though hematological parameters were normal. Further evaluation showed presence of associated distal renal tubular acidosis raising a possibility of CA II deficiency. Mutation analysis revealed a previously reported homozygous frameshift mutation c.143-146delCTGT (p.Ser48Phefs\*9) in CA2. Child has normal growth after initiation of alkali therapy.

DOI: 10.1055/s-0038-1675781

PMCID: PMC6499615 [Available on 2020-06-01]

PMID: 31061753

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119: Sen S, Singh P, Bajaj MS, Gaur N. Management of a case of orbital lymphangioma presenting in adulthood with negative-pressure aspiration and bleomycin injection. *BMJ Case Rep*. 2019 Jun 8;12(6). pii: e227697. doi: 10.1136/bcr-2018-227697. PubMed PMID: 31177193.

We hereby report a case of a 55-year-old woman, with complaints of sudden onset outward protrusion of left eye progressing over 2 months, along with pain and loss of vision. Visual acuity in the affected eye was light perception only. On imaging, a well-defined solitary cystic lesion was noted in the retrobulbar space, which showed no enhancement on contrast-enhanced MRI. We performed fluid aspiration from the cyst under negative pressure and injected bleomycin as a sclerosant, without attempting a surgical excision. The proptosis reduced visibly, and after a week, visual acuity improved to finger counting at 1 m. At the 6 months follow-up, the patient did not show any recurrence of proptosis. This report highlights the importance of sclerosant therapy without the need for

surgical excision in managing macrocystic lymphangiomas in adult age group.

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DOI: 10.1136/bcr-2018-227697

PMID: 31177193

120: Sethi A, Sankar MJ, Thukral A, Saxena R, Chaurasia S, Agarwal R. Prophylactic Vitamin K Administration in Neonates on Prolonged Antibiotic Therapy: A Randomized Controlled Trial. *Indian Pediatr.* 2019 Jun 15;56(6):463-467. PubMed PMID: 31278224.

**OBJECTIVE:** To compare the prevalence of vitamin K deficiency after intramuscular vitamin K or no treatment in neonates with sepsis on prolonged (>7 days) antibiotic therapy.

**STUDY DESIGN:** Open label randomized controlled trial.

**SETTING:** Level 3 Neonatal Intensive Care Unit (NICU).

**PARTICIPANTS:** Neonates with first episode of sepsis on antibiotics for  $\geq 7$  days were included. Neonates with clinical bleeding, vitamin K prior to start of antibiotic therapy (except the birth dose), cholestasis or prenatally diagnosed bleeding disorder were excluded.

**INTERVENTIONS:** Randomized to receive 1 mg vitamin K (n=41) or no vitamin K (n=39) on the 7th day of antibiotic therapy.

**MAIN OUTCOME MEASURES:** Vitamin K deficiency defined as Protein Induced by Vitamin K Absence (PIVKA-II)  $>> 2$  ng/mL after  $7 \pm 2$  days of enrolment.

**RESULTS:** The prevalence of vitamin K deficiency was 100% (n=80) at enrolment and it remained 100% even after  $7 \pm 2$  days of enrolment in both the groups.

**CONCLUSIONS:** Neonates receiving prolonged antibiotics have universal biochemical vitamin K deficiency despite vitamin K administration on 7th day of antibiotic therapy.

PMID: 31278224

121: Shankar C, Mathur P, Venkatesan M, Pragasam AK, Anandan S, Khurana S, Veeraraghavan B. Rapidly disseminating bla(OXA-232) carrying Klebsiella pneumoniae belonging to ST231 in India: multiple and varied mobile genetic elements. *BMC Microbiol.* 2019 Jun 24;19(1):137. doi: 10.1186/s12866-019-1513-8. PubMed PMID: 31234800; PubMed Central PMCID: PMC6591861.

**BACKGROUND:** Recently, in India, there has been a shift from NDM to OXA48-like carbapenemases. OXA-181 and OXA-232 are the frequently produced variants of OXA48-like carbapenemases. OXA48-like carbapenemases are also known to be carried on transposons such as Tn1999, Tn1999.2 and it is also associated with IS1R carried on Tn1999. In India, there are no previous reports studying the association of mobile genetic elements (MGEs) with OXA48-like carbapenemases. The present study was aimed at determining the genetic backbone of OXA48-like carbapenemases to determine the role of MGEs in its transfer and to investigate the Inc plasmid type carrying blaOXA48-like.

