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List of publications of AIIMS, New Delhi
for the month of March, 2017
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1: Agarwala S, Gupta A, Bansal D, Vora T, Prasad M, Arora B, Kapoor G, Chinnaswamy G, Radhakrishnan V, Laskar S, Kaur T, Dhaliwal RS, Rath GK, Bakhshi S. Management of Hepatoblastoma: ICMR Consensus Document. *Indian J Pediatr.* 2017 Jun;84(6):456-464. doi: 10.1007/s12098-017-2301-9. Epub 2017 Mar 29. Review. PubMed PMID: 28353129.

Dramatic advancement has been made in the management of children with hepatoblastoma (HB) over the past 3 decades owing to the improvement in diagnostic imaging, new chemotherapeutic agents, better surgical care and availability of liver transplantation. These advances are the end results of contributions from 4 major study groups across the globe including International Society of Pediatric Oncology - Liver Tumor Strategy Group (SIOPEL), Children's Oncology Group (COG), German Pediatric Hematology Oncology Group (GPOH) and Japanese Pediatric Liver Tumor Study Group (JPLT). The current manuscript is written with the objective of developing a consensus guideline for practitioners at a National level. Based on literature and personal experience over last 3 decades, the Indian Council of Medical Research (ICMR) Expert group has made recommendations for management of children with HB in resource-challenged nations including India.

DOI: 10.1007/s12098-017-2301-9
PMID: 28353129

2: Ahmed A, Bhatnagar S, Khurana D, Joshi S, Thulkar S. Ultrasound-Guided Radiofrequency Treatment of Intercostal Nerves for the Prevention of Incidental Pain Arising Due to Rib Metastasis. *Am J Hosp Palliat Care.* 2017 Mar;34(2):115-124. doi: 10.1177/1049909115617933. Epub 2016 Jul 11. PubMed PMID: 26656033.

BACKGROUND: Breakthrough pain (BTP) arising due to rib metastasis is very distressing and often very difficult to manage by titration of traditional analgesics. This study is undertaken to determine the efficacy of radiofrequency (RF) treatment of intercostal nerves for the prevention of BTP.

METHODS: The RF treatment of the intercostal nerves was carried out in 25 patients with uncontrolled BTP arising out of the rib metastasis. The intensity and episode of BTP, background pain, opioid dose, functional status (Karnofky score), and quality of life (Short-Form Health Survey [SF-36]) were noted at baseline visit and subsequently after the RF treatment.

RESULTS: After the RF treatment, there was more than 50% decrease in both intensity and frequency of BTP in more than 50% of patients for 3 months, and there was more than 50% decrease in BTP opioid dose in more than 50% of patients throughout the study period. There was also significant improvement in background pain, functional status, and the quality of life after the RF. Interestingly, pain relief, lowering of opioid dose, and functional status improvement were found mostly in patients with mixed and neuropathic type of pain and in patients in whom the metastasis were confined to the ribs only.

CONCLUSION: RF of the intercostal nerves is effective in preventing and decreasing the severity of BTP arising due to rib metastasis in selected group of patients with mixed and neuropathic type of pain and with the metastasis involving the ribs only.

DOI: 10.1177/1049909115617933
PMID: 26656033 [Indexed for MEDLINE]

3: Akhter MZ, Rajeswari MR. Triplex forming oligonucleotides targeted to hmgal selectively inhibit its expression and induce apoptosis in human cervical cancer. *J Biomol Struct Dyn.* 2017 Mar;35(4):689-703. doi: 10.1080/07391102.2016.1160257. Epub 2016 Mar 21. PubMed PMID: 26923360.

High-mobility group A1 (HMGA1) is a non-histone chromosomal protein, which is known as 'architectural' transcription factor that facilitates the assembly of

'enhanceosome.' Because of its elevated expression in a number of human malignancies, with barely minimal levels in healthy adults, HMGA1 is considered as potential 'tumor marker.' Therefore, we looked at the inhibition of hmgal using anti-gene strategy, as an attractive therapeutic approach. This was achieved by two triplex forming oligonucleotides (TFOs), TFO1 and TFO2 targeted to the promoter of hmgal at positions, -284--304 and -2800--2826, respectively. The stability of two DNA triplexes was characterized using a variety of biophysical and thermodynamics techniques and was confirmed by gel retardation assay using γ -(32)P [ATP]. The efficacy of TFOs on HMGA1 expression was evaluated in HeLa cells using MTT assay, Flow cytometry, Western blot, and RT-PCR. Results revealed that DNA Triplex1 formed by TFO1 is more stable and stronger than the corresponding Triplex2. Although both TFOs downregulated hmgal expression at mRNA and protein levels and caused apoptotic cell death in HeLa cell line, TFO1 demonstrated a greater effect at low concentration which corroborates well with the stability data. Thus, TFO-mediated inhibition of hmgal expression can be a promising strategy for the development of novel anti-cancer therapeutics.

DOI: 10.1080/07391102.2016.1160257

PMID: 26923360 [Indexed for MEDLINE]

4: Anand S, Kondal D, Montez-Rath M, Zheng Y, Shivashankar R, Singh K, Gupta P, Gupta R, Ajay VS, Mohan V, Pradeepa R, Tandon N, Ali MK, Narayan KM, Chertow GM, Kandula N, Prabhakaran D, Kanaya AM. Prevalence of chronic kidney disease and risk factors for its progression: A cross-sectional comparison of Indians living in Indian versus U.S. cities. PLoS One. 2017 Mar 15;12(3):e0173554. doi: 10.1371/journal.pone.0173554. eCollection 2017. PubMed PMID: 28296920; PubMed Central PMCID: PMC5351850.

BACKGROUND: While data from the latter part of the twentieth century consistently showed that immigrants to high-income countries faced higher cardio-metabolic risk than their counterparts in low- and middle-income countries, urbanization and associated lifestyle changes may be changing these patterns, even for conditions considered to be advanced manifestations of cardio-metabolic disease (e.g., chronic kidney disease [CKD]).

METHODS AND FINDINGS: Using cross-sectional data from the Center for cardiometabolic Risk Reduction in South Asia (CARRS, n = 5294) and Mediators of Atherosclerosis in South Asians Living in America (MASALA, n = 748) studies, we investigated whether prevalence of CKD is similar among Indians living in Indian and U.S. cities. We compared crude, age-, waist-to-height ratio-, and diabetes-adjusted CKD prevalence difference. Among participants identified to have CKD, we compared management of risk factors for its progression. Overall age-adjusted prevalence of CKD was similar in MASALA (14.0% [95% CI 11.8-16.3]) compared with CARRS (10.8% [95% CI 10.0-11.6]). Among men the prevalence difference was low (prevalence difference 1.8 [95% CI -1.6,5.3]) and remained low after adjustment for age, waist-to-height ratio, and diabetes status (-0.4 [-3.2,2.5]). Adjusted prevalence difference was higher among women (prevalence difference 8.9 [4.8,12.9]), but driven entirely by a higher prevalence of albuminuria among women in MASALA. Severity of CKD--i.e., degree of albuminuria and proportion of participants with reduced glomerular filtration fraction--was higher in CARRS for both men and women. Fewer participants with CKD in CARRS were effectively treated. 4% of CARRS versus 51% of MASALA participants with CKD had Alc < 7%; and 7% of CARRS versus 59% of MASALA participants blood pressure < 140/90 mmHg. Our analysis applies only to urban populations. Demographic--particularly educational attainment--differences among participants in the two studies are a potential source of bias.

CONCLUSIONS: Prevalence of CKD among Indians living in Indian and U.S. cities is similar. Persons with CKD living in Indian cities face higher likelihood of experiencing end-stage renal disease since they have more severe kidney disease and little evidence of risk factor management.

DOI: 10.1371/journal.pone.0173554

PMCID: PMC5351850

PMID: 28296920

5: Anjum R, Roy A, Farooque K, Sharma V. An Isolated Pure Dislocation of Fifth Carpometacarpal Joint: Case Report and Review of Literature. *J Orthop Case Rep.* 2017 Mar-Apr;7(2):14-16. doi: 10.13107/jocr.2250-0685.728. PubMed PMID: 28819593; PubMed Central PMCID: PMC5553826.

INTRODUCTION: Isolated pure dislocation of the fifth carpometacarpal (CMC) joint is a very rare injury and classified depending on displacement of the metacarpal base. This rare injury is often difficult to recognize and is liable to be overlooked. The purpose of this case report is to present a patient with an isolated dislocation of the fifth CMC joint that was satisfactorily treated with closed reduction and ulnar gutter pop slab.

CASE REPORT: A 21-year-old male presented with severe pain on the right carpus following a fall with injury to right hand. There was a mild swelling at fifth CMC joint region and a bony prominence was felt dorsally, little finger presented an abduction deformity, and there was apparent shortening of the fifth ray. A diagnosis of isolated dislocation of fifth CMC dislocation was made based on radiographs. Immediate closed reduction was done in emergency room by applying longitudinal traction and direct pressure on metacarpal base dorsally, reduction was stable and confirmed by postreduction radiographs.

CONCLUSION: Isolated pure dislocation of the fifth CMC joint is very rare injury and is prone to be missed in emergency room and particular attention should be made to diagnose it in polytrauma patients.

DOI: 10.13107/jocr.2250-0685.728

PMCID: PMC5553826

PMID: 28819593

Conflict of interest statement: Conflict of Interest: Nil

6: Anoop S, Misra A, Mani K, Pandey RM, Gulati S, Bhatt SP, Mahajan H. Estimation of Liver Span Using MRI for Prediction of Type 2 Diabetes in Non-obese Asian Indians. *J Diabetes Sci Technol.* 2017 Mar;11(2):446-447. doi: 10.1177/1932296816664916. Epub 2016 Aug 20. PubMed PMID: 27543273; PubMed Central PMCID: PMC5478024.

7: Anthwal D, Gupta RK, Bhalla M, Bhatnagar S, Tyagi JS, Haldar S. Direct Detection of Rifampin and Isoniazid Resistance in Sputum Samples from Tuberculosis Patients by High-Resolution Melt Curve Analysis. *J Clin Microbiol.* 2017 Jun;55(6):1755-1766. doi: 10.1128/JCM.02104-16. Epub 2017 Mar 22. PubMed PMID: 28330890; PubMed Central PMCID: PMC5442532.

Drug-resistant tuberculosis (TB) is a major threat to TB control worldwide. Globally, only 40% of the 340,000 notified TB patients estimated to have multidrug-resistant-TB (MDR-TB) were detected in 2015. This study was carried out to evaluate the utility of high-resolution melt curve analysis (HRM) for the rapid and direct detection of MDR-TB in *Mycobacterium tuberculosis* in sputum samples. A reference plasmid library was first generated of the most frequently observed mutations in the resistance-determining regions of *rpoB*, *katG*, and an *inhA* promoter and used as positive controls in HRM. The assay was first validated in 25 MDR *M. tuberculosis* clinical isolates. The assay was evaluated on DNA isolated from 99 *M. tuberculosis* culture-positive sputum samples that included 84 smear-negative sputum samples, using DNA sequencing as gold standard. Mutants were discriminated from the wild type by comparing melting-curve patterns with those of control plasmids using HRM software. Rifampin (RIF) and isoniazid (INH) monoresistance were detected in 11 and 21 specimens, respectively, by HRM. Six samples were classified as MDR-TB by sequencing, one of which was missed by HRM. The HRM-RIF, INH-*katG*, and INH-*inhA* assays had 89% (95% confidence interval [CI], 52, 100%), 85% (95% CI, 62, 97%), and 100% (95% CI, 74, 100%) sensitivity, respectively, in smear-negative samples, while all assays had 100% sensitivity in smear-positive samples. All assays had 100% specificity. Concordance of 97% to 100% (κ value, 0.9 to 1) was noted between sequencing and HRM. Heteroresistance

was observed in 5 of 99 samples by sequencing. In conclusion, the HRM assay was a cost-effective (Indian rupee [INR]400/US\$6), rapid, and closed-tube method for the direct detection of MDR-TB in sputum, especially for direct smear-negative cases.

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DOI: 10.1128/JCM.02104-16

PMCID: PMC5442532 [Available on 2017-12-01]

PMID: 28330890

8: Arora R, Bharti V, Gaur P, Aggarwal S, Mittal M, Das SN. Operculina turpethum extract inhibits growth and proliferation by inhibiting NF- κ B, COX-2 and cyclin D1 and induces apoptosis by up regulating P53 in oral cancer cells. Arch Oral Biol. 2017 Aug;80:1-9. doi: 10.1016/j.archoralbio.2017.03.015. Epub 2017 Mar 20. PubMed PMID: 28351666.

OBJECTIVES: Herbal drugs are popularly emerging as complementary and alternative medicines in cancer patients because of their cost effectiveness and minimal side-effects. The extract of Operculina turpethum (OT) is known to have antipyretic, anti-inflammatory and purgative properties. Since it is popularly known have antiinflammatory activity, we investigated its anti-tumor activity on four oral squamous cell carcinoma cell lines (OSCC) namely, (SCC-4, KB, SCC-9 and SCC-25).

DESIGN: Antitumor activities of Operculina turpethum extract (OTE) was investigated by MTT and clonogenic assay, effect on cell cycle and apoptosis induction by Annexin-V/propidium iodide (PI) staining and flow cytometry and invasive potential of the tumor was determined by matrigel assay. The expression of various proteins involved in these mechanisms was analysed by western blotting.

RESULTS: OTE specifically inhibited the growth and colony formation of OSCC cells in a dose-dependent manner via inhibiting NF- κ B and its downstream target COX-2. It further arrested cell cycle at G0/G1 phase by inhibiting cyclin-D1 and induced early apoptosis by up-regulating P53 in OSCC cells. It also limits the invasion capacity of OSCC cells by up to 55-60%.

CONCLUSIONS: OTE shows antitumor activities in OSCC cells by inhibiting NF- κ B, COX-2 and cyclin D1 and upregulation of p53 expression. It may be developed as a safe and promising alternative chemopreventive/chemotherapeutic agent for oral cancer.

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DOI: 10.1016/j.archoralbio.2017.03.015

PMID: 28351666

9: Ballal S, Soundararajan R, Bal C. Re-establishment of normal radioactive iodine uptake reference range in the era of universal salt iodization in the Indian population. Indian J Med Res. 2017 Mar;145(3):358-364. doi: 10.4103/ijmr.IJMR_1158_14. PubMed PMID: 28749399.

BACKGROUND & OBJECTIVES: The reference radioactive iodine uptake (RAIU) values established in the 1970s in the era of widespread iodine deficiency were relatively high. Now, after four decades of successful Universal Salt Iodization (USI) programme in India, there is a need to re-establish these reference ranges. The present study was aimed to quantify the two-hour and 24-h RAIU values in iodine sufficient euthyroid individuals and validate the results in Graves' and Hashimoto's thyroiditis patients.

METHODS: In this prospective study conducted from April 2012 to September 2013, euthyroid volunteers who consented for the investigations were enrolled in the study. Treatment-naive Graves' disease and Hashimoto's thyroiditis patients were recruited from the outpatient clinic. The investigations included neck ultrasonography, thyroid function tests, thyroglobulin (Tg), anti-Tg and anti-thyroid peroxidase antibody and urinary iodine concentration.

RESULTS: Three different groups comprising 110 euthyroid volunteers, 38 Graves' and 17 Hashimoto's thyroiditis patients were enrolled in the study. The mean 2-h RAIU values for the euthyroid group, Hashimoto's thyroiditis and Graves' patients were 3.83 ± 2.77 , 4.22 ± 3.41 and 32.67 ± 15.93 per cent, and mean 24-h RAIU values were 12.75 ± 5.51 , 11.66 ± 9.55 and 61.85 ± 12.9 per cent, respectively. The mean thyroid volumes were 7.63 ± 2.72 , 7.81 ± 1.67 and 20.76 ± 12.56 ml for the euthyroid, Hashimoto's thyroiditis and Graves' disease groups and the mean spot urinary iodine concentrations were 9.0, 7.8 and 13.9 $\mu\text{g}/\text{dl}$ in the three groups, respectively. The new reference range (95% confidence interval) for two-hour was 1-7 per cent and 24-h was 7-18 per cent.

INTERPRETATION & CONCLUSIONS: Compared to the previous values, there was a considerable decrease in the RAIU values in euthyroid individuals. This was further corroborated with increase in the urinary iodine concentration and decrease in thyroid volume, attributed to successful USI programme. Further studies with a large sample from different parts of India need to be done to confirm these findings.

DOI: 10.4103/ijmr.IJMR_1158_14
PMID: 28749399

10: Banerjee J, BanerjeeDixit A, Srivastava A, Ramanujam B, Kakkar A, Sarkar C, Tripathi M, Chandra PS. Altered glutamatergic tone reveals two distinct resting state networks at the cellular level in hippocampal sclerosis. *Sci Rep.* 2017 Mar 23;7(1):319. doi: 10.1038/s41598-017-00358-7. PubMed PMID: 28336943; PubMed Central PMCID: PMC5428248.

Hippocampal sclerosis (HS), the most common subset of drug-resistant epilepsy (DRE), is associated with large-scale network abnormalities, even under resting state. We studied the excitatory postsynaptic currents (EPSCs) recorded from pyramidal neurons in resected samples under resting conditions from the hippocampal and anterior temporal lobe (ATL) obtained from patients with HS (n=14) undergoing resective surgery. We observed higher frequency and amplitude of spontaneous EPSCs in both the samples compared to non-seizure control samples. Application of tetrodotoxin (TTX) reduced the frequency of spontaneous EPSCs by $49.6 \pm 4.3\%$ and $61.8 \pm 6.2\%$ in the hippocampal and ATL samples, respectively. The magnitude of reduction caused by TTX with respect to non-seizure controls was significantly higher in the ATL samples than in the hippocampal samples. The magnitude of the change in the expression of the NR2A subunit of the NMDA receptors also varied in these two regions. Thus, the mechanism of hyperexcitability mediated by glutamatergic network reorganization in the hippocampal region is different from that in the ATL region of patients with HS, suggesting two independent resting-state networks at the cellular level. Taken together, these findings will improve the understanding of the broadly distributed resting-state networks in HS.