**RESULTS:** A total of 49 carbapenem resistant K. pneumoniae which included 25 isolates from South India and 24 isolates from North India, were included in the study. Whole genome sequencing using Ion Torrent PGM was performed to study the isolates. OXA-232 was present in 35 isolates (71%). In 19 isolates (39%), blaOXA48-like was associated with MGEs. Insertion sequences such as ISX4, IS1, IS3, ISKpn1, ISKpn26, ISKpn25, ISSpu2, ISKox1, IS4321R, ISEc36, and ISPa38; and transposons such as TnAs3 and Tn2, were present. Isolates from northern and southern India belonging to same sequence type (ST) had diverse genetic backbone for blaOXA48-like. ST14 isolates from north had IS5 and Tn3 families while from south they had IS1, IS5 and IS630 families. ST231 from north had IS5, IS6 and Tn3 families with blaOXA-232 while from south, IS1, IS3 and IS5 families were observed; with ISKpn26 being present among isolates from both the regions.

blaOXA48-like was predominantly found on ColKP3 plasmid. ST231 was the predominant ST in 22 isolates (45%).

CONCLUSION: OXA-232 is the predominant variant of OXA48-like carbapenemase with ST231 being the commonest ST of OXA48-like carbapenemase producing *K. pneumoniae* in India. Diverse MGEs have been associated with both blaOXA-232 and blaOXA-181 which contribute to their spread. The MGEs in the present study are different from those reported earlier. There is no clonal expansion of blaOXA48-like producing *K. pneumoniae* since diverse STs were observed. Monitoring the genetic backbone of OXA48-like carbapenemase is essential to better understand the transmission dynamics of XDR *K. pneumoniae*.

DOI: 10.1186/s12866-019-1513-8

PMCID: PMC6591861

PMID: 31234800

122: Sharma V, Srinivasan A, Roychoudhury A, Rani K, Tyagi M, Dev K, Nikolajeff F, Kumar S. Characterization of protein extracts from different types of human teeth and insight in biomineralization. *Sci Rep.* 2019 Jun 27;9(1):9314. doi: 10.1038/s41598-019-44268-2. PubMed PMID: 31249316; PubMed Central PMCID: PMC6597790.

The present study describes an efficient method for isolation and purification of protein extracts from four types of human teeth i.e. molar, premolar, canine, and incisor. Detailed structural characterization of these protein extracts was done by Fourier transform infrared spectroscopy (FTIR) and circular dichroism (CD) which showed that a major fraction of the proteins present are unstructured in nature including primarily random coils in addition to the other structures like extended beta ( $\beta$ ) structure, poly-l-proline-type II (PPII) helix, turns, with only a small fraction constituting of ordered structures like alpha ( $\alpha$ ) helix and  $\beta$  sheets. These resultant labile structures give the proteins the necessary flexibility that they require to interact with a variety of substrates including different ions like calcium and phosphates and for other protein-protein interactions. We also did initial studies on the mineralization of calcium phosphate with the protein extracts. Nanoparticle tracking analysis (NTA) show an increase in the size of calcium phosphate accumulation in the presence of protein extracts. We propose that protein extracts elevate the crystallization process of calcium phosphate. Our current biophysical study provides novel insights into the structural characterization of proteins from human teeth and their implications in understanding the tooth biomineralization. As per our knowledge, this is the first report which focuses on the whole protein extraction from different types of human teeth as these extracts imitate the in vivo tooth mineralization.

DOI: 10.1038/s41598-019-44268-2

PMCID: PMC6597790

PMID: 31249316

123: Sharma VK, Gupta V, Bhari N, Singh V. Rituximab as an adjuvant therapy for pemphigus: experience in 61 patients from a single center with long-term follow-up. *Int J Dermatol.* 2019 Jun 30. doi: 10.1111/ijd.14546. [Epub ahead of print] PubMed PMID: 31257579.

BACKGROUND: Rituximab is increasingly being used as an adjuvant treatment for recalcitrant or relapsed pemphigus, but information on its use as a first-line agent is limited. We describe the long-term effectiveness and safety of rituximab in the treatment of pemphigus and compare the treatment outcomes when rituximab is used as first-line treatment vis-à-vis after treatment failure or relapse. METHODS: This was a retrospective review of 61 patients with pemphigus treated with rituximab at our center from March 2012 to October 2018. RESULTS: Of the 61 patients, 51 achieved complete remission (on or off treatment) and 10 had partial remission. Forty-nine (80.33%) patients achieved complete remission off prednisolone over a mean period of  $8.08 \pm 4.45$  (range 3-20) months.

Seventeen (27.9%) patients relapsed after a mean period of  $23.94 \pm 13.15$  months after first rituximab cycle and  $15.97 \pm 13.7$  months after stopping prednisolone. Treatment-related serious adverse effects were noted in six (9.8%) patients. Eighteen (29.5%) patients were administered rituximab as the first-line adjuvant, while 43 (70.5%) patients received it after treatment failure or relapse. In both groups, remission rates on prednisolone (88.9%, 81.4%) and off prednisolone (88.9%, 76.7%) were comparable ( $P > 0.05$ ). Relapse rates in the group which received rituximab as first-line treatment were about half of those who received rituximab after relapse or treatment failure (16.7% vs. 32.6%,  $P = 0.348$ ). No statistically significant difference was seen in the times to different treatment endpoints (disease control, complete remission on and off prednisolone, and relapse) between the two groups.

**CONCLUSIONS:** Rituximab is a safe and effective adjuvant in the treatment of pemphigus. Treatment outcomes were better for patients who received rituximab as first-line treatment, but the difference was not statistically significant.

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DOI: 10.1111/ijd.14546

PMID: 31257579

124: Shashni AK, Sen S, Meel R, Sharma MC, Nag TC. Primary apocrine adenocarcinoma of caruncle in an elderly male. *Can J Ophthalmol.* 2019 Jun;54(3):e123-e125. doi: 10.1016/j.jcjo.2018.08.011. Epub 2018 Oct 19. PubMed PMID: 31109498.

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126: Shivasabesan G, O'Reilly GM, Mathew J, Fitzgerald MC, Gupta A, Roy N, Joshipura M, Sharma N, Cameron P, Fahey M, Howard T, Cheung Z, Kumar V, Jarwani B, Soni KD, Patel P, Thakor A, Misra M, Gruen RL, Mitra B; Australia-India Trauma Systems Collaboration (AITSC). Establishing a Multicentre Trauma Registry in India: An Evaluation of Data Completeness. *World J Surg.* 2019 Jun 20. doi: 10.1007/s00268-019-05039-2. [Epub ahead of print] PubMed PMID: 31222639.

**BACKGROUND:** The completeness of a trauma registry's data is essential for its valid use. This study aimed to evaluate the extent of missing data in a new multicentre trauma registry in India and to assess the association between data completeness and potential predictors of missing data, particularly mortality. **METHODS:** The proportion of missing data for variables among all adults was determined from data collected from 19 April 2016 to 30 April 2017. In-hospital physiological data were defined as missing if any of initial systolic blood pressure, heart rate, respiratory rate, or Glasgow Coma Scale were missing. Univariable logistic regression and multivariable logistic regression, using manual stepwise selection, were used to investigate the association between mortality (and other potential predictors) and missing physiological data. **RESULTS:** Data on the 4466 trauma patients in the registry were analysed. Out of 59 variables, most ( $n=51$ ; 86.4%) were missing less than 20% of observations. There were 808 (18.1%) patients missing at least one of the first in-hospital physiological observations. Hospital death was associated with missing in-hospital physiological data (adjusted OR 1.4; 95% CI 1.02-2.01;  $p=0.04$ ). Other significant associations with missing data were: patient arrival time out of hours, hospital of care, 'other' place of injury, and specific injury mechanisms. Assault/homicide injury intent and occurrence of chest X-ray were associated with not missing any of first in-hospital physiological variables. **CONCLUSION:** Most variables were well collected. Hospital death, a proxy for more severe injury, was associated with missing first in-hospital physiological observations. This remains an important limitation for trauma registries.

DOI: 10.1007/s00268-019-05039-2  
PMID: 31222639

127: Singh A, Pramanik A, Acharya P, Makharia GK. Non-Invasive Biomarkers for Celiac Disease. *J Clin Med*. 2019 Jun 21;8(6). pii: E885. doi: 10.3390/jcm8060885. Review. PubMed PMID: 31234270.

Once thought to be uncommon, celiac disease has now become a common disease globally. While avoidance of the gluten-containing diet is the only effective treatment so far, many new targets are being explored for the development of new drugs for its treatment. The endpoints of therapy include not only reversal of symptoms, normalization of immunological abnormalities and healing of mucosa, but also maintenance of remission of the disease by strict adherence of the gluten-free diet (GFD). There is no single gold standard test for the diagnosis of celiac disease and the diagnosis is based on the presence of a combination of characteristics including the presence of a celiac-specific antibody (anti-tissue transglutaminase antibody, anti-endomysial antibody or anti-deamidated gliadin peptide antibody) and demonstration of villous abnormalities. While the demonstration of enteropathy is an important criterion for a definite diagnosis of celiac disease, it requires endoscopic examination which is perceived as an invasive procedure. The capability of prediction of enteropathy by the presence of the high titer of anti-tissue transglutaminase antibody led to an option of making a diagnosis even without obtaining mucosal biopsies. While present day diagnostic tests are great, they, however, have certain limitations. Therefore, there is a need for biomarkers for screening of patients, prediction of enteropathy, and monitoring of patients for adherence of the gluten-free diet. Efforts are now being made to explore various biomarkers which reflect different changes that occur in the intestinal mucosa using modern day tools including transcriptomics, proteomics, and metabolomics. In the present review, we have discussed comprehensively the pros and cons of available biomarkers and also summarized the current status of emerging biomarkers for the screening, diagnosis, and monitoring of celiac disease.