DOI: 10.1038/s41598-017-00358-7
PMCID: PMC5428248
PMID: 28336943

11: Bansal VK, Krishna A, Manek P, Kumar S, Prajapati O, Subramaniam R, Kumar A, Kumar A, Sagar R, Misra MC. A prospective randomized comparison of testicular functions, sexual functions and quality of life following laparoscopic totally extra-peritoneal (TEP) and trans-abdominal pre-peritoneal (TAPP) inguinal hernia repairs. *Surg Endosc.* 2017 Mar;31(3):1478-1486. doi: 10.1007/s00464-016-5142-0. Epub 2016 Aug 5. PubMed PMID: 27495344.

BACKGROUND: There is very scant literature on the impact of inguinal hernia mesh repair on testicular functions and sexual functions following open and laparoscopic repair. The present randomized study compares TAPP and TEP repairs in terms of testicular functions, sexual functions, quality of life and chronic groin pain.

METHODS: This study was conducted from April 2012 to October 2014. A total of 160 patients with uncomplicated groin hernia were randomized to either

trans-abdominal pre-peritoneal (TAPP) repair or totally extra-peritoneal (TEP) repair. Testicular functions were assessed by measuring testicular volume, testicular hormone levels preoperatively and at 3 months postoperatively. Sexual functions were assessed using BMSFI, and quality of life was assessed using WHO-QOL BREF scale preoperatively and at 3 and 6 months postoperatively. Chronic groin pain was evaluated using the VAS scale at 3 months, 6 months and at 1 year. RESULTS: The median duration of follow-up was 13 months (range 6-18 months). The mean preoperative pain scores (p value 0.35) as well as the chronic groin pain were similar between TEP and TAPP repairs at 3 months (p value 0.06) and 6 months (p value 0.86). The testicular resistive index and testicular volume did not show any significant change at follow-up of 3 months (p value 0.9) in the study population. No significant difference was observed in testicular resistive index and testicular volume when comparing TEP and TAPP groups at follow-up of 3 months (p value >0.05). There was a statistically significant improvement in the sexual drive score, erectile function and overall satisfaction over the follow-up period following laparoscopic inguinal hernia repair. However, sexual function improvement was similar in patients undergoing both TEP and TAPP repairs. All the domains of quality of life in the study population showed a significant improvement at a follow-up of 3 and 6 months. Subgroup analysis of all the domains of quality of life in both TAPP and TEP groups showed a similar increment as in the study population (p value <0.001); however, the mean scores of all the domains were comparable between the two subgroups (p value >0.05), preoperatively and 3 and 6 months follow-up. CONCLUSIONS: Laparoscopic groin hernia repair improves the testicular functions, sexual functions and quality of life, but TEP and TAPP repairs are comparable in terms of these long-term outcomes.

DOI: 10.1007/s00464-016-5142-0

PMID: 27495344 [Indexed for MEDLINE]

12: Batra SD, Nandi M, Sikri K, Tyagi JS. Genome-wide expression profiling establishes novel modulatory roles of vitamin C in THP-1 human monocytic cell line. BMC Genomics. 2017 Mar 23;18(1):252. doi: 10.1186/s12864-017-3635-4. PubMed PMID: 28335738; PubMed Central PMCID: PMC5364625.

BACKGROUND: Vitamin C (vit C) is an essential dietary nutrient, which is a potent antioxidant, a free radical scavenger and functions as a cofactor in many enzymatic reactions. Vit C is also considered to enhance the immune effector function of macrophages, which are regarded to be the first line of defence in response to any pathogen. The THP-1 cell line is widely used for studying macrophage functions and for analyzing host cell-pathogen interactions. RESULTS: We performed a genome-wide temporal gene expression and functional enrichment analysis of THP-1 cells treated with 100 μ M of vit C, a physiologically relevant concentration of the vitamin. Modulatory effects of vitamin C on THP-1 cells were revealed by differential expression of genes starting from 8 h onwards. The number of differentially expressed genes peaked at the earliest time-point i.e. 8 h followed by temporal decline till 96 h. Further, functional enrichment analysis based on statistically stringent criteria revealed a gamut of functional responses, namely, 'Regulation of gene expression', 'Signal transduction', 'Cell cycle', 'Immune system process', 'cAMP metabolic process', 'Cholesterol transport' and 'Ion homeostasis'. A comparative analysis of vit C-mediated modulation of gene expression data in THP-1 cells and human skin fibroblasts disclosed an overlap in certain functional processes such as 'Regulation of transcription', 'Cell cycle' and 'Extracellular matrix organization', and THP-1 specific responses, namely, 'Regulation of gene expression' and 'Ion homeostasis'. It was noteworthy that vit C modulated the 'Immune system' process throughout the time-course. CONCLUSIONS: This study reveals the genome-wide effects of physiological levels of vit C on THP-1 gene expression. The multitude of effects impacted by vit C in macrophages highlights its role in maintaining homeostasis of several cellular functions. This study provides a rational basis for the use of the Vitamin C-THP-1 cell model, to study biochemical and cellular responses to stresses, including infection with *M. tuberculosis* and other intracellular pathogens.

DOI: 10.1186/s12864-017-3635-4
PMCID: PMC5364625
PMID: 28335738

13: Benson R, Giridhar P, Venkatesulu BP, Mallick S, Raza MW, Rath GK. Re-irradiation for head and neck squamous cell carcinoma. *J Egypt Natl Canc Inst.* 2017 Mar;29(1):1-9. doi: 10.1016/j.jnci.2016.07.002. Epub 2016 Aug 29. Review. PubMed PMID: 27595192.

INTRODUCTION: Local recurrences after curative treatment have a potential for cure with salvage surgery or with re-irradiation.

METHODS: We reviewed the PubMed for articles published in English with key words squamous cell carcinoma, recurrent, re-irradiation, prognostic factors to find relevant articles describing prognostic factors, re-irradiation, and outcome for recurrent head and neck squamous cell carcinoma.

RESULTS: Various factors including age, performance status, time for recurrence, previous radiation dose volume and site of recurrence, previous use of chemotherapy are all prognostic factors in recurrent head and neck squamous cell carcinoma. Surgery is feasible in very select subgroup of patients and must be done when feasible. Re-irradiation with the aid of modern sophisticated technology is safe and confers durable and clinically meaningful survival benefit. Re-irradiation in head and neck recurrent squamous cell carcinoma may provide an expected median survival of 10-12months. Chemotherapy may be added along with radiation in the recurrent setting.

CONCLUSION: Treatment approaches may have to be personalized. Re surgery must be done in all patients in whom it is feasible. In patients in whom surgery is not feasible, re-irradiation must be evaluated as a therapeutic option especially in patients with limited volume recurrence.

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DOI: 10.1016/j.jnci.2016.07.002
PMID: 27595192 [Indexed for MEDLINE]

14: Bhadada SK, Arya AK, Mukhopadhyay S, Khadgawat R, Sukumar S, Lodha S, Singh DN, Sathya A, Singh P, Bhansali A. Primary hyperparathyroidism: insights from the Indian PHPT registry. *J Bone Miner Metab.* 2017 Mar 31. doi: 10.1007/s00774-017-0833-8. [Epub ahead of print] PubMed PMID: 28364324.

The presentation of primary hyperparathyroidism (PHPT) is variable throughout the world. The present study explored retrospective data submitted to the Indian PHPT registry (<http://www.indianphptregistry.com>) between July 2005 and June 2015 from 5 centres covering four different geographical regions. The clinical, biochemical, radiological and histopathological characteristics of PHPT patients across India were analysed for similarity and variability across the centres. A total of 464 subjects (137 men and 327 women) with histopathologically proven PHPT were analysed. The mean age was 41 ± 14 years with a female:male ratio of 2.4:1. The majority (95%) of patients were symptomatic. Common clinical manifestations among all the centres were weakness and fatigability (58.7%), bone pain (56%), renal stone disease (31%), pancreatitis (12.3%) and gallstone disease (11%). Mean serum calcium, parathyroid hormone and inorganic phosphorus levels were 11.9 ± 1.6 mg/dL, 752.4 ± 735.2 pg/mL and 2.8 ± 0.9 mg/dL, respectively. Sestamibi scanning had better sensitivity than ultrasonography in the localisation of parathyroid adenoma; however, when these two modalities were combined, 93% of the cases were correctly localised. Mean parathyroid adenoma weight was 5.6 ± 6.5 g (0.1-54 g). It was concluded that the majority of PHPT patients within India are still mainly symptomatic with >50% of patients presenting with bone disease and one-third with renal impairment. Compared to Western countries, Indian patients with PHPT are younger, biochemical abnormalities are more severe, and adenoma weight is higher. As our observation is largely derived from a tertiary care hospital (no routine screening of serum

calcium level), the results do not reflect racial differences in susceptibility to PHPT.

DOI: 10.1007/s00774-017-0833-8
PMID: 28364324

15: Bhari N, Mahajan R, Singh S, Sharma VK. Fixed drug eruption due to three antihistamines of a same chemical family: Cetirizine, levocetirizine, and hydroxyzine. *Dermatol Ther*. 2017 Mar;30(2). doi: 10.1111/dth.12412. Epub 2016 Sep 9. PubMed PMID: 27612321.

16: Bhari N, Pahadiya P, Arava S, Gupta S. Histoplasmosis mimicking non-Hodgkin lymphoma in a 40-year-old man with AIDS. *Int J STD AIDS*. 2017 Mar;28(3):312-314. doi: 10.1177/0956462416665942. Epub 2016 Aug 20. PubMed PMID: 27535728.

In patients with acquired immunodeficiency syndrome (AIDS), advanced immunosuppression is associated with atypical presentation of dermatological conditions. Our patient presented with a single crusted plaque over the lower lip and large tender cervical lymphadenopathy. The enzyme-linked immunosorbent assay for human immunodeficiency virus was found to be positive, and his CD4+ lymphocyte cell count was 4 cells/mm³. The presence of multiple histoplasma spores in the biopsies from the crusted plaque over lip and cervical lymph node helped in the confirmation of the diagnosis of histoplasmosis, and the patient showed significant improvement within two months of treatment with conventional injection amphotericin B initially followed by oral itraconazole.

DOI: 10.1177/0956462416665942
PMID: 27535728

17: Bhatia R, Gupta V, Khanna N. Oral involvement in disseminated superficial porokeratosis. *Indian J Dermatol Venereol Leprol*. 2017 Mar-Apr;83(2):244-246. doi: 10.4103/0378-6323.197386. PubMed PMID: 28071607.

18: Bhatia R, Mahajan R, Arava S, Singh S, Kandasamy D. A non-healing oral ulcer as a manifestation of systemic tuberculosis in an immunocompetent man. *Indian J Dermatol Venereol Leprol*. 2017 Mar-Apr;83(2):238-241. doi: 10.4103/0378-6323.197385. PubMed PMID: 28071606.

19: Bhattacharjee HK, Jalaludeen A, Bansal V, Krishna A, Kumar S, Subramaniam R, Ramachandran R, Misra M. Impact of standard-pressure and low-pressure pneumoperitoneum on shoulder pain following laparoscopic cholecystectomy: a randomised controlled trial. *Surg Endosc*. 2017 Mar;31(3):1287-1295. doi: 10.1007/s00464-016-5108-2. Epub 2016 Jul 21. PubMed PMID: 27444831.

BACKGROUND: The incidence of shoulder pain (SP) following laparoscopic cholecystectomy (LC) varies between 21 and 80 %. A few randomised controlled trials and meta-analysis have shown lesser SP in LC performed under low-pressure carbon dioxide pneumoperitoneum (LPCP) than under standard-pressure carbon dioxide pneumoperitoneum (SPCP). However, the possible compromise in adequate exposure and effective working space during LPCP has negatively influenced its uniform adoption for LC.

MATERIALS AND METHODS: All consecutive patients undergoing elective LC for gallstone disease who met the inclusion and exclusion criteria were enrolled. Forty patients were randomised to SPCP group (pressure of 14 mmHg) and 40 to LPCP group (pressure of 9-10 mmHg). Primary outcome measured was incidence of SP and its severity on visual analogue scale (VAS) at 4, 8, 24 h and 7 days after LC. Secondary outcomes measured were procedural time, technical difficulty, surgeons' satisfaction score on exposure and working space, intra-operative changes in heart rate and blood pressure, abdominal pain and analgesic requirement. Analyses were performed using Stata software.

RESULTS: There was no conversion to open surgery, bile duct injury or need to increase intra-abdominal pressure on either group. Twenty-three patients (57.5 %) in SPCP group and nine patients (22.5 %) in LPCP group had SP ($p = 0.001$). The severity of SP was significantly more in SPCP group at 8 and 24 h ($p = 0.009$ and 0.005 , respectively). Both the groups had similar procedural time, surgeons' satisfaction score, intra-operative changes in heart rate and blood pressure. CONCLUSION: The incidence and severity of SP following LC performed at LPCP are significantly less compared to that in SPCP. The safety, efficacy and surgeons' satisfaction appear to be comparable in both the groups. Hence, a routine practice of low-pressure carbon dioxide pneumoperitoneum may be recommended in selected group of patients undergoing laparoscopic cholecystectomy. CLINICAL TRIAL REGISTRATION NUMBER: CTRI/2016/02/006590.

DOI: 10.1007/s00464-016-5108-2
PMID: 27444831

20: Bhattacharjee S, Soni KD, Maitra S, Baidya DK. Levosimendan does not provide mortality benefit over dobutamine in adult patients with septic shock: A meta-analysis of randomized controlled trials. *J Clin Anesth.* 2017 Jun;39:67-72. doi: 10.1016/j.jclinane.2017.03.011. Epub 2017 Mar 30. PubMed PMID: 28494911.

OBJECTIVES: Despite of advancement in intensive care medicine, sepsis and septic shock carry a high mortality. Levosimendan, an inodilator, may be promising for septic shock patients with myocardial dysfunction; however, firm evidence is lacking. In this meta- analysis of randomized controlled trials, levosimendan has been compared with dobutamine in adult patients with sepsis and septic shock. DESIGN: Meta-analysis of randomized controlled trial. SETTING: Intensive-care unit. PARTICIPANTS: Adult septic shock patients. INTERVENTION: Adult septic shock patients received dobutamine or levosimendan. MAIN OUTCOME MEASURE: Mortality at longest follow-up, blood lactate level, cardiac index and noradrenaline requirement. RESULTS: Data from 7 randomized trials have been included in this meta-analysis. Levosimendan has no benefit in terms of mortality at longest follow up in comparison to dobutamine (Odds ratio 0.77, 95% CI 0.45, 132; $p=0.34$) and length of ICU stay (MD -4.7days, 95% CI -10.3, 0.9days, $p=0.10$). Patients received levosimendan had less blood lactate level (standardized mean difference -0.95; 95% CI -1.64, -0.27; $p=0.006$) and higher cardiac index (mean difference 0.44; 95% CI 0.17, 0.71; $p=0.001$). Noradrenaline requirements are similar in both the groups. CONCLUSION: There is no evidence that levosimendan is superior to dobutamine in adult patients with sepsis and septic shock. Further large randomized trials are necessary in this area.

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DOI: 10.1016/j.jclinane.2017.03.011
PMID: 28494911

21: Bherwani S, Ahirwar AK, Saumya AS, Sandhya AS, Prajapat B, Patel S, Jibhkate SB, Singh R, Ghotekar LH. The study of association of Vitamin B(12) deficiency in type 2 diabetes mellitus with and without diabetic nephropathy in North Indian Population. *Diabetes Metab Syndr.* 2017 Mar 6. pii: S1871-4021(16)30319-8. doi: 10.1016/j.dsx.2017.03.017. [Epub ahead of print] PubMed PMID: 28283394.

AIM: Diabetic Mellitus is the chronic metabolic disorder associated with various complications of heart, eyes, nerves, kidney etc. Diabetic Nephropathy is one of the leading causes of death in diabetic patient. We hypothesized that decrease Vitamin B12 levels is associated with Diabetic Nephropathy. Aim of our study is to study the serum Vitamin B12 levels in type 2 diabetes mellitus patients with and without nephropathy. METHODS: Our study population consist of 100 subjects out of which 50 cases of Diabetes Mellitus without Diabetic Nephropathy and 50 cases of Diabetes Mellitus

with Diabetic Nephropathy. We measured various routine lab parameters, apart from it, we measured spot urinary albumin to creatinine ratio to assess diabetic nephropathy and in special investigation we measured serum Vitamin B12 by chemiluminescence based immunoassay.

RESULT: Serum Vitamin B12 level in the group with nephropathy (181.6 ± 17.6 pg/dl) was significantly lower than in the group without nephropathy (286 ± 30.1 pg/dl) ($p=0.03$).

CONCLUSION: Our study points towards the decrease levels of serum Vitamin B12 levels associated with the complication of diabetic mellitus such as diabetic nephropathy. So treatment of Vitamin B12 deficiency by supplementing could prevent the development and progression of diabetic nephropathy and improves the overall management of diabetic patient.

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DOI: 10.1016/j.dsx.2017.03.017

PMID: 28283394

22: Bhethanabhotla S, Bakhshi S. Presence of risk factors does not affect outcome in early stage pediatric Hodgkin lymphoma treated with ABVD. *Ann Hematol.* 2017 Mar;96(3):521-522. doi: 10.1007/s00277-016-2880-y. Epub 2016 Nov 18. PubMed PMID: 27864603.

23: Bindal S, Sharma S, Singh TP, Gupta R. Evolving transpeptidase and hydrolytic variants of γ -glutamyl transpeptidase from *Bacillus licheniformis* by targeted mutations of conserved residue Arg109 and their biotechnological relevance. *J Biotechnol.* 2017 May 10;249:82-90. doi: 10.1016/j.jbiotec.2017.03.034. Epub 2017 Mar 30. PubMed PMID: 28365292.

γ -Glutamyl transpeptidase (GGT) catalyzes the transfer of the γ -glutamyl moiety from donor compounds such as l-glutamine (Gln) and glutathione (GSH) to an acceptor. During the biosynthesis of various γ -glutamyl-containing compounds using GGT enzyme, auto-transpeptidation reaction leads to the formation of unwanted byproducts. Therefore, in order to alter the auto-transpeptidase activity of the GGT enzyme, the binding affinity of Gln should be modified. Structural studies of the *Bacillus licheniformis* GGT (BlGT) complexed with the glutamic acid has shown that glutamic acid has strong ionic interactions through its α -carboxylic group with the guanidine moiety of Arg109. This interaction appears to be an important contributor for the binding affinity of Gln. In view of this, six mutants of *Bacillus licheniformis* ER15 GGT (BlGGT) viz. Arg109Lys, Arg109Ser, Arg109Met, Arg109Leu, Arg109Glu and Arg109Phe were prepared. As seen from the structure of BlGT, the mutation of Arg109 to Lys109 may reduce the affinity for Gln to some extent, whereas the other mutations are expected to lower the affinity much more. Biophysical characterization and functional studies revealed that Arg109Lys mutant has increased transpeptidation activity and catalytic efficiency than the other mutants. The Arg109Lys mutant showed high conversion rates for l-theanine synthesis as well. Moreover, the Arg109Met mutant showed increased hydrolytic activity as it completely altered the binding of Gln at the active site. Also, the salt stability of the enzyme was significantly improved on replacing Arg109 by Met109 which is required for hydrolytic applications of GGTs in food industries.

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DOI: 10.1016/j.jbiotec.2017.03.034

PMID: 28365292

24: Chandrasekaran A, Thukral A, Jeeva Sankar M, Agarwal R, Paul VK, Deorari AK. Nasal masks or binasal prongs for delivering continuous positive airway pressure in preterm neonates—a randomised trial. *Eur J Pediatr.* 2017 Mar;176(3):379-386. doi: 10.1007/s00431-017-2851-x. Epub 2017 Jan 13. PubMed PMID: 28091776.

The objective of this study was to compare the efficacy and safety of continuous positive airway pressure (CPAP) delivered using nasal masks with binasal prongs. We randomly allocated 72 neonates between 26 and 32 weeks gestation to receive bubble CPAP by either nasal mask (n = 37) or short binasal prongs (n = 35). Primary outcome was mean FiO₂ requirement at 6, 12 and 24 h of CPAP initiation and the area under curve (AUC) of FiO₂ against time during the first 24 h (FiO₂ AUC₀₋₂₄). Secondary outcomes were the incidence of CPAP failure and nasal trauma. FiO₂ requirement at 6, 12 and 24 h (mean (SD); 25 (5.8) vs. 27.9 (8); 23.8 (4.5) vs. 25.4 (6.8) and 22.6 (6.8) vs. 22.7 (3.3)) as well as FiO₂ AUC₀₋₂₄ (584.0 (117.8) vs. 610.6 (123.6)) were similar between the groups. There was no difference in the incidence of CPAP failure (14 vs. 20%; relative risk 0.67; 95% confidence interval 0.24-1.93). Incidence of severe nasal trauma was lower with the use of nasal masks (0 vs. 31%; p < .001). CONCLUSIONS: Nasal masks appear to be as efficacious as binasal prongs in providing CPAP. Masks are associated with lower risk of severe nasal trauma.

TRIAL REGISTRATION: CTRI2012/08/002868 What is Known? • Binasal prongs are better than single nasal and nasopharyngeal prongs for delivering continuous positive airway pressure (CPAP) in preventing need for re-intubation. • It is unclear if they are superior to newer generation nasal masks in preterm neonates requiring CPAP. What is New? • Oxygen requirement during the first 24 h of CPAP delivery is comparable with use of nasal masks and binasal prongs. • Use of nasal masks is, however, associated with significantly lower risk of severe grades of nasal injury.

DOI: 10.1007/s00431-017-2851-x

PMID: 28091776 [Indexed for MEDLINE]

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Molecular genetic testing for fragile X (FX) is complicated due to the large variation in the size of CGG expansion. The aim of this study was to apply this new technique using AmpliX FMR1 PCR assay, which is considered a better diagnostic tool for detecting expanded alleles in Indian population. The primary objective was to identify the carrier status of females and to correlate the instability of premutation alleles in females with the repeat sizes. 24 children with FX based on rapid PCR and 29 female relatives of these patients were included. Out of the 29 females screened, those whose child (or children) was affected by FX, were all premutation carriers confirming their role in transmission. The smallest PM allele that expanded into FM in the next generation was 78 repeats and the smallest PM allele detected was 63 repeats, and when transmitted from mother to offspring remained in the premutation range. In 4 families, the repeat size of the allele reduced from PM to normal repeat numbers in their daughters and in 1 case to borderline PM range. Thus, apart from the reduced turnaround time, this PCR based assay offers advantage by its sensitivity to detect CGG repeats in the intermediate region and lower range of premutation alleles. It also provides added information of AGG interruptions, which may have an impact on the counseling of women with intermediate and PM alleles.

DOI: 10.1177/0883073816683075

PMID: 28193118

27: Chowdhury T, Garg R, Sheshadri V, Venkatraghavan L, Bergese SD, Cappellani RB, Schaller B. Perioperative Factors Contributing the Post-Craniotomy Pain: A Synthesis of Concepts. *Front Med (Lausanne)*. 2017 Mar 1;4:23. doi:

10.3389/fmed.2017.00023. eCollection 2017. Review. PubMed PMID: 28299313; PubMed Central PMCID: PMC5331036.

The perioperative management of post-craniotomy pain is controversial. Although the concept of pain control in non-neurosurgical fields has grown substantially, the understanding of neurosurgical pain and its causative factors in such a population is inconclusive. In fact, the organ that is the center of pain and its related mechanisms receives little attention to alleviate distress during neurosurgical procedures. In contrast to the old belief that pain following intracranial surgery is minimal, recent data suggest the exact opposite. Despite the evolution of various multimodal analgesic techniques for optimal pain control, the concern of post-craniotomy pain remains. This paradox could be due to the lack of thorough understanding of different perioperative factors that can influence the incidence and intensity of pain in post-craniotomy population. Therefore, this review aims to give an in-depth insight into the various aspects of pain and its related factors in adult neurosurgical patients.

DOI: 10.3389/fmed.2017.00023

PMCID: PMC5331036

PMID: 28299313

28: Chua SK, Qureshi AM, Krishnan V, Pai DR, Kamal LB, Gunasegaran S, Afzal MZ, Ambawatta L, Gan JY, Kew PY, Winn T, Sood S. The impact factor of an open access journal does not contribute to an article's citations. *F1000Res*. 2017 Mar 2;6:208. doi: 10.12688/f1000research.10892.1. eCollection 2017. PubMed PMID: 28649365; PubMed Central PMCID: PMC5464220.

Background Citations of papers are positively influenced by the journal's impact factor (IF). For non-open access (non-OA) journals, this influence may be due to the fact that high-IF journals are more often purchased by libraries, and are therefore more often available to researchers, than low-IF journals. This positive influence has not, however, been shown specifically for papers published in open access (OA) journals, which are universally accessible, and do not need library purchase. It is therefore important to ascertain if the IF influences citations in OA journals too. Methods 203 randomized controlled trials (102 OA and 101 non-OA) published in January 2011 were included in the study. Five-year citations for papers published in OA journals were compared to those for non-OA journals. Source papers were derived from PubMed. Citations were retrieved from Web of Science, Scopus, and Google Scholar databases. The Thompson-Reuter's IF was used. Results OA journals were found to have significantly more citations overall compared to non-OA journals (median 15.5 vs 12, $p=0.039$). The IF did not correlate with citations for OA journals (Spearman's $\rho=0.187$, $p=0.60$). The increase in the citations with increasing IF was minimal for OA journals (beta coefficient = 3.346, 95% CI -0.464, 7.156, $p=0.084$). In contrast, the IF did show moderate correlation with citations for articles published in non-OA journals (Spearman's $\rho=0.514$, $p<0.001$). The increase in the number of citations was also significant (beta coefficient = 4.347, 95% CI 2.42, 6.274, $p<0.001$). Conclusion It is better to publish in an OA journal for more citations. It may not be worth paying high publishing fees for higher IF journals, because there is minimal gain in terms of increased number of citations. On the other hand, if one wishes to publish in a non-OA journal, it is better to choose one with a high IF.

DOI: 10.12688/f1000research.10892.1

PMCID: PMC5464220

PMID: 28649365

Conflict of interest statement: Competing interests: No competing interests were disclosed.

29: de Raaff CAL, Gorter-Stam MAW, de Vries N, Sinha AC, Jaap Bonjer H, Chung F, Coblijn UK, Dahan A, van den Helder RS, Hilgevoord AAJ, Hillman DR, Margaron MP, Mattar SG, Mulier JP, Ravesloot MJL, Reiber BMM, van Rijswijk AS, Singh PM, Steenhuis R, Tenhagen M, Vanderveken OM, Verbraecken J, White DP, van der Wielen

N, van Wagenveld BA. Perioperative management of obstructive sleep apnea in bariatric surgery: a consensus guideline. *Surg Obes Relat Dis*. 2017 Jul;13(7):1095-1109. doi: 10.1016/j.soard.2017.03.022. Epub 2017 Mar 30. PubMed PMID: 28666588.

BACKGROUND: The frequency of metabolic and bariatric surgery (MBS) is increasing worldwide, with over 500,000 cases performed every year. Obstructive sleep apnea (OSA) is present in 35%-94% of MBS patients. Nevertheless, consensus regarding the perioperative management of OSA in MBS patients is not established.

OBJECTIVES: To provide consensus based guidelines utilizing current literature and, when in the absence of supporting clinical data, expert opinion by organizing a consensus meeting of experts from relevant specialties.

SETTING: The meeting was held in Amsterdam, the Netherlands.

METHODS: A panel of 15 international experts identified 75 questions covering preoperative screening, treatment, postoperative monitoring, anesthetic care and follow-up. Six researchers reviewed the literature systematically. During this meeting, the "Amsterdam Delphi Method" was utilized including controlled acquisition of feedback, aggregation of responses and iteration.

RESULTS: Recommendations or statements were provided for 58 questions. In the judgment of the experts, 17 questions provided no additional useful information and it was agreed to exclude them. With the exception of 3 recommendations (64%, 66%, and 66% respectively), consensus (>70%) was reached for 55 statements and recommendations. Several highlights: polysomnography is the gold standard for diagnosing OSA; continuous positive airway pressure is recommended for all patients with moderate and severe OSA; OSA patients should be continuously monitored with pulse oximetry in the early postoperative period; perioperative usage of sedatives and opioids should be minimized.

CONCLUSION: This first international expert meeting provided 58 statements and recommendations for a clinical consensus guideline regarding the perioperative management of OSA patients undergoing MBS.

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DOI: 10.1016/j.soard.2017.03.022
PMID: 28666588

30: Deshpande S, Singh N. Influence of Cubosome Surface Architecture on Its Cellular Uptake Mechanism. *Langmuir*. 2017 Apr 11;33(14):3509-3516. doi: 10.1021/acs.langmuir.6b04423. Epub 2017 Mar 29. PubMed PMID: 28325047.

Interaction of nanoparticles with biological systems is a key factor influencing their efficacy as a drug delivery vehicle. The inconsistency in defining the optimal design parameters across different nanoparticle types suggests that information gained from one model system need not apply to other systems. Therefore, selection of a versatile model system is critical for such studies. Cubosomes are one of the potential drug delivery vehicles due to their biocompatibility, stability, ability to carry hydrophobic, hydrophilic, and amphiphilic drugs, and ease of surface modification. Here we report the importance of surface architecture of cubosomes by comparing their cellular uptake mechanism with poly- ϵ -lysine (P ϵ L)-coated cubosomes. Uncoated cubosomes entered cells by an energy-independent, cholesterol-dependent mechanism, whereas P ϵ L-coated cubosomes relied on energy-dependent mechanisms to enter the endosomes. As endosomal entrapment was evaded by uncoated cubosomes, they can be preferably used for cytosolic delivery of therapeutic agents.

DOI: 10.1021/acs.langmuir.6b04423
PMID: 28325047

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Indian College of Physicians (ICP) Position Statement on Pharmacovigilance. J Assoc Physicians India. 2017 Mar;65(3):63-66. PubMed PMID: 28462545.

Pharmacovigilance is the art and science of detection, understanding and prevention of adverse drug reactions and not merely a critical analysis of prescriptions and errors. This field starts with reporting by clinicians of a suspected adverse drug reaction (ADR) to the pharmacologist followed by joint causality analysis and ends at the application of new information by a clinician for benefit of patients. There are a number of ways, which can be utilised for reporting adverse effects using pen and paper format to software applications for smart phones. Varied types of activities spreading from systematic reviews to the mechanistic evaluation of ADR can be performed under the umbrella of pharmacovigilance. It is of utmost importance for clinicians to understand how to identify, communicate and understand adverse effects of drugs with an aim to prevent harm to patients.

© Journal of the Association of Physicians of India 2011.

PMID: 28462545

32: Farooqui FA, Sharma SK, Kumar A, Soneja M, Mani K, Radhakrishnan R, Farooqui N. Endothelial function and carotid intima media thickness in obstructive sleep apnea without comorbidity. Sleep Breath. 2017 Mar;21(1):69-76. doi: 10.1007/s11325-016-1371-7. Epub 2016 Jun 25. PubMed PMID: 27344563.

PURPOSE: The objective of this study was to evaluate endothelial function and carotid intima media thickness (CIMT) in moderate to severe obstructive sleep apnea (OSA) without comorbidities.

METHODS: It is an observational case control study in which endothelial function was assessed using flow-mediated dilatation (FMD) and peripheral arterial tonometry (PAT), and carotid artery ultrasound was used to measure CIMT in study group subjects that included 20 normotensive, non-diabetic, treatment naïve, and moderate to severe OSA patients, and 20 normotensive, non-diabetic, and non-OSA subjects served as a control group. Study was conducted in Polysomnography Laboratory, Department of Internal Medicine, All India Institute of Medical Sciences (AIIMS) Hospital, New Delhi.

RESULTS: FMD was significantly lower in the moderate to severe OSA group compared to non-OSA group (mean±SD, 8.3±2.8 vs. 13.4±4.1 %; p=0.0001). Reactive hyperemia index (RHI) was also significantly lower in the OSA group (1.55±0.27 vs. 2.01±0.48, p=0.0007). CIMT was observed to be significantly higher in the OSA group compared to the non-OSA group (0.54±0.09 vs. 0.48±0.08 mm; p=0.049). In the OSA group, FMD, RHI, and CIMT did not show a significant correlation with OSA disease severity indices [apnea hypopnea index (AHI), oxygen desaturation index (ODI), and minimum O₂ saturation].

CONCLUSION: Endothelial function in macrovascular and microvascular circulation is significantly impaired in moderate to severe OSA patients without comorbidities. These patients also show evidence of subclinical atherosclerosis, in the form of increased CIMT.

DOI: 10.1007/s11325-016-1371-7

PMID: 27344563

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India has a rapidly growing population inflicted with cancer diagnosis. From an estimated incidence of 1.45 million cases in 2016, the cancer incidence is expected to reach 1.75 million cases in 2020. With the limitation of facilities for cancer treatment, the only effective way to tackle the rising and humongous

cancer burden is focusing on preventable cancer cases. Approximately, 70% of the Indian cancers (40% tobacco related, 20% infection related and 10% others) are caused by potentially modifiable and preventable risk factors. We review these factors with special emphasis on the Indian scenario. The results may help in designing preventive strategies for a wider application.

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DOI: 10.1016/j.jnci.2016.08.002
PMID: 27591115 [Indexed for MEDLINE]

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38: Giri AK, Bharadwaj S, Banerjee P, Chakraborty S, Parekatt V, Rajashekar D, Tomar A, Ravindran A, Basu A, Tandon N, Bharadwaj D. DNA methylation profiling reveals the presence of population-specific signatures correlating with phenotypic characteristics. *Mol Genet Genomics.* 2017 Jun;292(3):655-662. doi: 10.1007/s00438-017-1298-0. Epub 2017 Mar 7. PubMed PMID: 28271161.

Phenotypic characteristics are known to vary substantially among different ethnicities around the globe. These variations are mediated by number of stochastic events and cannot be attributed to genetic architecture alone. DNA methylation is a well-established mechanism that sculpts our epigenome influencing phenotypic variation including disease manifestation. Since DNA methylation is an important determinant for health issues of a population, it demands a thorough investigation of the natural differences in genome wide DNA methylation patterns across different ethnic groups. This study is based on comparative analyses of methylome from five different ethnicities with major focus on Indian subjects. The current study uses hierarchical clustering approaches, principal component analysis and locus specific differential methylation analysis on Illumina 450K methylation data to compare methylome of different ethnic subjects. Our data indicates that the variations in DNA methylation patterns of Indians are less among themselves compared to other global population. It empirically correlated with dietary, cultural and demographical divergences across different ethnic groups. Our work further suggests that Indians included in this study, despite their genetic similarity with the Caucasian population, are in close proximity with Japanese in terms of their methylation signatures.