DOI: 10.3390/jcm8060885  
PMCID: PMC6616864  
PMID: 31234270

128: Singh AP, Ramana G, Bajaj T, Singh V, Dwivedi S, Behari M, Dey AB, Dey S. Elevated Serum SIRT 2 May Differentiate Parkinson's Disease From Atypical Parkinsonian Syndromes. *Front Mol Neurosci*. 2019 Jun 12;12:129. doi: 10.3389/fnmol.2019.00129. eCollection 2019. PubMed PMID: 31244600; PubMed Central PMCID: PMC6581755.

Atypical Parkinson syndromes (APSS) often have symptoms that overlap with those of Parkinson's disease (PD), especially early in the disease, making these disorders difficult to diagnose. Previous studies have demonstrated an association of oligomeric  $\alpha$ -synuclein ( $\alpha$ -Syn), a key element in the pathogenesis of PD, with Sirtuin (SIRT)2 proteins for modulating PD. We aimed to evaluate SIRT protein expression in serum of PD patients and compare it with APSS and normal elderly control (GC) and to correlate this with  $\alpha$ -Syn. SIRT protein expression was evaluated in sera of 68 PD; 34 APS and 68 GC without any neuro-psychiatric illness as controls by surface plasmon resonance (SPR). SIRT2 expression was correlated with  $\alpha$ -Syn in PD and GC. Significant ( $p < 0.0001$ ) differences were observed between serum SIRT2 concentration in PD and APS and GC as well as between APS and GC. Receiver operating characteristic (ROC) analysis revealed the strong cut-off value to differentiate PD from APS and GC and also APS from GC. Significant correlation was observed among SIRT2 levels in early PD patients with Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn & Yahr (H & Y) and increased duration of disease. In addition, a strong positive correlation of SIRT2 with  $\alpha$ -Syn ( $p < 0.0001$ ) was observed. However, no such difference was detected for serum SIRT1 in cases of PD and APS or for GC. The present study is the first to report elevated serum SIRT2 in PD. The study also provided a simple

test to distinguish PD from APS and may have translational utility for diagnosis.

DOI: 10.3389/fnmol.2019.00129

PMCID: PMC6581755

PMID: 31244600

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

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

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PMID: 30880045

130: Singh MK, Singh L, Pushker N, Saini N, Meel R, Chosdol K, Bakhshi S, Sen S, Venkatesh P, Chawla B, Kaur J, Kashyap S. Identification of canonical NF $\kappa$ B (C-NF $\kappa$ B) pathway in uveal melanoma and their relation with patient outcome. *Clin Exp Metastasis.* 2019 Jun;36(3):271-290. doi: 10.1007/s10585-019-09969-y. Epub 2019 May 8. PubMed PMID: 31069565.

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 NF $\kappa$ B (C-NF $\kappa$ B) pathway is known to play a crucial role in tumor inflammation. We therefore, studied the expression of canonical NF $\kappa$ B proteins and their prognostic relevance in UM. Our study evaluated the expression of C-NF $\kappa$ B proteins (p65, p50, and c-Rel) by using immunohistochemistry on sections from 75 formalin-fixed UM. Activation of the NF $\kappa$ B subunit was determined on fresh tumor specimens by measuring the DNA-binding activity in nuclei using an NF $\kappa$ B ELISA assay. Real-time PCR was performed on frozen material on 58 tumors. The presence of native C-NF $\kappa$ B 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-NF $\kappa$ B 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-NF $\kappa$ B proteins expressed are more often in UM with inflammation than those without inflammation. Activation of the canonical NF $\kappa$ B 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-NF $\kappa$ B proteins contributing to tumor aggressiveness.

DOI: 10.1007/s10585-019-09969-y  
PMID: 31069565

131: Singh P, Rajput R, Mehra NK, Vajpayee M, Sarin R. Cytokine gene polymorphisms among North Indians: Implications for genetic predisposition? *Infect Genet Evol.* 2019 Jun 4;73:450-459. doi: 10.1016/j.meegid.2019.06.004. [Epub ahead of print] PubMed PMID: 31173933.

Variations in the production and activity of cytokines influence the susceptibility and/or resistance to various infectious agents, autoimmune diseases, as well as the post-transplant engraftment/ rejection. Differences in the production of cytokines between individuals have been correlated to single nucleotide polymorphisms (SNPs) in the promoter, coding or non-coding regions of cytokine genes. The present study aimed at understanding distribution of cytokine gene variants among HIV seropositive subjects including HIV+TB+ subjects of Indian origin. Our findings indicate significant association of pro-inflammatory (IL2, IFN- $\gamma$ , TNF- $\alpha$ ) and anti-inflammatory cytokine gene variants (IL4, IL10) with the risk to acquire the HIV infection and development of AIDS related illness in Indian population. Since distribution of genetic polymorphisms varies significantly across different populations, different genotypes might exhibit different disease-modifying effects. An understanding of the immunogenetic factors or AIDS restriction genes is important not only for elucidating the mechanisms of disease pathogenesis but also for vaccine design and its application.

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DOI: 10.1016/j.meegid.2019.06.004  
PMID: 31173933

132: Singh V, Kabra SK. *Advances in Tuberculosis: Therapeutics.* Indian J Pediatr. 2019 Aug;86(8):700-702. doi: 10.1007/s12098-019-03005-3. Epub 2019 Jun 18. PubMed PMID: 31209764.

133: Singh Y, Mirdha BR, Guleria R, Kabra SK, Mohan A, Chaudhry R, Kumar L, Dwivedi SN, Agarwal SK. Novel dihydropteroate synthase gene mutation in *Pneumocystis jirovecii* among HIV-infected patients in India: Putative association with drug resistance and mortality. *J Glob Antimicrob Resist.* 2019 Jun;17:236-239. doi: 10.1016/j.jgar.2019.01.007. Epub 2019 Jan 15. PubMed PMID: 30658203.

**OBJECTIVES:** *Pneumocystis pneumonia* (PCP) remains a debilitating cause of death among HIV-infected patients. The combination trimethoprim/sulfamethoxazole (SXT) is the most effective anti-*Pneumocystis* treatment and prophylaxis. However, long-term use of this combination has raised alarms about the emergence of resistant organisms. This study was performed to investigate mutations in the dihydropteroate synthase (DHPS) gene and their clinical consequences in HIV-infected patients with PCP.

**METHODS:** A total of 76 clinically suspected cases of PCP among HIV-seropositive adult patients from March 2014 to March 2017 were included. Clinical samples (bronchoalveolar lavage fluid and sputum) were investigated for the detection of *Pneumocystis jirovecii* using both microscopy and nested PCR. DHPS genotyping and mutational analyses were performed and the data were correlated with clinical

characteristics.

**RESULTS:** Among the 76 enrolled HIV-positive patients, only 17 (22.4%) were positive for *P. jirovecii*. DHPS gene sequencing showed a novel nucleotide substitution at position 288 (Val96Ile) in three patients (3/12; 25.0%). Patients infected with the mutant *P. jirovecii* genotype had severe episodes of PCP, did not respond to SXT and had a fatal outcome ( $P=0.005$ ). All three patients had a CD4+ T-cell count  $<100$  cells/ $\mu$ L, and two also had co-infections.

**CONCLUSION:** This study suggests that the emergence of a mutant *P. jirovecii* genotype is probably associated with drug resistance and mortality. The data also suggest that DHPS mutational analyses should be performed in HIV-seropositive patients to avoid treatment failure and death due to PCP. However, the role of underlying disease severity and co-morbidities should not be underestimated.

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DOI: 10.1016/j.jgar.2019.01.007

PMID: 30658203

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135: Sirolia V, Jauhari P. Clinical Concepts in Infantile Onset Epilepsy. *Indian J Pediatr*. 2019 Aug;86(8):669-670. doi: 10.1007/s12098-019-02996-3. Epub 2019 Jun 3. PubMed PMID: 31161418.

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137: Surve A, Sharma MC, Pushker N, Bajaj MS, Meel R, Kashyap S. A study of changes in levator muscle in congenital ptosis. *Int Ophthalmol*. 2019 Jun;39(6):1231-1238. doi: 10.1007/s10792-018-0931-1. Epub 2018 Apr 28. PubMed PMID: 29705893.

**PURPOSE:** To study microscopic and ultrastructural changes of levator palpebrae superioris (LPS) muscle in congenital ptosis.

**METHODS:** In this prospective observational study, LPS muscle was studied in 77 eyelids with congenital ptosis; 35-simple congenital ptosis (SCP), 12-Marcus Gunn jaw winking phenomenon (MGJWP), and 30-blepharophimosis epicanthus inversus syndrome (BPES). Light microscopy, enzyme histochemistry, immunohistochemistry and electron microscopy were performed, and results were analyzed.

**RESULTS:** Muscle fibers were detected in 83.33% of MGJWP, 22.86% of SCP and 16.67% of BPES eyelids. Fibers were detected significantly more in individuals with moderate ptosis, LPS action  $>4$  mm, present eyelid crease and eyelid fold. Severe endomysial and perimysial fibrosis was seen significantly more in individuals with MGJWP. Fat infiltration and nuclei internalization were seen in all three groups. The absence of degenerating or regenerating fibers and inflammatory cells, normal staining pattern on immunohistochemistry and absence of accumulation of any abnormal substance were found in all three groups. Abnormal mitochondrial staining pattern was seen occasionally in three groups. On electron microscopy, muscle was detected in 1 SCP eyelid and 8 MGJWP eyelids out of which 4 had myofibrillary disruption. All other eyelids where muscle fibers were not detected had only fibrocollagenous tissue.