DOI: 10.1007/s00438-017-1298-0
PMID: 28271161 [Indexed for MEDLINE]

39: Gogia A, Raina V, Kumar L, Sharma A, Sharma MCh, Mallick SR. Follicular lymphoma: an Institutional Analysis. Asian Pac J Cancer Prev. 2017 Mar 1;18(3):681-685. PubMed PMID: 28440975.

Background: Follicular lymphoma (FL) is second most common lymphoma in adult, constituted 20% of all lymphoma cases in the west. There is limited information is available on FL from India. Methods: The clinico-pathological profile, treatment outcome and prognostic factors for survival were assessed retrospectively in 181 patients of FL seen at our center over a period of 17 years (1996-2012). Results: There were 120 males and 61 females. The median age was 51 years (24-80 years). The common presenting features were lymphadenopathy 71%, fatigue 23% and fever 20%. Ann Arbor stage distribution was: stage I - 9%, stage II - 11%, stage III -22 % and stage IV - 58%. Extra nodal involvement and bulky disease were present in 22% and 19% patients respectively. Follicular Lymphoma International Prognostic Index (FLIPI) 1 score : Low -25%, Intermediate-45% and high risk in 30% of cases. One forty five patients (80%) received treatment at presentation or during follow-up. Chemotherapeutic regimen used were: CHOP-45 , CVP-51, chlorambucil and prednisolone -7 , BR (bendamustine and rituximab)-12, RCHOP- 14 RCVP - 7 and other regimen were used in 5 cases. The overall response (ORR) and complete remission (CR) rates were 70% and 35% respectively. Median overall survival (OS) and event free survival (EFS) was 5.5 years and 2.5 years respectively, with median follow up period of 3.0 years. Grade 3 histology, failure to attain CR, low serum albumin, and high risk FLIPI were significantly associated with lower event free survival. High risk FLIPI (HR 1.46, 95% CI 1.03-2.10, p=0.003) and failure to attain CR (HR 2.64, CI 1.10-4.30, p=0.001) were predictors of poor OS. Conclusions: FL represents 9 % of all lymphoma in adult. This is the largest data from single institute from India. Eighty percentage of patients presented in stage III/IV disease. High risk FLIPI and failure to attain CR were important prognostic variables for OS.

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DOI: 10.22034/APJCP.2017.18.3.681
PMID: 28440975

40: Gogna P, Gaba S, Mukhopadhyay R, Rohilla R, Singh A. Neglected epiphyseal injuries of the distal end of the radius with ulnar impaction: analysis of distal osteotomy of both bones using a dorsal midline approach. J Orthop Traumatol. 2017 Mar;18(1):31-36. doi: 10.1007/s10195-016-0423-x. Epub 2016 Jul 28. PubMed PMID: 27468849; PubMed Central PMCID: PMC5311000.

BACKGROUND: To evaluate results of a technique for treating neglected epiphyseal injuries of the distal radius with ulnar impaction. MATERIALS AND METHODS: This retrospective study involved six cases (four males; two females), all of whom sustained the primary injury during childhood (range 9-12 years of age). All presented with wrist deformity and ulnar-sided wrist pain. They were managed with osteotomy of the distal radius, osteotomy and shortening of the ulna, harvesting the bone grafts, and distal radioulnar joint (DRUJ) reduction performed simultaneously through a dorsal midline approach. Mean follow-up was 30 months (range 24-36). RESULTS: Deformity correction and pain relief was observed in all patients. Flexion arc increased from an average of 60° to 102.5°, supination from an average of 31.67° to 67.50°, and pronation from an average of 30.83° to 61.67°.

The mean preoperative DASH score was 87.5, which improved to 18.72 postoperatively.

CONCLUSION: Neglected epiphyseal injuries of the distal radius are difficult to manage and many variations are described for handling each of the associated problems. Our technique provides an option for managing this injury with an easy surgical approach, single incision, and cost effectiveness. All the four components of the surgery, which include osteotomy of the distal radius, osteotomy of the ulna, harvesting the bone grafts, and DRUJ reduction were done through a single incision and in a single sitting. Level of evidence IV.

DOI: 10.1007/s10195-016-0423-x

PMCID: PMC5311000

PMID: 27468849

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Urban Asian Indians generally have low serum 25(OH)D. Information on serum bioavailable 25(OH)D and the effect of prolonged sun-exposure in them is not known. We assessed serum 25(OH)D and bioavailable 25(OH)D in males with varying durations of sun-exposure in Delhi during August-September. Serum 25(OH)D, vitamin D-binding protein (DBP), bioavailable 25(OH)D, free 25(OH)D index, iPTH, ionized calcium and sun-index were assessed in outdoor, mixed outdoor-indoor and indoor workers (n = 88, 32 and 74, respectively). The mean sun-index (12.0 ± 6.25 , 4.3 ± 2.20 and 0.7 ± 0.62 , respectively; $P < 0.001$) was highest outdoors and lowest indoors. Serum 25(OH)D (29.0 ± 8.61 , 19.1 ± 5.73 and 10.9 ± 4.19 ng/ml, respectively; $P < 0.001$), bioavailable 25(OH)D and free 25(OH)D index were maximum in outdoor workers followed by mixed-exposure and indoor workers. Their mean serum DBP levels (241.2 ± 88.77 , 239.3 ± 83.40 and 216.6 ± 63.93 µg/ml, respectively; $P = 0.12$) were comparable. Mean serum iPTH was significantly lower in outdoor than indoor workers and showed inverse correlations with serum 25(OH)D, bioavailable 25(OH)D and free 25(OH)D index ($r = -0.401$, -0.269 and -0.236 , respectively; $P < 0.001$ in all). Daily dietary-calorie intake was higher and calcium lower in outdoor than indoor workers. On regression analysis, sun-exposure was the only significant variable, increasing serum 25(OH)D by 2.03 ng/ml per hour of sun-exposure (95 % confidence interval 1.77-2.28; $P < 0.001$). Outdoor workers with prolonged sun-exposure were vitamin D-sufficient, with higher serum bioavailable 25(OH)D than the indoor workers during summer. Use of serum DBP levels did not affect the interpretation of their vitamin D status.

DOI: 10.1007/s00774-016-0739-x

PMID: 26832389 [Indexed for MEDLINE]

42: Goudra B, Singh PM. More Questions Than Answers: Comparison of the Risk of Cardiopulmonary Adverse Events Between Propofol and Traditional Anesthesia for Gastrointestinal Endoscopy. *Clin Gastroenterol Hepatol.* 2017 Mar;15(3):468. doi: 10.1016/j.cgh.2016.09.137. Epub 2016 Sep 23. PubMed PMID: 27670384.

43: Goudra B, Nuzat A, Singh PM, Borle A, Carlin A, Gouda G. Association between Type of Sedation and the Adverse Events Associated with Gastrointestinal Endoscopy: An Analysis of 5 Years' Data from a Tertiary Center in the USA. *Clin Endosc.* 2017 Mar;50(2):161-169. doi: 10.5946/ce.2016.019. Epub 2016 Apr 29. PubMed PMID: 27126387; PubMed Central PMCID: PMC5398365.

BACKGROUND/AIMS: The landscape of sedation for gastrointestinal (GI) endoscopic procedures and the nature of the procedures themselves have changed over the last decade. In this study, an attempt is made to analyze the frequency and etiology

of all major adverse events associated with GI endoscopy.

METHODS: All adverse events extracted from the electronic database and local registry were analyzed. Although the data analysis was retrospective, the adverse events themselves were documented prospectively. These events were evaluated after subdivision into propofol-based anesthesia and intravenous conscious sedation groups.

RESULTS: Cardiorespiratory events, including cardiac arrest, were the most common adverse events during esophagogastroduodenoscopy, while bleeding was more frequent in patients undergoing colonoscopy. Pancreatitis was the most frequent adverse event in patients undergoing endoscopic retrograde cholangiopancreatography. The frequencies of most adverse events were significantly higher in patients anesthetized with propofol. Automatic regression modeling showed that the type of sedation, the American Society of Anesthesiologists physical status classification, and the procedure type were some of the predictors of immediate life-threatening complications.

CONCLUSIONS: Clearly, our regression modeling suggests a strong association between the type of sedation as well as various patient factors and the frequency of adverse events. The possible reasons for our results are the changing demographics, the worsening comorbidities of the patient population, and the increasing technical complexity of these procedures. Although extensive use of propofol has increased patient satisfaction and procedure acceptability, its use is also associated with more frequent adverse events.

DOI: 10.5946/ce.2016.019

PMCID: PMC5398365

PMID: 27126387

44: Guha S, Sethi R, Ray S, Bahl VK, Shanmugasundaram S, Kerkar P, Ramakrishnan S, Yadav R, Chaudhary G, Kapoor A, Mahajan A, Sinha AK, Mullasari A, Pradhan A, Banerjee AK, Singh BP, Balachander J, Pinto B, Manjunath CN, Makhale C, Roy D, Kahali D, Zachariah G, Wander GS, Kalita HC, Chopra HK, Jabir A, Tharakan J, Paul J, Venogopal K, Bakshi KB, Ganguly K, Goswami KC, Somasundaram M, Chhetri MK, Hiremath MS, Ravi MS, Das MK, Khanna NN, Jayagopal PB, Asokan PK, Deb PK, Mohanan PP, Chandra P, Girish CR, Rabindra Nath O, Gupta R, Raghu C, Dani S, Bansal S, Tyagi S, Routray S, Tewari S, Chandra S, Mishra SS, Datta S, Chatterjee SS, Kumar S, Mookerjee S, Victor SM, Mishra S, Alexander T, Samal UC, Trehan V.

Cardiological Society of India: Position statement for the management of ST elevation myocardial infarction in India. *Indian Heart J.* 2017 Apr;69 Suppl 1:S63-S97. doi: 10.1016/j.ihj.2017.03.006. Epub 2017 Mar 23. PubMed PMID: 28400042; PubMed Central PMCID: PMC5388060.

45: Gupta A, Khenduja P, Pandey RM, Sati HC, Sofi NY, Kapil U. Dietary Intake of Minerals, Vitamins, and Trace Elements Among Geriatric Population in India. *Biol Trace Elem Res.* 2017 Mar 20. doi: 10.1007/s12011-017-0972-8. [Epub ahead of print] PubMed PMID: 28321633.

The geriatric population is at a high risk of developing deficiencies of essential micronutrients such as minerals, vitamins, and trace elements and their related deficiency signs and symptoms. Scarce data is available on the dietary intake of essential micronutrients among geriatric subjects in India. Hence, to fill the gap in the existing knowledge, a community-based cross-sectional study was conducted during 2015-2016 in District Nainital, Uttarakhand State, India. A total of 255 geriatric subjects were enrolled from 30 clusters (villages) identified by using population proportionate to size sampling methodology. Data were collected on sociodemographic profile and dietary intake of essential micronutrients (24-h dietary recall, food frequency questionnaire) from all the geriatric subjects. A high percentage of geriatric subjects did not consume the recommended daily intake for essential micronutrients such as energy (78%), protein (78%), calcium (51%), thiamine (33%), riboflavin (64%), niacin (88%), vitamin C (42%), iron (72%), folic acid (72%), magnesium (48%), zinc (98%), copper (81%) and chromium (89%) adequately. Food groups rich in essential micronutrients such as pulses, green leafy vegetables, roots and tubers, other

vegetables, fruits, nonvegetarian food items, and milk and milk products were consumed irregularly by the subjects. The overall intake of energy and essential micronutrients was inadequate among the geriatric population in India, possibly due to poor quality and quantity of the diet consumed.

DOI: 10.1007/s12011-017-0972-8

PMID: 28321633

46: Gupta N, Agarwal R. Prophylactic sustained lung inflation followed by early CPAP vs. early CPAP at birth in extreme preterm neonates. *Acta Paediatr.* 2017 Mar;106(3):517. doi: 10.1111/apa.13692. Epub 2017 Jan 25. PubMed PMID: 28120525.

47: Gupta PK, Krishna M, Chullikana A, Desai S, Murugesan R, Dutta S, Sarkar U, Raju R, Dhar A, Parakh R, Jeyaseelan L, Viswanathan P, Vellotare PK, Seetharam RN, Thej C, Rengasamy M, Balasubramanian S, Majumdar AS. Administration of Adult Human Bone Marrow-Derived, Cultured, Pooled, Allogeneic Mesenchymal Stromal Cells in Critical Limb Ischemia Due to Buerger's Disease: Phase II Study Report Suggests Clinical Efficacy. *Stem Cells Transl Med.* 2017 Mar;6(3):689-699. doi: 10.5966/sctm.2016-0237. Epub 2016 Oct 5. PubMed PMID: 28297569; PubMed Central PMCID: PMC5442769.

Critical limb ischemia (CLI) due to Buerger's disease is a major unmet medical need with a high incidence of morbidity. This phase II, prospective, nonrandomized, open-label, multicentric, dose-ranging study was conducted to assess the efficacy and safety of i.m. injection of adult human bone marrow-derived, cultured, pooled, allogeneic mesenchymal stromal cells (BMMSC) in CLI due to Buerger's disease. Patients were allocated to three groups: 1 and 2 million cells/kg body weight (36 patients each) and standard of care (SOC) (18 patients). BMMSCs were administered as 40-60 injections in the calf muscle and locally, around the ulcer. Most patients were young (age range, 38-42 years) and ex-smokers, and all patients had at least one ulcer. Both the primary endpoints-reduction in rest pain (0.3 units per month [SE, 0.13]) and healing of ulcers (11% decrease in size per month [SE, 0.05])-were significantly better in the group receiving 2 million cells/kg body weight than in the SOC arm. Improvement in secondary endpoints, such as ankle brachial pressure index (0.03 [SE, 0.01] unit increase per month) and total walking distance (1.03 [SE, 0.02] times higher per month), were also significant in the group receiving 2 million cells/kg as compared with the SOC arm. Adverse events reported were remotely related or unrelated to BMMSCs. In conclusion, i.m. administration of BMMSC at a dose of 2 million cells/kg showed clinical benefit and may be the best regimen in patients with CLI due to Buerger's disease. However, further randomized controlled trials are required to confirm the most appropriate dose. *Stem Cells Translational Medicine* 2017;6:689-699.

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DOI: 10.5966/sctm.2016-0237

PMCID: PMC5442769

PMID: 28297569

48: Gupta RK, Saran RK, Srivastava AK, Jagetia A, Garg L, Sharma MC. T cell lymphoblastic lymphoma/leukemia within an adrenocorticotrophic hormone and thyroid stimulating hormone positive pituitary adenoma: A cytohistological correlation emphasizing importance of intra-operative squash smear. *Neuropathology.* 2017 Aug;37(4):358-364. doi: 10.1111/neup.12375. Epub 2017 Mar 13. PubMed PMID: 28295636.

We present a rare case of primary pituitary T cell lymphoma/leukemia (T-LBL) in association with adrenocorticotrophic hormone (ACTH) and thyroid stimulating hormone (TSH) expressing pituitary adenoma in a 55-year-old woman highlighting the importance of intra-operative squash smears examination. The patient

presented with complaints of headache, diminution of vision and recent onset altered sensorium. MRI revealed a mass lesion in the sellar-suprasellar region with non-visualization of pituitary gland separately, extending to involve adjacent structures diagnosed as invasive pituitary macroadenoma. Intra-operative tissue was sent for squash smear examination. The cytology showed a tumor comprising of sheets of immature lymphoid cells intermixed with clusters of pituitary acinar cells with many mitoses and tingible body macrophages. A diagnosis of presence of immature lymphoid cells within the pituitary was offered and differentials of infiltration by lymphoma cells from systemic disease versus primary central nervous lymphoma-like lymphoma arising in the pituitary adenoma were considered. Later paraffin section examination and immunohistochemistry corroborated with the squash findings and a final diagnosis of primary pituitary T cell lymphoma/leukemia in association with ACTH and TSH expressing pituitary adenoma was made. To date, only six cases of primary pituitary T cell lymphomas, including three T-LBL cases, have been reported. This is the seventh case and first one additionally describing cytohistological correlation and importance of intra-operative cytology.

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DOI: 10.1111/neup.12375

PMID: 28295636

49: Gupta SK, Kothari SS, Ramakrishnan S, Saxena A. Large ventricular septal defect and coexisting chronic constrictive pericarditis: "reversible Eisenmenger syndrome"-5 years after corrective surgery. *Catheter Cardiovasc Interv.* 2017 Mar 17. doi: 10.1002/ccd.27028. [Epub ahead of print] PubMed PMID: 28303664.

50: Gupta T, Sarkar C, Rajshekhar V, Chatterjee S, Shirsat N, Muzumdar D, Pungavkar S, Chinnaswamy G, Jalali R. Indian Society of Neuro-Oncology consensus guidelines for the contemporary management of medulloblastoma. *Neurol India.* 2017 Mar-Apr;65(2):315-332. doi: 10.4103/0028-3886.201841. PubMed PMID: 28290395.

INTRODUCTION: The high success rate in the management medulloblastoma achieved in the western world is not exactly mirrored in developing countries including India. Socio-demographic differences, health-care disparity, and lack in uniformity of care with resultant widespread variations in the clinical practice are some of the reasons that may partly explain this difference in outcomes. Patients with medulloblastoma require a multi-disciplinary team approach involving but not limited to neuro-radiology, neurosurgery; neuropathology, molecular biology, radiation oncology, pediatric medical oncology and rehabilitative services for optimizing outcomes.

METHODS: The Indian Society of Neuro-Oncology (ISNO) constituted an expert multi-disciplinary panel with adequate representation from all stakeholders to prepare national consensus guidelines for the contemporary management of medulloblastoma.

RESULTS: Minimum desirable, as well as preferable though optional recommendations (as appropriate), were developed and adopted for the pre-surgical work-up including neuroimaging; neurosurgical management including surgical principles, techniques, and complications; neuropathology reporting and molecular testing; contemporary risk-stratification in the molecular era; appropriate adjuvant therapy (radiotherapy and chemotherapy); and follow-up schedule in medulloblastoma.

CONCLUSIONS: The current document represents a broad consensus reached amongst various stakeholders within the neuro-oncology community involved in the contemporary curative-intent management of children with medulloblastoma. It provides both general as well as specific guidelines and recommendations to be adopted by physicians and health care providers across India to achieve uniformity of care, improve disease-related outcomes, and compare results between institutions within the country.

DOI: 10.4103/0028-3886.201841

PMID: 28290395

51: Gupta V, Pandey PM, Gupta RK, Mridha AR. Rotary ultrasonic drilling on bone: A novel technique to put an end to thermal injury to bone. Proc Inst Mech Eng H. 2017 Mar;231(3):189-196. doi: 10.1177/0954411916688500. Epub 2017 Jan 24. PubMed PMID: 28116985.

Bone drilling is common in orthopedic procedures and the heat produced during conventional experimental drilling often exceeds critical temperature of 47°C and induces thermal osteonecrosis. The osteonecrosis may be the reason for impaired healing, early loosening and implant failure. This study was undertaken to control the temperature rise by interrupted cutting and reduced friction effects at the interface of drill tool and the bone surface. In this work, rotary ultrasonic drilling technique with diamond abrasive particles coated on the hollow drill tool without any internal or external cooling assistance was used. Experiments were performed at room temperature on the mid-diaphysis sections of fresh pig bones, which were harvested immediately after sacrifice of the animal. Both rotary ultrasonic drilling on bone and conventional surgical drilling on bone were performed in a five set of experiments on each process using identical constant process parameters. The maximum temperature of each trial was recorded by K-type thermocouple device. Ethylenediaminetetraacetic acid decalcification was done for microscopic examination of bone. In this comparative procedure, rotary ultrasonic drilling on bone produced much lower temperature, that is, 40.2°C±0.4°C and 40.3°C±0.2°C as compared to that of conventional surgical drilling on bone, that is, 74.9°C±0.8°C and 74.9°C±0.6°C with respect to thermocouples fixed at first and second position, respectively. The conventional surgical drilling on bone specimens revealed gross tissue burn, microscopic evidence of thermal osteonecrosis and tissue injury in the form of cracks due to the generated force during drilling. But our novel technique showed no such features. Rotary ultrasonic drilling on bone technique is robust and superior to other methods for drilling as it induces no thermal osteonecrosis and does not damage the bone by generating undue forces during drilling.

DOI: 10.1177/0954411916688500

PMID: 28116985

52: Gupta V, Rawat R, Shalimar, Saraya A. Carvedilol versus propranolol effect on hepatic venous pressure gradient at 1 month in patients with index variceal bleed: RCT. Hepatol Int. 2017 Mar;11(2):181-187. doi: 10.1007/s12072-016-9765-y. Epub 2016 Sep 13. PubMed PMID: 27624505.

BACKGROUND AND AIMS: Endoscopic variceal ligation (EVL) plus beta blocker is the mainstay treatment after index bleed to prevent rebleed. Primary objective of this study was to compare EVL plus propranolol versus EVL plus carvedilol on reduction of HVPG after 1 month of therapy.

METHODS: Patients of cirrhosis presenting with index esophageal variceal bleed received standard treatment (Somatostatin therapy f/b EVL) following which HVPG was measured and patients were randomized to propranolol or carvedilol group if HVPG was >12 mmHg. Standard endotherapy protocol was continued in both groups. HVPG was again measured at 1 month of treatment.

RESULTS: Out of 129 patients of index esophageal variceal bleed, 59 patients were eligible and randomized into carvedilol (n = 30) and propranolol (n = 29). At 1 month of treatment, decrease in heart rate, mean arterial blood pressure (MAP) and HVPG was significant within each group (p = 0.001). Percentage decrease in MAP was significantly more in carvedilol group as compared to propranolol group (p = 0.04). Number of HVPG responders (HVPG decrease >20 % or below 12 mmHg) was significantly more in carvedilol group (22/29) as compared to propranolol group (14/28), p = 0.04.

CONCLUSION: Carvedilol is more effective in reducing portal pressure in patients with cirrhosis with esophageal bleed. Though a larger study is required to substantiate this, the results in this study are promising for carvedilol. Clinical trials online government registry (CTRI/2013/10/004119). Trial registration number CTRI/2013/10/004119.

DOI: 10.1007/s12072-016-9765-y
PMID: 27624505 [Indexed for MEDLINE]

53: Harivenkatesh N, Kumar L, Bakhshi S, Sharma A, Kabra M, Velpandian T, Gogia A, Shastri SS, Biswas NR, Gupta YK. Influence of MDR1 and CYP3A5 genetic polymorphisms on trough levels and therapeutic response of imatinib in newly diagnosed patients with chronic myeloid leukemia. *Pharmacol Res.* 2017 Jun;120:138-145. doi: 10.1016/j.phrs.2017.03.011. Epub 2017 Mar 19. PubMed PMID: 28330783.

Polymorphisms in genes coding for imatinib transporters and metabolizing enzymes may affect imatinib pharmacokinetics and clinical response. Aim of this study was to assess the influence of polymorphisms in MDR1 and CYP3A5 genes on imatinib trough levels, cytogenetic and molecular response in patients with CML. Newly diagnosed patients with chronic-phase CML started on imatinib therapy were enrolled and followed up prospectively for 24 months. The following single nucleotide polymorphisms were genotyped; C1236T, C3435T, G2677T/A in MDR1 gene and A6986G in CYP3A5 gene. Genotyping was done using PCR-RFLP method and validated by direct gene sequencing. Trough levels of imatinib were measured using LC-MS/MS. Cytogenetic response was assessed by conventional bone-marrow cytogenetics. Molecular response was assessed by qRT-PCR using international scale. A total of 173 patients were included, out of which 71 patients were imatinib responders, while 102 were non-responders. Marked inter-individual variability in trough levels of imatinib was seen. Patients with GG genotype for CYP3A5-A6986G ($P=0.016$) and TT genotype for MDR1-C3435T ($P=0.013$) polymorphisms had significantly higher trough levels of imatinib. Patients with AA genotype for CYP3A5-A6986G [RR=1.448, 95% CI (1.126, 1.860), $P=0.029$] and CC genotype for MDR1-C1236T [RR=1.397, 95% CI (1.066, 1.831), $P=0.06$] & MDR1-C3435T [RR=1.508, 95% CI (1.186, 1.917), $P=0.018$] polymorphisms were at high risk for failure of imatinib therapy. Patients with CGC haplotype for MDR1 polymorphisms had significantly lower imatinib trough levels and were at a higher risk of imatinib failure [RR=1.547, 95% CI (1.324, 1.808), $P<0.001$]. GG vs. non-GG genotype for CYP3A5-A6986G [adjusted OR: 0.246; 95% CI (0.116, 0.519); $P<0.001$] and TT vs. non-TT genotype for MDR1-C1236T [adjusted OR: 0.270; 95% CI (0.110, 0.659); $P=0.004$] & MDR1-C3435T [adjusted OR: 0.289; 95% CI (0.135, 0.615); $P=0.001$] polymorphisms were independent factors predicting imatinib response in multivariate analysis. To conclude, MDR1 and CYP3A5 genetic polymorphisms significantly influence plasma trough levels and therapeutic response of imatinib in patients with CML. Genotyping of these polymorphisms could be of value to individualize the therapy and optimize the clinical outcomes.

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DOI: 10.1016/j.phrs.2017.03.011
PMID: 28330783

54: Honnekeri BS, Goel A, Umate M, Shah N, De Sousa A. Social anxiety and Internet socialization in Indian undergraduate students: An exploratory study. *Asian J Psychiatr.* 2017 Jun;27:115-120. doi: 10.1016/j.ajp.2017.02.021. Epub 2017 Mar 2. PubMed PMID: 28558881.

BACKGROUND: Social Anxiety Disorder (SAD) is a globally prevalent, chronic, debilitating psychiatric disorder affecting youth. With comorbidities including major depression, substance abuse, lower educational and work attainment, and increased suicide risk, it has a significant public health burden. The objective of this study was to estimate the prevalence of SAD in urban Indian undergraduate students and to study their Facebook (FB) usage patterns.

METHODS: In this exploratory cross-sectional study, 316 undergraduate students were screened for social anxiety using validated instruments, Social Interaction Anxiety Scale (SIAS) and Social Phobia Scale (SPS), and divided into two groups based on scores obtained. The groups were then compared with regards to behaviors and attitudes toward Facebook, obtained from a self-report questionnaire.

RESULTS: SAD was estimated to be a significant, prevalent (7.8%) disorder in otherwise productive youth, and showed female preponderance. Higher specific social phobia scores were associated with the inability to reduce Facebook use, urges toward increasing use, spending more time thinking about Facebook, negative reactions to restricting use, and using it to forget one's problems.

CONCLUSIONS: SAD was estimated to have a prevalence of 7.8% in our study, and was associated with stronger FB usage attitudes and patterns. We recommend that the relationship between social anxiety and Internet use be explored further, to study the possibility of Internet-based screening and intervention strategies having wider reach and appeal in socially anxious individuals.

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DOI: 10.1016/j.ajp.2017.02.021

PMID: 28558881

55: Hooda B, Chouhan RS, Rath GP, Bithal PK, Suri A, Lamsal R. Effect of tranexamic acid on intraoperative blood loss and transfusion requirements in patients undergoing excision of intracranial meningioma. *J Clin Neurosci*. 2017 Jul;41:132-138. doi: 10.1016/j.jocn.2017.02.053. Epub 2017 Mar 7. PubMed PMID: 28283245.

Surgical excision of meningioma is often complicated by significant blood loss requiring blood transfusion with its attendant risks. Although tranexamic acid is used to reduce perioperative blood loss, its blood conservation effect is uncertain in neurosurgery. Sixty adults undergoing elective craniotomy for meningioma excision were randomized to receive either tranexamic acid or placebo, initiated prior to skin incision. Patients in the tranexamic acid group received intravenous bolus of 20mg/kg over 20min followed by an infusion of 1mg/kg/h till the conclusion of surgery. Intraoperative blood loss, transfusion requirements and estimation of surgical hemostasis using a 5-grade scale were noted. Postoperatively, the extent of tumor excision on CT scan and complications were observed. Demographics, tumor characteristics, amount of fluid infusion, and duration of surgery and anesthesia were comparable between the two groups. The amount of blood loss was significantly less in tranexamic acid group compared to placebo (830ml vs 1124ml; $p=0.03$). The transfusion requirement was less in tranexamic acid group ($p>0.05$). The patients in tranexamic acid group fared better on a 5-grade surgical hemostasis scale with more patients showing good hemostasis ($p=0.007$). There were no significant differences between the groups with regards to extent of tumor removal, perioperative complications, hospital stay or neurologic outcome. To conclude, administration of tranexamic acid significantly reduced blood loss in patients undergoing excision of meningioma. Fewer patients in the tranexamic acid group received blood transfusions. Surgical field hemostasis was better achieved in patients who received tranexamic acid.

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DOI: 10.1016/j.jocn.2017.02.053

PMID: 28283245

56: Jain S, Sharma N, Maharana PK, Agarwal T, Sinha R, Vajpayee RB. Comparative Evaluation of Use of 400- μ m and 350- μ m Microkeratome Head to Prepare Donor Tissue in Cases of Descemet Stripping Automated Endothelial Keratoplasty. *Eye Contact Lens*. 2017 Mar;43(2):130-134. doi: 10.1097/ICL.0000000000000243. PubMed PMID: 26808701.

PURPOSE: To compare the outcomes of 400- μ m microkeratome head with 350- μ m microkeratome head Descemet stripping automated endothelial keratoplasty (DSAEK) in a prospective comparative study.

METHODS: Twenty cases of pseudophakic bullous keratopathy were randomly allocated into two groups. Group 1 underwent slow, single-pass 400- μ m microkeratome head, whereas group 2 underwent the standard technique of DSAEK using a 350- μ m microkeratome head. The primary outcome measures were best-corrected visual

acuity (BCVA) at 6 months.

RESULTS: Groups were comparable in baseline characteristics. The mean central graft thickness (GT) at 6 months in group 1 was significantly thinner than group 2 (90.44±28.67 vs. 165.60±62.74 µm; P=0.003). The BCVA and contrast sensitivity were significantly better in group 1 than in group 2 (BCVA: 0.34±0.15 vs. 0.53±0.19 logMAR units, P=0.02; contrast sensitivity: 1.48±0.13 vs. 1.06±0.22, P=0.001). A significant correlation was found between both postoperative BCVA and contrast sensitivity, with the postoperative GT using Spearman rho correlation analysis (R=0.534, P=0.01 for BCVA and R=-0.522, P=0.02 for contrast sensitivity). The percentage endothelial cell loss was comparable between the 2 groups at the last follow-up (P=0.3). No major complications were observed during the study period.

CONCLUSIONS: The use of a 400-µm microkeratome head instead of 350-µm head can improve the visual outcomes in DSAEK without increasing the risk of complications. The thickness of the DSAEK graft can affect the visual acuity and contrast sensitivity.

DOI: 10.1097/ICL.0000000000000243

PMID: 26808701 [Indexed for MEDLINE]

57: Jakhetiya A, Shukla NK, Muduly D, Kale SS. Extraskelatal orbital mesenchymal chondrosarcoma: surgical approach and mini review. *BMJ Case Rep.* 2017 Mar 3;2017. pii: bcr2016218744. doi: 10.1136/bcr-2016-218744. Review. PubMed PMID: 28258179.

Extraskelatal orbital mesenchymal chondrosarcoma (MC) is an extremely rare and highly aggressive tumour. It has characteristic radiological features and pathognomic histological biphasic pattern. Radical resection with negative margins is the mainstay of treatment; role of adjuvant chemotherapy and radiotherapy is yet not well defined. We report a rare case of 18-year-old man who was diagnosed to have orbital MC. He presented with locally advanced disease with no vision in the affected eye. He underwent right orbital exenteration; a transcranial intradural approach was used to divide the optic nerve, and the temporalis muscle flap was utilised to fill the exenterated orbit. Though optic nerve involvement is rare in orbital MCs, a transcranial approach may be used effectively to avoid traction on optic chiasma and ensure margin-free resection in case of optic nerve involvement up to orbital apex. Unfortunately, prognosis remains dismal in MCs despite treatment.

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DOI: 10.1136/bcr-2016-218744

PMID: 28258179 [Indexed for MEDLINE]

58: Jhanjee S, Lal R, Mishra A, Yadav D. A Randomized Pilot Study of Brief Intervention versus Simple Advice for Women Tobacco Users in an Urban Community in India. *Indian J Psychol Med.* 2017 Mar-Apr;39(2):131-136. doi: 10.4103/0253-7176.203121. PubMed PMID: 28515547; PubMed Central PMCID: PMC5385739.

AIM: The study aimed to assess the efficacy of providing brief intervention (BI) for women tobacco users in a community-based setting.

METHODS: In this open-labeled randomized study, a representative sample of women (n = 100) from a community in East Delhi were screened using Alcohol, Smoking and Substance Involvement Screening Test. Eligible women were randomized to BI or simple advice (SA) arms. At baseline, they were assessed for tobacco use characteristics and severity of nicotine dependence using Fagerstrom's test for nicotine dependence. Intervention in the form of a single session of BI or SA to quit tobacco was provided at baseline. All participants were assessed at 1 week and 3 months following intervention. The principal outcome was self-reported abstinence from tobacco use at 3 months follow-up.

RESULTS: The mean age of the sample was 43 years (standard deviation = 13). Most women were married (80%), housewives (69%), illiterate (61%), socioeconomically

disadvantaged and were smokeless tobacco users (94%). The subjects in the BI group were twice more likely to stop tobacco use as compared to individuals in the SA group (odds ratio = 2.2, 95% confidence interval: 0.962-5.197, P = 0.06). CONCLUSION: The study results are suggestive of beneficial effect of BI. A larger study might provide more significant results.

DOI: 10.4103/0253-7176.203121

PMCID: PMC5385739

PMID: 28515547

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

59: Joshi R, Tripathi M, Gupta P, Gulati S, Gupta YK. Adverse effects & drug load of antiepileptic drugs in patients with epilepsy: Monotherapy versus polytherapy. Indian J Med Res. 2017 Mar;145(3):317-326. doi: 10.4103/ijmr.IJMR_710_15. PubMed PMID: 28749393.

BACKGROUND & OBJECTIVES: Although the need for a combination of antiepileptic drugs (AEDs) in the treatment of epilepsy is well justified, but an associated increase in adverse effects (AEs) lends a restriction to polytherapy. The aim of this study was to evaluate AEs and drug load (prescribed daily dose/defined daily doses) of AEDs in patients with epilepsy (PWE).

METHODS: Consecutive PWEs attending Epilepsy clinic in a tertiary care hospital in New Delhi, India, were enrolled in the study. Demographic variables, such as age, gender, diagnosis, age at onset of seizures, frequency of seizures, use of all AEDs and adverse event profile (AEP) score were noted. Routine laboratory tests including lipid profile, fasting blood glucose, haematological parameters and liver and kidney function tests were done.

RESULTS: A total of 697 consecutive patients were included in this study. Of them, 64.4 per cent were male; mean age was 29.6 ± 10.6 yr. Generalized seizures and focal seizures were recorded in $n=386$ (55.4%) and $n=311$ (44.6%), respectively. Monotherapy and polytherapy with two and greater than or equal to three AEDs were prescribed in 264 (37.9%), 243 (34.9%) and 190 (27.2%) patients, respectively. The average AED load, duration of treatment as well as AEP score were found to be significantly higher in combination of greater than or equal to three AEDs as compared to both monotherapy and combination of two AEDs, whereas no significant difference was observed between monotherapy and combination of two AEDs. Patients on monotherapy were in good control of seizures as compared to polytherapy. There was no significant change in biochemical parameters between the groups.