**CONCLUSION:** Fibrocollagenous tissue predominated in all the cases, and muscle fibers detected correlated inversely with the severity of ptosis. The absence of degenerating, regenerating fibers and inflammatory cells supported the theory of dysgenesis of muscle. However, internalization of nucleus seen in all the

subtypes is a feature favoring dystrophy.

DOI: 10.1007/s10792-018-0931-1

PMID: 29705893 [Indexed for MEDLINE]

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An interatrial communication is essential for adequate mixing and survival in cases of total anomalous pulmonary venous connection. We report a 5-month-old infant with total anomalous pulmonary venous connection (cardiac type) without an interatrial communication and a large ventricular septal defect.

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DOI: 10.1016/j.athoracsur.2018.10.031

PMID: 30476472

139: Taneja N, Gupta S, Gupta S. High precision freezing in cryotherapy using customized and pre-designed templates. *J Am Acad Dermatol*. 2019 Jun 21. pii: S0190-9622(19)31021-7. doi: 10.1016/j.jaad.2019.06.033. [Epub ahead of print] PubMed PMID: 31233854.

140: Tarik M, Ramakrishnan L, Sinha S, Sachdev HPS, Tandon N, Roy A, Bhargava SK. Association of birth outcomes and postnatal growth with adult leukocyte telomere length: Data from New Delhi Birth Cohort. *Matern Child Nutr*. 2019 Jun 19:e12857. doi: 10.1111/mcn.12857. [Epub ahead of print] PubMed PMID: 31216382.

Born small for gestational age due to undernutrition in utero and subsequent catch-up growth is associated with risk of developing chronic diseases in adulthood. Telomere length has been shown to be a predictor of these age-related diseases and may be a link between birth size, a surrogate for foetal undernutrition, and adult chronic diseases. We assessed the relationship of leukocyte telomere length in adult life with birth outcomes and serial change in body mass index (BMI) from birth to adulthood. Leukocyte relative telomere length (RTL) was measured by MMqPCR in 1,309 subjects from New Delhi Birth Cohort who participated in two phases of the study between 2006-2009 (Phase 6) and 2012-2015 (Phase 7) at a mean age of 39.08 ( $\pm 3.29$ ), and its association with birth outcomes and conditional BMI gain at 2, 11, and 29 years was assessed in a mixed regression model. We did not find any significant association of RTL with body size at birth including birthweight, birth length, and birth BMI. Gestational age was positively associated with RTL ( $P = .017$ , multivariate model:  $P = .039$ ). Conditional BMI gain at 2 and 11 years was not associated with RTL. BMI gain at 29 year was negatively associated with RTL in multivariate model ( $P = .015$ ). Born small for gestational age was not associated with RTL in adulthood. Leukocyte telomere attrition was observed in those born before 37 weeks of gestational age as well as in those who gained weight as adults, which may predispose to chronic diseases.

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DOI: 10.1111/mcn.12857

PMID: 31216382

141: Temkar S, Azad SV, Chawla R, Damodaran S, Garg G, Regani H, Nawazish S, Raj N, Venkatraman V. Ultra-widefield fundus fluorescein angiography in pediatric retinal vascular diseases. *Indian J Ophthalmol*. 2019 Jun;67(6):788-794. doi: 10.4103/ijo.IJO\_1688\_18. PubMed PMID: 31124488; PubMed Central PMCID: PMC6552605.

**Purpose:** To describe the utility of RetCam ultra-wide-field fundus fluorescein angiography in pediatric retinal vascular diseases.

**Methods:** A retrospective chart review was carried out in 43 eyes of 22 pediatric patients who were diagnosed or suspected to have a retinal vascular disease. Fluorescein angiography was carried out using the 130 degree lens of RetCam 3. Fluorescein angiography guided treatment (laser/cryotherapy) was carried out wherever required.

**Results:** Diseases studied included - coats disease, familial exudative vitreoretinopathy, retinopathy of prematurity, congenital retinal folds, double optic nerve head, persistent fetal vasculature and incontinentia pigmenti. RetCam assisted fluorescein angiography was helpful in establishing a diagnosis in 4 patients (18%), in decision making regarding treatment in 18 patients (82%), in deciding need for retreatment in 5 patients (23%), helped in staging of disease in 5 patients (23%) and in detecting clinically subtle findings in 6 patients (27%).

**Conclusion:** RetCam assisted FFA is extremely useful to document peripheral retinal vascular pathologies in pediatric patients and helps to take crucial therapeutic and retreatment decisions.