INTERPRETATION & CONCLUSIONS: Polytherapy with combination of greater than or equal to three AEDs was associated with higher AEs and lower seizure control as compared to both monotherapy and combination of two AEDs. AEs did not correlate with AED load, seizure type, gender and age of the patients but were associated with both numbers of AEDs as well as seizure frequency in PWE.

DOI: 10.4103/ijmr.IJMR_710_15

PMID: 28749393

60: Julka PK, Sharma DN, Madan R, Mallick S, Benson R, Kunhi P H, Gupta S, Rath GK. Patterns of care and survival among small cell lung cancer patients: Experience from a tertiary center in India. J Egypt Natl Canc Inst. 2017 Mar;29(1):47-51. doi: 10.1016/j.jnci.2016.10.001. Epub 2016 Nov 14. PubMed PMID: 27856126.

BACKGROUND/PURPOSE: Lung cancer is the commonest malignancy and the most common cause of cancer related mortality in males worldwide. Non-small cell lung cancer (NSCLC) is the commonest histology while small cell lung cancer (SCLC) contributes to only 15% of all cases of lung cancer. This report intended to present the patterns of care, survival outcomes and prognostic factors of SCLC treated in a tertiary care institute.

RESULTS: A total of 85 patients of SCLC were registered in radiotherapy unit I during the period January, 2005 to December, 2012. The median age of the cohort

was 56.5years (95% CI 34-72). The majority of the patients were male with a male:female ratio of 6.7:1. Sixty eight percent of the patients were smokers. Sixty percent patients presented with extensive stage disease. Radiotherapy (RT) was used in 76% of the patients while chemotherapy was used in 75% of the patients. Platinum Etoposide was the most common regimen which was used in 70% of the patients who received chemotherapy. The median progression free survival (PFS) of the entire cohort was 11.4months (95% CI 9.11-13.58months). Stage, performance status, and use of chemotherapy were found to be significant factors affecting survival outcome in patients with SCLC.

CONCLUSION: The pattern of care and survival outcomes in the present study parallels that of the various published retrospective reviews. Basic research and development of targeted agents may be the way forward in improving the outcome of patients with SCLC.

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DOI: 10.1016/j.jnci.2016.10.001
PMID: 27856126 [Indexed for MEDLINE]

61: Kar M, Singla M, Chandele A, Kabra SK, Lodha R, Medigeshi GR. Dengue Virus Entry and Replication Does Not Lead to Productive Infection in Platelets. *Open Forum Infect Dis*. 2017 Mar 23;4(2):ofx051. doi: 10.1093/ofid/ofx051. eCollection 2017 Spring. PubMed PMID: 28491890; PubMed Central PMCID: PMC5420081.

Thrombocytopenia is a characteristic feature during the acute phase of dengue infection and has been found to associate with vascular leakage in severe dengue. Although dengue antigens have been observed in platelets, there is no strong evidence to suggest a direct infection of platelets by dengue virus as a contributing factor for thrombocytopenia. We show that dengue virus can enter platelets but replicate viral ribonucleic acid to a minimal extent and, therefore, cannot produce infectious virus. Dengue antigen was undetectable in platelets isolated from dengue patients; however, we observed an increase in CD14(+)CD16(+) monocyte-platelet complexes, suggesting a mechanism for platelet clearance.

DOI: 10.1093/ofid/ofx051
PMCID: PMC5420081
PMID: 28491890

62: Kariya P, Tandon S, Singh S, Tewari N. Polymorphism in emergence of deciduous dentition: A cross-sectional study of Indian children. *J Investig Clin Dent*. 2017 Mar 27. doi: 10.1111/jicd.12266. [Epub ahead of print] PubMed PMID: 28349669.

AIM: The aim of the present study was to evaluate the timing and sequence of the eruption of deciduous teeth in Indian children.

METHOD: This cross-sectional study focused on children aged 5-36 months. One hospital was randomly selected from four geographic zones of the city. A total of 400 children from each hospital, fulfilling the inclusion criteria, constituted the sample. The examination was carried out by a single, trained examiner. The tooth was recorded as "present" or "absent" on the day of examination. The mean age of emergence was calculated using a probit model. Independent sample t-test was used to assess the statistical significance of differences in the mean age of tooth emergence.

RESULTS: The deciduous mandibular central incisor was the first tooth to erupt in the oral cavity (8.15±1.69 months). Girls showed delayed eruption compared to boys; however, no interarch variation was observed in the mean age of tooth eruption. There was also no difference in the sequence of eruption of deciduous teeth, as reported in other studies.

CONCLUSIONS: The present study establishes a chronological table for the eruption of deciduous teeth in Indian children. There was delayed eruption of deciduous teeth when compared to the reference ranges of Western populations.

DOI: 10.1111/jicd.12266

PMID: 28349669

63: Kavitha V, Mohan A, Madan K, Hadda V, Khilnani GC, Guleria R. Fractional exhaled nitric oxide is a useful adjunctive modality for monitoring bronchial asthma. *Lung India*. 2017 Mar-Apr;34(2):132-137. doi: 10.4103/0970-2113.201322. PubMed PMID: 28360460; PubMed Central PMCID: PMC5351354.

BACKGROUND AND OBJECTIVE: To evaluate the utility of fractional exhaled nitric oxide (FeNO) in monitoring asthma control.

MATERIALS AND METHODS: Steroid naïve nonsmoking asthmatics were recruited and followed for 6-8 weeks on standard treatment. Serial measurements of FeNO, peak expiratory flow rate (PEFR) variability, forced expiratory volume in 1 s (FEV1), bronchodilator reversibility (BDR), and asthma control test (ACT) score were measured at baseline and after 6-8 weeks of treatment.

RESULTS: One hundred and fifty-one patients were recruited over an 18-month period. These comprised 79 males (52.3%) with mean (standard deviation) age of 34.2 (11.6). Mean (SD) FeNO levels at baseline and after therapy were 45.4 (35.9) and 38.4 (23.7) ppb, respectively ($P = 0.01$). Baseline FeNO correlated strongly with FEV1 ($r = -0.78$, $P < 0.001$), ACT score ($r = -0.76$, $P < 0.001$), PEFR variability ($r = -0.74$, $P < 0.001$), and moderately with BDR ($r = 0.50$, $P < 0.001$). After treatment with inhaled steroids, the correlation remained strong with ACT score ($r = -0.68$, $P < 0.001$) but weakened with PEFR variability ($r = -0.34$, $P = 0.01$) and FEV1 ($r = -0.36$, $P = 0.01$).

CONCLUSIONS: FeNO may be useful as an adjunctive noninvasive modality to assess asthma control in both steroid naïve asthmatics and asthmatics on treatment. However, the suboptimal sensitivity and specificity may limit its utility as a point-of-care single monitoring tool.

DOI: 10.4103/0970-2113.201322

PMCID: PMC5351354

PMID: 28360460

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

64: Khan L, Kumar R, Thiruvengadam R, Parray HA, Makhdoomi MA, Kumar S, Aggarwal H, Mohata M, Hussain AW, Das R, Varadarajan R, Bhattacharya J, Vajpayee M, Murugavel KG, Solomon S, Sinha S, Luthra K. Cross-neutralizing anti-HIV-1 human single chain variable fragments(scFvs) against CD4 binding site and N332 glycan identified from a recombinant phage library. *Sci Rep*. 2017 Mar 23;7:45163. doi: 10.1038/srep45163. PubMed PMID: 28332627; PubMed Central PMCID: PMC5362912.

More than 50% of HIV-1 infection globally is caused by subtype_C viruses. Majority of the broadly neutralizing antibodies (bnAbs) targeting HIV-1 have been isolated from non-subtype_C infected donors. Mapping the epitope specificities of bnAbs provides useful information for vaccine design. Recombinant antibody technology enables generation of a large repertoire of monoclonals with diverse specificities. We constructed a phage recombinant single chain variable fragment (scFv) library with a diversity of 7.8×10^8 clones, using a novel strategy of pooling peripheral blood mononuclear cells (PBMCs) of six select HIV-1 chronically infected Indian donors whose plasma antibodies exhibited potent cross neutralization efficiency. The library was panned and screened by phage ELISA using trimeric recombinant proteins to identify viral envelope specific clones. Three scFv monoclonals D11, C11 and 1F6 selected from the library cross neutralized subtypes A, B and C viruses at concentrations ranging from $0.09 \mu\text{g/mL}$ to $100 \mu\text{g/mL}$. The D11 and 1F6 scFvs competed with mAbs b12 and VRC01 demonstrating CD4bs specificity, while C11 demonstrated N332 specificity. This is the first study to identify cross neutralizing scFv monoclonals with CD4bs and N332 glycan specificities from India. Cross neutralizing anti-HIV-1 human scFv monoclonals can be potential candidates for passive immunotherapy and for guiding

immunogen design.

DOI: 10.1038/srep45163

PMCID: PMC5362912

PMID: 28332627

65: Khandelwal D, Dutta D, Singla R, Surana V, Aggarwal S, Gupta Y, Kalra S, Khadgawat R, Tandon N. Perceptions about Training during Endocrinology Residency Programs in India over the Years: A Cross-sectional Study (PEER India Study). *Indian J Endocrinol Metab.* 2017 Mar-Apr;21(2):271-276. doi: 10.4103/ijem.IJEM_530_16. PubMed PMID: 28459024; PubMed Central PMCID: PMC5367229.

BACKGROUND: Residents' perception on quality of endocrinology training in India is not known. This study aimed to evaluate the perceptions about endocrinology residency programs in India among current trainees as compared to practicing endocrinologists.

METHODS: Trainees attending a preconference workshop at the annual conference of Endocrine Society of India (ESI) were given a questionnaire designed to evaluate their perceptions on their training. These evaluated the reasons for choosing endocrinology, their experiences during residency, and career plans. Practicing endocrinologists attending ESICON with at least 5-year experience were evaluated as controls.

RESULTS: Questionnaires from 63 endocrine trainees and 78 practicing endocrinologists were analyzed. Endocrinology is perceived to be the super-specialty with the best quality of life (QOL) but fair with regard to financial remuneration. Among current trainees, 61.89%, 31.74%, and 34.91% are satisfied with training in clinical endocrinology, laboratory endocrinology, and clinical/translational research, respectively. The corresponding figures for practicing endocrinologists are 71.78%, 25.63%, and 30.75%, respectively. Exposure to national endocrinology conferences during their endocrinology residency was adequate. However, exposure to international endocrinology conferences, research publications, project writing, and grant application are limited. Laboratory endocrinology is rated as the most neglected aspect during endocrine residency. Most of the trainees want to establish their own clinical practice in the long run. Very few trainees (17.46%) wish to join the medical education services.

CONCLUSION: There is a good perception of QOL in endocrinology in spite of average financial remuneration. There is dissatisfaction with the quality of training in laboratory endocrinology and clinical research. Very few endocrine trainees consider academics as a long-term career option in India.

DOI: 10.4103/ijem.IJEM_530_16

PMCID: PMC5367229

PMID: 28459024

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

66: Khetan A, Purushothaman R, Zullo M, Gupta R, Hejjaji V, Agarwal S, Mohan SK, Josephson R. Rationale and design of a cluster-randomized controlled trial to evaluate the effects of a community health worker-based program for cardiovascular risk factor control in India. *Am Heart J.* 2017 Mar;185:161-172. doi: 10.1016/j.ahj.2016.10.027. Epub 2016 Dec 21. PubMed PMID: 28267470.

BACKGROUND: The increasing burden of cardiovascular disease (CVD) in low- and middle-income countries is largely driven by the increasing prevalence of hypertension, diabetes, and tobacco use. We hypothesize that the utilization of community health workers (CHWs) to screen for and manage these 3 determinants of CVD in an integrated manner would be an effective approach to favorably affecting public health.

METHODS: We have designed and set up the infrastructure to implement a 2-year community-based cluster randomized controlled trial in an underserved region of West Bengal, India. Participants include around 1200 adults, aged between 35 and

70 years, with ≥ 1 cardiovascular risk factor. They are recruited through home-based screening into a total of 12 clusters, which are randomized to either a control or intervention arm before screening. After the screening, CHWs follow up with participants enrolled in the intervention arm for a period of 2 years through home visits. The control arm receives usual care in the community. The CHW arm follows a behavioral strategy focused on modifying the individual's lifestyle, increasing knowledge of CVD, promoting smoking cessation, increasing physician-seeking behavior, and promoting medication adherence. The main project office is based in Cleveland, OH, at University Hospitals/CWRU, and the local site office is located in Dalkhola, West Bengal, at a local nonprofit set up for the study. Institutional review board approval was obtained both in Cleveland as well as in India.

OUTCOME EVALUATION: The 2-year primary outcome of the study is the absolute reduction in systolic blood pressure among hypertensive participants, absolute reduction in fasting blood glucose among diabetic participants, and absolute reduction in average number of cigarettes smoked per day among smokers.

DISCUSSION: We believe that this study infrastructure serves as a useful model for international collaboration. It builds on unique local resources, attends to important domestic requirements, and will ultimately provide an evidence-based approach that will help manage the increasing burden of CVD worldwide.

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DOI: 10.1016/j.ahj.2016.10.027

PMID: 28267470 [Indexed for MEDLINE]

67: Kumar A, Kumar A, Singh PK, Mishra S, Garg K, Sharma BS. Letter to the Editor: Beta-blocker therapy. *J Neurosurg.* 2017 Mar;126(3):1026-1027. doi: 10.3171/2016.10.JNS162509. Epub 2017 Jan 20. PubMed PMID: 28106496.

68: Kumar S, Vatsa R, Bharti J, Roy KK, Sharma JB, Singh N, Meena J, Singhal S. Urinary fistula-A continuing problem with changing trends. *J Turk Ger Gynecol Assoc.* 2017 Mar 15;18(1):15-19. doi: 10.4274/jtgga.2016.0211. PubMed PMID: 28506945; PubMed Central PMCID: PMC5450205.

OBJECTIVE: Urinary fistula is a distressing complication after difficult vaginal deliveries, obstetric, and gynecologic surgeries. The present study describes a single center's experience in the management of urinary fistula at a tertiary care hospital. It was performed to analyze the etiology of genitourinary fistula, to assess the outcome after surgical repair, and to determine the changing trends in the etiology and management of urinary fistula.

MATERIAL AND METHODS: This retrospective study was conducted over 5 years in the department of obstetrics and gynecology, All India Institute of Medical Sciences, New Delhi. Twenty patients who underwent surgical repair of urinary fistula were included in the study and analyzed for their etiology, presentation, site, size, previous failed repair, approach of surgical repair, and outcome. The findings of the present study were compared with a previous study at our center to determine the changing trends of urinary fistula.

RESULTS: The mean age of the study population was 37.05 ± 8.08 years. The majority (65%) of the fistulae occurred following gynecologic surgeries, whereas 25% were due to obstructed labor, and 10% after cesarean section for other indications. The vaginal approach was used in all except one case of uterovesical fistula, which was repaired abdominally. The outcome was successful in 85% of cases. The success rate was similar in primary versus previous failed repair ($p=0.270$).

CONCLUSION: The most common cause of urinary fistula in the present study was gynecologic surgery. The vaginal approach can be used even in cases with previous failed repairs with a high success rate.

DOI: 10.4274/jtgga.2016.0211

PMCID: PMC5450205

PMID: 28506945

69: Kumar V, Kumawat D, Bhari A, Chandra P. TWENTY-FIVE-GAUGE PARS PLANA VITRECTOMY IN COMPLEX RETINAL DETACHMENTS ASSOCIATED WITH GIANT RETINAL TEAR. *Retina*. 2017 Mar 22. doi: 10.1097/IAE.0000000000001592. [Epub ahead of print] PubMed PMID: 28333880.

PURPOSE: To study the structural and functional outcomes of 25-gauge pars plana vitrectomy in giant retinal tear-associated retinal detachments.

METHODS: Seventeen eyes of 17 patients with giant retinal tear, who underwent 25-gauge pars plana vitrectomy over a period of 15 months at a tertiary eye care center by a single surgeon, were recruited in this retrospective interventional study.

RESULTS: Giant retinal tears were mostly traumatic (35.3%) or associated with myopia (35.3%) and occurred in young (mean age 25.7 years) males (94.1%). Most eyes had best-corrected visual acuity $\leq 20/1,200$ (in 82.3%), foveal detachment (in 88.2%), and proliferative vitreoretinopathy \leq Grade B (in 82.3%). The giant retinal tear extent was more than 180° in 29.4% and the fellow eye was involved in 35.2% of eyes. All eyes underwent 25-gauge pars plana vitrectomy with encircling band in 41.1%, perfluorocarbon liquid use in 82.3%, and endotamponade with sulphur hexafluoride (23.6%) or silicone oil (76.4%). At mean follow-up of 10.2 months, reattachment rate was 88.2%. Only 35.2% of eyes achieved final visual acuity $\geq 20/80$ with a cause of poor vision being cataract, secondary glaucoma, macular pucker, and corneal edema.

CONCLUSION: Twenty-five-gauge pars plana vitrectomy can achieve excellent attachment rates in eyes with giant retinal tear-associated retinal detachment. It can be as efficient as larger-gauge vitrectomy, at the same time retaining all advantages of smaller-gauge surgery.

DOI: 10.1097/IAE.0000000000001592

PMID: 28333880

70: Kumar V, Kumawat D. Multimodal imaging in a case of butterfly pattern dystrophy of retinal pigment epithelium. *Int Ophthalmol*. 2017 Mar 15. doi: 10.1007/s10792-017-0497-3. [Epub ahead of print] PubMed PMID: 28299497.

AIMS: To report multi-modal imaging findings in a case of butterfly pattern dystrophy of retinal pigment epithelium.

METHODS: A middle-aged female with butterfly pattern dystrophy, who presented with progressive loss of vision, was examined using coloured fundus photographs, short wave autofluorescence, swept source optical coherence tomography (SS-OCT), fundus fluorescein angiography and enface optical coherence tomography.

RESULTS: Multi-modal imaging was useful in the characterization of the various disease features. Autofluorescence pattern was opposite to that of fluorescein angiogram and SS-OCT showed disruption in the outer retinal layers. Enface OCT images depicted the pigment deposition prominently.

CONCLUSION: The features of butterfly pattern dystrophy on these modalities correlated well with the histopathological findings described in the literature. Enface imaging highlights the deposition of pigment/lipofuscin and has never been described in BPD.

DOI: 10.1007/s10792-017-0497-3

PMID: 28299497

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72: Kumar V, Nayak M, Ansari T, Malhotra R. Sudden peroneal nerve palsy in an osteoarthritic knee: a case report. *SICOT J*. 2017;3:22. doi: 10.1051/sicotj/2017005. Epub 2017 Mar 10. PubMed PMID: 28287389; PubMed Central PMCID: PMC5347368.

Peroneal nerve injuries have been reported in association with various causes around the knee such as traumatic varus injury, traumatic dislocation, upper tibial osteotomy, knee arthroscopy and total knee arthroplasty. Two instances of varus arthritic knee associated with a peroneal nerve palsy have been reported so far. One presented with gradual onset peroneal nerve palsy that recovered with time and the other with sudden onset peroneal nerve palsy that did not recover. We describe the case of a 63-year-old man who presented with a symptomatic varus arthritic knee and sudden onset peroneal nerve palsy with synovial cysts over the lateral aspect of the knee. We performed a total knee arthroplasty with decompression of the synovial cyst in the same patient. Three months following the surgery the patient was walking pain free with a completely recovered nerve palsy.

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DOI: 10.1051/sicotj/2017005

PMCID: PMC5347368

PMID: 28287389

73: Kumar Y, Jain V, Chauhan SS, Bharate V, Koli D, Kumar M. Influence of different forms and materials (zirconia or titanium) of abutments in periimplant soft-tissue healing using matrix metalloproteinase-8: A randomized pilot study. *J Prosthet Dent.* 2017 Mar 23. pii: S0022-3913(16)30693-X. doi: 10.1016/j.prosdent.2016.11.017. [Epub ahead of print] PubMed PMID: 28343676.

STATEMENT OF PROBLEM: It is unclear how pathogenic bacteria adhere to different implant materials and whether biomarker matrix metalloproteinase-8 (MMP-8) level provides a reliable method of evaluating the connective tissue status of periimplant tissues.

PURPOSE: The purpose of this pilot clinical study was to evaluate periimplant connective tissue response by assessing the MMP-8 levels in periimplant crevicular fluid around titanium and zirconia abutments.

MATERIAL AND METHODS: The study was designed as a prospective, within-subject comparison with left-right randomization. Twelve participants with partial edentulism were selected according to inclusion and exclusion criteria. Periimplant sulcal fluid sampling and pocket probing depths were assessed at 1, 3, and 12 months after placing the abutments. The MMP-8 protein level of the periimplant sulcal fluid was determined by MMP-8-specific sandwich enzyme-linked immunosorbent assay system. The independent t test or Wilcoxon test was used to compare MMP-8 levels and probing depth assessment between the zirconia and titanium groups at different time points (1, 3, and 12 months). Repeated measures ANOVA was used for within-group comparison of the MMP-8 levels at 3 time points ($\alpha=.05$).

RESULTS: At 1 and 3 months, the titanium abutments showed significantly higher MMP-8 levels and probing depths than the zirconia abutments ($P<.05$), but no significant differences were found at 12 months for either variable ($P>.05$).

CONCLUSIONS: This study suggests the presence of more remodeling and/or inflammatory phenomena around titanium implant abutments than around zirconia abutments of a different design during the early stages but not at 1 year.

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DOI: 10.1016/j.prosdent.2016.11.017

PMID: 28343676

74: Kusuma YS, Burman D, Kumari R, Lamkang AS, Babu BV. Impact of health education based intervention on community's awareness of dengue and its prevention in Delhi, India. *Glob Health Promot.* 2017 Mar 1:1757975916686912. doi: 10.1177/1757975916686912. [Epub ahead of print] PubMed PMID: 28349734.

Dengue is endemic in India. The capital, Delhi, continues to witness a higher number of cases due to urbanization-related factors. This study is intended to

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

DOI: 10.1177/1757975916686912

PMID: 28349734

75: Lokdarshi G, Pushker N, Kashyap S, Shameer A. Canaliculops: clinical examination. *Can J Ophthalmol*. 2017 Aug;52(4):e132-e134. doi: 10.1016/j.jcjo.2017.01.012. Epub 2017 Mar 18. PubMed PMID: 28774536.

76: Madan K, Shrestha P, Garg R, Hadda V, Mohan A, Guleria R. Bronchoscopic management of critical central airway obstruction by thyroid cancer: Combination airway stenting using tracheal and inverted-Y carinal self-expanding metallic stents. *Lung India*. 2017 Mar-Apr;34(2):202-205. doi: 10.4103/0970-2113.201297. PubMed PMID: 28360477; PubMed Central PMCID: PMC5351371.

Central airway obstruction (CAO) can result from various benign and malignant etiologies. Anaplastic thyroid cancer (ATC) is the most aggressive form of thyroid cancer. Rapid airway compromise is the main cause of death in ATC. We report a patient with ATC who presented with a large neck mass leading to CAO with long segment tracheal and right main bronchial compression and respiratory failure. Urgent Rigid Bronchoscopy was performed for airway stabilization and patient was managed with a combination airway stenting approach. A combination of self expanding, metallic, covered inverted Y and straight tracheal stents was used to stabilize the near complete airway structure. We herein highlight the role of therapeutic rigid bronchoscopy with airway stenting as an efficacious treatment modality for management of malignant CAO.

DOI: 10.4103/0970-2113.201297

PMCID: PMC5351371

PMID: 28360477

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

77: Madhusudhan KS, Sharma R, Kilambi R, Shylendran S, Shalimar, Sahni P, Gupta AK. 2D Shear Wave Elastography of Liver in Patients with Primary Extrahepatic Portal Vein Obstruction. *J Clin Exp Hepatol*. 2017 Mar;7(1):23-27. doi: 10.1016/j.jceh.2016.12.001. Epub 2016 Dec 29. PubMed PMID: 28348467; PubMed Central PMCID: PMC5357710.

AIMS: To evaluate liver stiffness (LS) in patients of primary extrahepatic portal vein obstruction (EHPVO) using 2D shear wave elastography (SWE) and compare it with healthy volunteers.

METHODS: Fifty patients (mean age: 22.4 years) of EHPVO and 25 healthy volunteers were included in the study. Liver function tests and viral markers were done in both groups and endoscopy in EHPVO group, followed by ultrasonography and SWE of liver. Liver elastography was done with patients/volunteers in supine position

through right intercostal space. The LS for right lobe of liver was recorded in kilopascals. Three such measurements were taken and the mean of both groups were compared. The variables were also correlated with mean LS using Pearson's correlation coefficient in EHPVO group.

RESULTS: There was no significant difference in the mean LS in patients of EHPVO (5.96 kPa) and healthy volunteers (5.47 kPa) (P = 0.093). There was no significant correlation between LS with duration of symptoms, hematemesis, esophageal varices, total bilirubin, serum alkaline phosphatase and aspartate aminotransferase levels in EHPVO group.

CONCLUSION: SWE of liver may be used as a simple additional tool in the diagnosis of patients of EHPVO who show LS values similar to normal liver.

DOI: 10.1016/j.jceh.2016.12.001

PMCID: PMC5357710 [Available on 2018-03-01]

PMID: 28348467

78: Maitra S, Baidya DK, Bhattacharjee S, Som A. [Perioperative gabapentin and pregabalin in cardiac surgery: a systematic review and meta-analysis]. *Rev Bras Anesthesiol.* 2017 May - Jun;67(3):294-304. doi: 10.1016/j.bjan.2016.07.005. Epub 2017 Mar 1. Portuguese. PubMed PMID: 28258733.

OBJECTIVES: Sternotomy for cardiac surgeries causes significant postoperative pain and when not properly managed may cause significant morbidity. As neuropathic pain is a significant component here, gabapentin and pregabalin may be effective in these patients and may reduce postoperative opioid consumption. The purpose of this systematic review was to find out efficacy of gabapentin and pregabalin in acute postoperative pain after cardiac surgery.

METHODS: Published prospective human randomized clinical trials, which compared preoperative and/or postoperative gabapentin/pregabalin with placebo or no treatment for postoperative pain management after cardiac surgery has been included in this review.

RESULTS: Four RCTs each for gabapentin and pregabalin have been included in this systematic review. Three gabapentin and two pregabalin studies reported decrease in opioid consumption in cardiac surgical patients while one gabapentin and two pregabalin studies did not. Three RCTs each for gabapentin and pregabalin reported lower pain scores both during activity and rest. The drugs are not associated with any significant complications.

CONCLUSION: Despite lower pain scores in the postoperative period, there is insufficient evidence to recommend routine use of gabapentin and pregabalin to reduce opioid consumption in the cardiac surgical patients.

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DOI: 10.1016/j.bjan.2016.07.005

PMID: 28258733

79: Malhotra R, Gautam D, Wahal N. Tuberculous periprosthetic infection precipitated by infliximab therapy. *BMJ Case Rep.* 2017 Mar 7;2017. pii: bcr2016218726. doi: 10.1136/bcr-2016-218726. PubMed PMID: 28270399.

Biological therapy with TNF- α inhibitors have been increasingly used in the treatment of inflammatory arthritis. Systemic tuberculosis infections are often known to occur following treatment with these biological agents. However, no case of periprosthetic tuberculous infection of the hip following this therapy has been reported. We report a case of a 45-year-old man who developed periprosthetic tuberculous infection soon after infliximab injection. We also discuss the need of pretreatment awareness, high index of suspicion, early diagnosis and management of such case.

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DOI: 10.1136/bcr-2016-218726

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To identify novel coding association signals and facilitate characterization of mechanisms influencing glycemic traits and type 2 diabetes risk, we analyzed 109,215 variants derived from exome array genotyping together with an additional 390,225 variants from exome sequence in up to 39,339 normoglycemic individuals from five ancestry groups. We identified a novel association between the coding variant (p.Pro50Thr) in AKT2 and fasting plasma insulin (FI), a gene in which rare fully penetrant mutations are causal for monogenic glycemic disorders. The low-frequency allele is associated with a 12% increase in FI levels. This variant is present at 1.1% frequency in Finns but virtually absent in individuals from other ancestries. Carriers of the FI-increasing allele had increased 2-h insulin values, decreased insulin sensitivity, and increased risk of type 2 diabetes (odds ratio 1.05). In cellular studies, the AKT2-Thr50 protein exhibited a partial loss of function. We extend the allelic spectrum for coding variants in

AKT2 associated with disorders of glucose homeostasis and demonstrate bidirectional effects of variants within the pleckstrin homology domain of AKT2.

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DOI: 10.2337/db16-1329

PMCID: PMC5482074 [Available on 2018-01-01]

PMID: 28341696

82: Meena R, Aggarwal A, Bhattacharya A, Gupta V, Dhandapani S, Chhabra R. Non traumatic vertebral lesions: incremental utility of PET-CT over MRI and FNAC in a suggested diagnostic algorithm. *Br J Neurosurg.* 2017 Mar 10:1-5. doi: 10.1080/02688697.2017.1301377. [Epub ahead of print] PubMed PMID: 28282998.

OBJECTIVE: To prospectively compare positron emission tomography-computed tomography (PET-CT) with conventional magnetic resonance imaging (MRI) and FNAC for diagnosis of non-traumatic vertebral lesions fracture in countries like India where tuberculosis is endemic.

METHODS: Fifty four patients with non-traumatic spontaneous vertebral lesions were prospectively studied. All patients underwent CEMRI focusing on the spinal lesions, whole-body PET-CT and FNAC. Results were then analysed and compared with final diagnosis obtained either by FNAC or clinical follow up.

RESULTS: Out of total 54 patients, FNAC from the spinal lesion could establish diagnosis in 36 patients (26 TB, 1 Fungal and 9 tumors). Of the remaining 18 patients, diagnosis could be established in 7 utilizing FNAC from other sites as dictated by PET-CT. In the remaining 11 patients, the diagnosis and management was decided on the concordance of MRI and PET-CT.

CONCLUSION: All three investigations have their own advantages and pitfalls and they complement each other in reaching the final diagnosis. MRI has a better pick up rate (than PET-CT) for inflammatory lesions. PET-CT on the other hand has better sensitivity for malignant vertebral disease. Diagnosis was established if FNAC was conclusive. In cases where FNAC was inconclusive, an additional 38.9% patients' diagnosis could be established by FNAC from other sites of involvement as dictated by PET-CT. This was an incremental utility of PET-CT. When even this fails, there were two possible scenarios-MRI and PET-CT in concordance with each other. In such a scenario, the combined report of MRI and PET-CT was relied upon. The last sub group (where MRI and PET-CT were discordant and FNAC was inconclusive) still remains achilles' heel. Wide bore biopsy may help in establishing diagnosis in such group.

DOI: 10.1080/02688697.2017.1301377

PMID: 28282998

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The management of hemodynamically normal patients with retained intra-pericardial foreign body remains a matter of conjecture. The available literature supports non-operative management of such innocuous foreign bodies. We report our experience of a hemodynamically normal patient with a retained intra-pericardial pellet from a firearm injury. He initially received successful non-operative management but developed fatal hemopericardium 21 days after injury. In this paper, we discussed the pitfalls in the management of such injuries in light of the available literature and summarized the clinical experience.

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DOI: 10.1016/j.cjtee.2016.05.006

PMCID: PMC5392712

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Auditory impulses perceived by the hair cells of the organ of Corti are relayed in the cochlear nucleus, the first relay station in the brainstem, by the cochlear nerve. The human foetus is well known to respond to sound during the last trimester of gestation. On the contrary, studies conducted in rat, cat and mouse have shown that these mammals have an immature auditory system at the time of birth. There are very few reports available regarding the morphological and functional maturation of the cochlear nucleus in human. Although the human cochlear nucleus neurons attain adult morphological characters by mid-gestation, there are hardly any studies discussing the functional maturation of the cochlear nucleus. Hence the present study was aimed at observing the morphological as well as functional maturation of the human foetal cochlear nuclei at various gestational ages. Morphological maturation was observed qualitatively while stereological estimation of the volume of well defined ventral cochlear nucleus (VCN) was calculated by the Cavalieri principle; neuronal count and density was estimated by dissector principle. The functional maturation was assessed by observing the expression of synaptophysin, a synaptic marker, at different gestational ages and by the presence of parvalbumin, a calcium binding functional neuronal marker by immunohistochemistry. Neurons showed coarse Nissl's substance and well developed cell processes and gradual increase in cell size by the 24th-30th gestational week. Synaptophysin labeling in the complete cochlear nucleus was observed at 20 weeks of gestation. Adult pattern of synaptophysin labeling was observed finally at 37 weeks of gestation. Earliest presence of parvalbumin expression was detected at 16 weeks of gestation and a distinct adult pattern was seen at 37 weeks of gestation. This study concluded that morphological and functional maturation of the human cochlear nuclei occurs simultaneously during mid-gestation which represents the critical period of development and continues up to term.

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DOI: 10.1016/j.jchemneu.2017.03.002
PMID: 28341180

86: Mondal D, Julka PK, Sharma DN, Jana M, Laviraj MA, Deo SV, Roy S, Guleria R, Rath GK. Accelerated hypofractionated adjuvant whole breast radiation with simultaneous integrated boost using volumetric modulated arc therapy for early breast cancer: A phase I/II dosimetric and clinical feasibility study from a tertiary cancer care centre of India. *J Egypt Natl Canc Inst*. 2017 Mar;29(1):39-45. doi: 10.1016/j.jnci.2017.01.005. PubMed PMID: 28343538.

BACKGROUND: Hypofractionation has become standard of care after Breast Conserving Therapy (BCT) in many European and few others western countries. Though still debatable, tumor cavity boost is routinely practised in our centre. Hypofractionation is not yet the current standard of practice in Asian countries. Employing hypofractionation and simultaneous integrated boost to lumpectomy cavity with conformal technique is not the current practice in this region. Hence the study was performed to see whether accelerated hypofractionation and simultaneous boost can be combined using volumetric modulated arc therapy (VMAT) in treating early breast cancer (EBC) patients.

PATIENTS AND METHODS: Female patients with EBC treated by whole breast radiation and boost were treated simultaneously to a dose of 40.5Gy and 48Gy in fifteen fractions over three weeks to entire breast and tumor cavity respectively with VMAT. Dosimetry including target coverage, OAR (organ at risk) sparing and acute radiation toxicity were evaluated.

RESULTS: Ten consecutive patients were treated. Planning target volume (PTV) coverage and OAR sparing were mostly satisfactory. Mean volume of PTVWB and PTVBoost were 786.18cm(3) and 228.9cm(3) respectively. Mean Dmean to PTVWB and PTVBOOST were 41.9Gy and 49.1Gy respectively. Dmax to PTVWB and PTVBOOST were 127.56% and 110.67% respectively. Ipsilateral lung mean dose and V20 were 13.92Gy and 21.53% respectively. V40 and V25 of heart were 0.17% and 2.25% respectively. All patients are disease free after a median follow up of two years. Most acute toxicities were Grade 1. Only two patients out of ten developed Grade 2 skin reaction during radiation. Early cosmesis using Harvard cosmesis scale is good to excellent.

CONCLUSIONS: Accelerated hypofractionated RT using SIB-VMAT is a clinically feasible technique with acceptable initial result. Initial results are encouraging.