DOI: 10.4103/ijo.IJO\_1688\_18

PMCID: PMC6552605

PMID: 31124488

142: Tewari N, Bansal K, Mathur VP. Dental Trauma in Children: A Quick Overview on Management. Indian J Pediatr. 2019 Jun 13. doi: 10.1007/s12098-019-02984-7. [Epub ahead of print] PubMed PMID: 31197645.

Traumatic dental injuries (TDI) or tooth trauma have a global prevalence of 10-15%. These are often the cause of first visit to emergency room. Prognosis of teeth after injury is dependent on type of TDI, emergency treatment and time elapsed till definitive care. The low level of awareness among general public and medical practitioners often leads to delay in seeking treatment which often leads to pain, severe symptoms and poor prognosis. Pediatricians can play a significant role in identification of TDI, health advise, emergency care and referral to dentists. This paper highlights the important features to be noted in children with history of TDI and the key steps which needs to be taken in these situations.

DOI: 10.1007/s12098-019-02984-7

PMID: 31197645

143: Tewari R, Chandra P, Agarwal R, Azad R. Posterior laser barrage in advancing retinopathy of prematurity: A prospective randomized study. Indian J Ophthalmol. 2019 Jun;67(6):866-870. doi: 10.4103/ijo.IJO\_1608\_18. PubMed PMID: 31124504; PubMed Central PMCID: PMC6552574.

**Purpose:** To compare the outcomes of conventional laser photocoagulation versus additional posterior barrage laser in advanced stage 3 retinopathy of prematurity (ROP).

**Methods:** A total of 20 infants with bilateral symmetric zone 2 stage 3 advancing ROP were treated with conventional laser treatment followed by randomization of one eye to receive additional posterior retinal laser treatment. Disc-fovea and inter-arcade distance was measured. The patients were followed up prospectively for 3 months. Structural and functional outcomes and safety profile were analyzed.

**Results:** 18/20 (90%) eyes in the study group and 19/20 (95%) eyes in the control group achieved regression of disease. Faster and complete regression was observed at 4 weeks after posterior laser compared to the control group (P = 0.024).

Disc-fovea and inter-arcade distance was comparable in both groups.

**Conclusion:** Additional posterior barrage laser is a safe technique that led to faster and more complete regression in eyes with advancing ROP. Final regression

profile was comparable in both treatment modalities.

DOI: 10.4103/ijo.IJO\_1608\_18  
PMCID: PMC6552574  
PMID: 31124504

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

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

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DOI: 10.1016/j.jcrs.2018.12.024  
PMID: 30876785

145: Tripathy S, Kumar R, Kakkar A, Kumar R, Sharma P, Shamim SA. Esthesioneuroblastoma on 68Ga DOTANOC PET/CT. *Clin Nucl Med.* 2019 Jun 1. doi: 10.1097/RLU.0000000000002644. [Epub ahead of print] PubMed PMID: 31162250.

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

DOI: 10.1097/RLU.0000000000002644  
PMID: 31162250

146: 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.

147: Wei J, Anjana RM, Goenka S, Lobelo F, Shivashankar R, Kadir MM, Tandon N, Mohan V, Narayan K MV, Prabhakaran D, Ali MK. Physical activity, sitting, and risk

factors of cardiovascular disease: a cross-sectional analysis of the CARRS study. *J Behav Med.* 2019 Jun;42(3):502-510. doi: 10.1007/s10865-018-9989-5. Epub 2018 Nov 16. PubMed PMID: 30446920.

We aimed to estimate the associations between substituting 30-min/day of walking or moderate-to-vigorous physical activity (MVPA) for 30 min/day of sitting and cardiovascular risk factors in a South Asian population free of cardiovascular disease. We collected information regarding sitting and physical activity from a representative sample of 6991 participants aged 20 years and above from New Delhi, India and Karachi, Pakistan enrolled in 2010-2011 in the Center for cArdio-metabolic Risk Reduction in South Asia study using the International Physical Activity Questionnaire (short form). We conducted isotemporal substitution analyses using multivariable linear regression models to examine the cross-sectional associations between substituting MVPA and walking for sitting with cardiovascular risk factors. Substituting 30 min/day of MVPA for 30 min/day of sitting was associated with 0.08 mmHg lower diastolic blood pressure ( $\beta = -0.08$  [-0.15, -0.0003]) and 0.13 mg/dl higher high-density lipoprotein cholesterol ( $\beta = 0.13$  [0.04, 0.22]). Substituting 30 min/day of walking for 30 min/day of sitting was associated with 0.08 kg/m<sup>2</sup> lower body mass index ( $\beta = -0.08$  [-0.15, -0.02]), and 0.25 cm lower waist circumference ( $\beta = -0.25$  [-0.39, -0.11]). In conclusion, substituting time engaged in more-active pursuits for time engaged in less-active pursuits was associated with modest but favorable cardiovascular risk factor improvements among South Asians.

DOI: 10.1007/s10865-018-9989-5  
PMID: 30446920

148: Zafar A, Singh S, Ahmad S, Khan S, Imran Siddiqi M, Naseem I. Interaction of C20-substituted derivative of pregnenolone acetate with copper (II) leads to ROS generation, DNA cleavage and apoptosis in cervical cancer cells: Therapeutic potential of copper chelation for cancer treatment. *Bioorg Chem.* 2019 Jun;87:276-290. doi: 10.1016/j.bioorg.2019.03.031. Epub 2019 Mar 19. PubMed PMID: 30908970.

Cervical cancer is a leading cause of cancer-related deaths among women in developing countries. Therefore, development of new chemotherapeutic agents is required. Unlike normal cells, cancer cells contain elevated copper levels which play an integral role in angiogenesis. Thus, targeting copper via copper-specific chelators in cancer cells can serve as effective anticancer strategy. In this work, a copper chelator pregnenolone acetate nucleus-based tetrazole derivative (ligand-L) was synthesized and characterized by elemental analysis, ESI-MS, <sup>1</sup>H NMR and <sup>13</sup>C NMR. DNA binding ability of ligand-L was studied using UV-Vis and fluorescence spectroscopy. Fluorescence spectroscopy studies reveal that quenching constant of ligand-L-DNA and ligand-L-Cu(II) were found to be  $7.4 \times 10^3$  M<sup>-1</sup> and  $8.8 \times 10^3$  M<sup>-1</sup>, respectively. In vitro toxicity of ligand-L was studied on human cervical cancer C33A cancer cells. Results showed that ligand-L exhibit significant cytotoxic activity against cervical cancer C33A cells with IC<sub>50</sub> value  $5.0 \pm 1.8 \mu\text{M}$ . Further, it was found that ligand-L cytotoxicity is due to redox cycling of copper to generate ROS which leads to DNA damage and apoptosis. In conclusion, this is the report where we synthesized pregnenolone acetate-based tetrazole derivative against C33A cells that targets cellular copper to induce pro-oxidant death in cancer cells. These findings will provide significant insights into the development of new chemical molecules with better copper chelating and pro-oxidant properties against cancer cells.

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DOI: 10.1016/j.bioorg.2019.03.031  
PMID: 30908970

149: Zheng D, Xu Y, You S, Hackett ML, Woodman RJ, Li Q, Woodward M, Loffler KA, Rodgers A, Drager LF, Lorenzi-Filho G, Wang X, Quan WW, Tripathi M, Mediano O, Ou

Q, Chen R, Liu Z, Zhang X, Luo Y, McArdle N, Mukherjee S, McEvoy RD, Anderson CS. Effects of continuous positive airway pressure on depression and anxiety symptoms in patients with obstructive sleep apnoea: results from the sleep apnoea cardiovascular Endpoint randomised trial and meta-analysis. *EClinicalMedicine*. 2019 Jun 13;11:89-96. doi: 10.1016/j.eclinm.2019.05.012. eCollection 2019 May-Jun. PubMed PMID: 31312807; PubMed Central PMCID: PMC6610775.

**Background:** Whether continuous positive airway pressure (CPAP) treatment can improve depression or anxiety symptoms in obstructive sleep apnoea (OSA) patients remains uncertain.

**Methods:** Secondary analysis of the Sleep Apnea Cardiovascular Endpoints (SAVE) trial, combined with a systematic review of randomised evidence. The SAVE secondary analyses involved 2410 patients with co-existing moderate-severe OSA and established cardiovascular disease randomly allocated to CPAP treatment plus usual care or usual care alone and followed up for 3.7 (SD 1.6) years. We evaluated the effect of CPAP treatment on depression and anxiety caseness (scores  $\geq 8$  on the Hospital Anxiety and Depression Scale depression and anxiety subscales [HADS-D and HADS-A]) for OSA patients.

**Findings:** CPAP treatment was associated with reduced odds of depression caseness (adjusted odds ratio [OR] 0.80, 95% confidence interval [CI] 0.65-0.98,  $P=0.031$ ) compared to usual care in the SAVE trial and the treatment effect was greater in those with pre-existing depression symptoms. A systematic review of 20 randomised trials including 4255 participants confirmed a benefit of CPAP in reducing depression symptoms in OSA patients: the overall effect (standardised mean difference) was - 0.18 (95% CI - 0.24 to - 0.12). No effect of CPAP treatment on anxiety caseness was found both in patients of the SAVE study (adjusted OR 0.98, 95% CI 0.78-1.24,  $P=0.89$ ) and the systematic review.

**Interpretation:** CPAP reduces depression symptoms in patients with co-existing OSA and CVD independently of improvements in sleepiness.

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PMID: 31312807