MINI ABSTRACT: Simultaneous integrated boost with accelerated hypofractionated whole breast radiotherapy using Volumetric Modulated Arc Therapy is a novel approach. Patient selection and technical considerations are of paramount importance. The present study describes successful implementation of this approach.

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DOI: 10.1016/j.jnci.2017.01.005

PMID: 28343538 [Indexed for MEDLINE]

87: Myatra SN, Ahmed SM, Kundra P, Garg R, Ramkumar V, Patwa A, Shah A, Raveendra US, Shetty SR, Doctor JR, Pawar DK, Ramesh S, Das S, Divatia JV. Republication: All India Difficult Airway Association 2016 Guidelines for Tracheal Intubation in the Intensive Care Unit. Indian J Crit Care Med. 2017 Mar;21(3):146-153. doi: 10.4103/ijccm.IJCCM_57_17. PubMed PMID: 28400685; PubMed Central PMCID: PMC5363103.

Tracheal intubation (TI) is a routine procedure in the Intensive Care Unit (ICU) and is often lifesaving. In contrast to the controlled conditions in the operating room, critically ill patients with respiratory failure and shock are physiologically unstable. These factors, along with under evaluation of the airway and suboptimal response to preoxygenation, are responsible for a high incidence of life-threatening complications such as severe hypoxemia and cardiovascular collapse during TI in the ICU. The All India Difficult Airway Association (AIDAA) proposes a stepwise plan for safe management of the airway in critically ill patients. These guidelines have been developed based on available evidence; Wherever, robust evidence was lacking, recommendations were arrived at by consensus opinion of airway experts, incorporating the responses to a questionnaire sent to members of the (AIDAA) and Indian Society of Anaesthesiologists. Noninvasive positive pressure ventilation for preoxygenation provides adequate oxygen stores during TI for patients with respiratory pathology. Nasal insufflation of oxygen at 15 L/min can increase the duration of apnea before hypoxemia sets in. High flow nasal cannula oxygenation at 60-70 L/min may also increase safety during intubation of critically ill patients. Stable hemodynamics and gas exchange must be maintained during rapid sequence induction. It is necessary to implement an intubation protocol during routine airway management in the ICU. Adherence to a plan for difficult airway management incorporating the use of intubation aids and airway rescue devices and strategies is useful.

DOI: 10.4103/ijccm.IJCCM_57_17

PMCID: PMC5363103

PMID: 28400685

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

88: Naglot S, Aggarwal P, Dey S, Dalal K. Estimation of Serum YKL-40 by Real-Time Surface Plasmon Resonance Technology in North-Indian Asthma Patients. *J Clin Lab Anal.* 2017 Mar;31(2). doi: 10.1002/jcla.22028. Epub 2016 Sep 12. PubMed PMID: 27616735.

BACKGROUND: Many studies reported for estimating serum YKL-40 using ELISA or RIA methods. This study introduces the plausible utilization of real-time surface plasmon resonance (SPR) technology in investigating the expression of serum YKL-40 protein levels and ELISA method for serum IgE in bronchial asthma. **METHODS:** A commercially available BIAcore 2000 instrument, based on SPR technology, was utilized for assessing serum YKL-40 levels in a control sample size of 45 and active sample size of 97. Antibody immobilization was optimized to obtain the best sensor performance and a sensitive analytic detection. A commercially available ELISA kit was utilized for detecting serum IgE to estimate allergic condition-associated asthma. **RESULTS:** The results of SPR technology could distinctly classify with highly statistical significance, the asthma severities by estimating the elevated levels of YKL-40 in blood sera of minute quantities (up to 0.33 ng/ml), and thus differentiates superior utility in comparison with ELISA method. No statistically significant correlation of YKL-40 and IgE was observed. **CONCLUSIONS:** Serum YKL-40 may be used as a protein marker in classifying asthma severity by applying SPR technology as a reliable, label-free, highly sensitive, and cost-effective tool.

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DOI: 10.1002/jcla.22028

PMID: 27616735 [Indexed for MEDLINE]

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Human calcium/calmodulin-dependent protein kinase IV (CAMKIV), a member of Ser/Thr kinase family, is associated with cancer, cerebral hypoxia and neurodegenerative diseases. β -carotene is a colored organic compound, abundant in plants and fruits and is used in cancer prevention. Here, we report a strong binding affinity of β -carotene with CAMKIV using molecular docking, fluorescence binding and isothermal titration calorimetry methods. Furthermore, β -carotene also reduces the enzyme activity of CAMKIV moderately as observed during ATPase assay. To see the role of β -carotene on cell proliferation and apoptosis, cancerous cells (HeLa, HuH7 and MCF-7) and normal (HEK-293-T) cell lines were used. Admirable anticancer activity of β -carotene was observed. We further performed propidium iodide and DAPI (4',6-diamidino-2-phenylindole) assays to understand the mechanism of anticancer activity of β -carotene at molecular level. Our findings provide a newer insight into the use of β -carotene in cancer prevention and protection via inhibition of CAMKIV by regulating the signaling pathways.

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DOI: 10.1016/j.ijbiomac.2016.12.024

PMID: 27956097 [Indexed for MEDLINE]

91: Nehate C, Aji Alex MR, Kumar A, Koul V. Combinatorial delivery of superparamagnetic iron oxide nanoparticles ($\gamma\text{Fe}(2)\text{O}(3)$) and doxorubicin using folate conjugated redox sensitive multiblock polymeric nanocarriers for enhancing the chemotherapeutic efficacy in cancer cells. *Mater Sci Eng C Mater Biol Appl*. 2017 Jun 1;75:1128-1143. doi: 10.1016/j.msec.2017.03.024. Epub 2017 Mar 6. PubMed PMID: 28415398.

Redox sensitive, folate conjugated multiblock polymeric system of (-PLGA-PEG-PLGA-urethane-ss-) demonstrated self-assembly into stable nanoplateforms. The polymeric nanocarriers were encapsulated with doxorubicin and highly crystalline $\gamma\text{Fe}_2\text{O}_3$ superparamagnetic iron oxide nanoparticles (SPIONs), for co-delivery of the same to cancer cells, with average particle size of ~170nm and zeta potential of ~-33mV. Furthermore, the designed formulation was evaluated for protein adsorption, hemo-cytocompatibility and stability. Glutathione (GSH) induced redox sensitivity of the nanocarriers was depicted by ~4.47 fold increase in drug release in the presence of 10mM GSH. In vitro cellular uptake studies of the designed nanocarriers showed synergistic cytotoxic effect in folate overexpressing cells (HeLa and MDA-MB-231), after subjecting the cells to radio frequency (RF) induced hyperthermia (~43°C). Negligible effect of the combinatorial therapy was observed in normal cells (L929). The developed polymeric system depicted facile synthesis, reproducibility and potential for achieving combinatorial and targeted delivery of drug and SPIONs to cancer cells. This combinatorial approach can help in achieving better therapeutic effect with minimal side effects of chemotherapy.

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DOI: 10.1016/j.msec.2017.03.024
PMID: 28415398 [Indexed for MEDLINE]

92: Noh DY, Roh JK, Kim YH, Yoshida K, Baba H, Samson-Fernando MC, Misra S, Aziz Z, Umbas R, P Singh Y, Shu Kam Mok T, Yang HK, Akaza H. Symposium: "Oncology Leadership in Asia". *Cancer Res Treat*. 2017 Apr;49(2):283-291. doi: 10.4143/crt.2017.090. Epub 2017 Mar 9. PubMed PMID: 28279063; PubMed Central PMCID: PMC5398385.

The symposium on "Oncology Leadership in Asia" was held as part of the official program of the 42nd Annual Meeting of the Korean Cancer Association with International Cancer Conference. Given the increasing incidence of cancer in all countries and regions of Asia, regardless of developmental stage, and also in light of the recognized need for Asian countries to enhance collaboration in cancer prevention, research, treatment and follow-up, the symposium was held with the aim of bringing together oncology specialists from eight countries and regions in Asia to present the status in their own national context and discuss the key challenges and requirements in order to establish a greater Asian presence in the area of cancer control and research. The task of bringing together diverse countries and regions is made all the more urgent in that while Asia now accounts for more than half of all new cancer cases globally, clinical guidelines are based predominantly on practices adopted in Western countries, which may not be optimized for unique ethnic, pharmacogenomic and cultural characteristics in Asia. Recognizing the need for Asia to better gather information and data for the compilation of Asia-specific clinical guidelines, the participants discussed the current status in Asia in the national and regional contexts and identified future steps towards integrated and collaborative initiatives in Asia. A key outcome of the symposium was a proposal to combine and integrate the activities of existing pan-Asian societies, including the Asian Pacific Federation of Organizations for Cancer Research and Control (APFOCC) and Asian Clinical Oncology Society (ACOS). Further proposals included the expansion of pan-Asian society membership to include individuals and the essential need to encourage the participation of young researchers in order to ensure self-sustainability of cancer control efforts in the future.

DOI: 10.4143/crt.2017.090
PMCID: PMC5398385
PMID: 28279063

93: Pal S, George J, Singh AN, Mathur S, Dash NR, Garg P, Sahni P, Chattopadhyay TK. Posterior Superior Mesenteric Artery (SMA) First Approach vs. Standard Pancreaticoduodenectomy in Patients with Resectable Periampullary Cancers: a Prospective Comparison Focusing on Circumferential Resection Margins. *J Gastrointest Cancer*. 2017 Mar 18. doi: 10.1007/s12029-017-9933-x. [Epub ahead of print] PubMed PMID: 28315190.

BACKGROUND: The 'SMA-first' (P-SMA) pancreatoduodenectomy (PD) allows dissection directly on the right lateral aspect of superior mesenteric artery (SMA) which may decrease circumferential resection margin (CRM) positivity. This comparative study between standard PD (sPD) and P-SMA approach was planned focusing on CRM involvement.

METHODS: This was a prospective study comparing consecutive patients with resectable periampullary cancers (PACA) undergoing PD using the standard or P-SMA approach. The perioperative outcomes and the CRM positivity rates (specimens analysed according to the standardized Leeds pathology protocol (LEEPP)) were compared.

RESULTS: Overall, 39 patients (28 men; mean age 54 years; sPD 21, P-SMA 18) were included. Both groups were comparable with regard to demographic/tumour characteristics and perioperative outcomes. The P-SMA technique was significantly faster (321.1 ± 54.0 vs. 357.6 ± 55.8 min; $p = 0.05$). Though the mean tumour size (2.2 vs. 2.1 cm; $p = 0.84$) and T stage (T2 and T3) distribution were similar in both groups, lymph node yield was significantly higher in the P-SMA group (10.7 vs. 5.95; $p = 0.001$; mean 8 (2-21)). Though CRM positivity (margin <1 mm) occurred in 8 (21.1%), we did not find the P-SMA PD to yield significantly lower CRM positivity rates compared to the sPD (3/17 (17.6%) vs. 5/21 (23.8%); $p = 0.71$). At a median follow-up of 28 months, fewer patients in the P-SMA PD group developed recurrence (2/15 vs. 5/19; $p = 0.3$) or died (3/15 vs. 7/19; $p = 0.19$), though this difference was not significant.

CONCLUSIONS: In patients with resectable PACA, P-SMA PD was significantly faster and yielded higher lymph node counts in the specimen but did not lower the rate of CRM positivity as determined by the LEEPP.

DOI: 10.1007/s12029-017-9933-x
PMID: 28315190

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Butyrate is one of the short chain fatty acids, produced by the gut microbiota during anaerobic fermentation of dietary fibres. It has been shown that it can inhibit tumor progression via suppressing histone deacetylase and can induce apoptosis in cancer cells. However, the comprehensive pathway by which butyrate mediates apoptosis and growth arrest in cancer cells still remains unclear. In this study, the role of miR-22 in butyrate-mediated ROS release and induction of apoptosis was determined in hepatic cells. Intracellular expression of miR-22 was increased when the Huh 7 cells were incubated with sodium butyrate.

Over-expression of miR-22 or addition of sodium butyrate inhibited SIRT-1 expression and enhanced the ROS production. Incubation of cells with anti-miR-22 reversed the effects of butyrate. Butyrate induced apoptosis via ROS production, cytochrome c release and activation of caspase-3, whereas addition of N-acetyl cysteine or anti-miR-22 reversed these butyrate-induced effects. Furthermore, sodium butyrate inhibited cell growth and proliferation, whereas anti-miR-22 inhibited these butyrate-mediated changes. The expression of PTEN and gsk-3 was found to be increased while p-akt and β -catenin expression was decreased significantly by butyrate. These data showed that butyrate modulated both apoptosis and proliferation via miR-22 expression in hepatic cells.

DOI: 10.1016/j.redox.2017.03.006
PMCID: PMC5350572
PMID: 28288414

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96: Parajuli P, Kumar S, Gupta A, Bansal VK, Sagar S, Mishra B, Singhal M, Kumar A, Gamangatti S, Gupta B, Sawhney C, Misra MC. Role of Laparoscopy in Patients With Abdominal Trauma at Level-I Trauma Center. *Surg Laparosc Endosc Percutan Tech.* 2017 Mar 8. doi: 10.1097/SLE.0000000000000379. [Epub ahead of print] PubMed PMID: 28277439.

INTRODUCTION: Abdominal trauma is one of the preventable causes of death in polytrauma patients. Decision and timing of laparotomy is a major challenge. Rate of nontherapeutic laparotomy is still high. Laparoscopy can avoid nontherapeutic laparotomy and also provide a reliable and accurate diagnosis of injury.

MATERIALS AND METHODS: This ambispective observational study was conducted in the division of Trauma Surgery and Critical Care, JPN Apex Trauma Centre, All India Institute Medical Sciences, New Delhi. Retrospective analysis of prospectively maintained data of cases from January 1, 2008 through April 30, 2013 and prospective analysis of cases from May 1, 2013 through March 31, 2015 was done using appropriate measures. Hemodynamically stable or responders fulfilling inclusion criteria were included. Selected patients underwent the laparoscopic procedure and if required converted to laparotomy.

RESULTS: Of the 3610 patients of abdominal trauma, laparotomy was done in 1666 (46.14%) patients and laparoscopy was done in 119 (3.29%) patients. Rate of reduction of nontherapeutic laparotomy in patients with abdominal trauma using diagnostic laparoscopy was 55.4%. However laparotomy could be avoided in 59.7%. Laparoscopy was 100% accurate in identifying injuries in our study. No injuries were missed in these patients. Fever and wound infection were significantly higher in laparotomy group. Chest infection and sepsis were also higher in laparotomy group but the difference was not statistically significant. Median length of hospital stay in laparoscopy group was 4 days (range: 1 to 28 d) and in laparotomy group was 9.5 days (range: 2 to 55 d) with P-value of 0.001.

CONCLUSIONS: Laparoscopy has a role in management of hemodynamically stable patients with suspected abdominal injury to prevent nontherapeutic laparotomies, and thereby decreasing postoperative complications.

DOI: 10.1097/SLE.0000000000000379
PMID: 28277439

97: Patil AL, Sood SK, Goyal V, Kochhar KP. Cortical Potentials Prior to Movement in Parkinson's Disease. *J Clin Diagn Res.* 2017 Mar;11(3):CC13-CC16. doi: 10.7860/JCDR/2017/25520.9598. Epub 2017 Mar 1. PubMed PMID: 28511378; PubMed Central PMCID: PMC5427304.

INTRODUCTION: Recording cortical potentials prior to movement (bereitschaftspotentials, BP) offer a good non invasive method for studying activity of motor related cortices in Parkinson's Disease (PD). Dopaminergic medications provide some symptomatic relief in advanced stages but they do not stop the progression of the disease. Assessing BP may be a good idea to see the response of anti PD drugs. It remains unclear whether the anti PD medications also improve cortical activity prior to movement even in advanced stages of the disease.

AIM: In this study we recorded scalp BP in patients with varying grades of severity to study the relationship between disease severity and various

components of BP.

MATERIALS AND METHODS: We successfully recorded BP at Cz, C3 and C4 sites during self-initiated 100 right wrist movements in 12 male patients with PD having severity Hoehn and Yahn (H&Y) scale 4 (PD3 group). These potentials were compared with age matched patients with H&Y scale 2 (PD1) and scale 3 (PD2) and also with age matched healthy controls.

RESULTS: We found flatter waveforms with increasing severity of disease. Amplitude is first to be affected in mild severity as compared to controls ($p=0.011$); while with increasing severity early as well as late part of potentials is affected. Such changes are prominently seen at Cz site across the groups.

CONCLUSION: These findings imply that there is increasing defect in cortical activity during movement especially in supplementary motor area with increasing severity in PD in spite of dopaminergic medications. This dynamic nature of dysfunction in supplementary motor cortices must be taken in account while treating advanced cases using newer stimulation techniques.

DOI: 10.7860/JCDR/2017/25520.9598

PMCID: PMC5427304

PMID: 28511378

98: Paul SB, Dhamija E, Gamanagatti SR, Sreenivas V, Yadav DP, Jain S, Shalimar, Acharya SK. Evaluation of tumor response to intra-arterial chemoembolization of hepatocellular carcinoma: Comparison of contrast-enhanced ultrasound with multiphase computed tomography. *Diagn Interv Imaging*. 2017 Mar;98(3):253-260. doi: 10.1016/j.diii.2016.09.002. Epub 2016 Sep 28. PubMed PMID: 27692674.

PURPOSE: To compare the diagnostic accuracy of contrast-enhanced ultrasound (CEUS) with that of multiphase computed tomography (CT) in the evaluation of tumor response to transarterial chemoembolization (TACE) of hepatocellular carcinoma (HCC).

MATERIAL AND METHODS: Fifty patients (41 men, 9 women; mean age, 53 years \pm 12.5 [SD]) with a total of 70 HCCs (mean size, 5cm \pm 3 [SD]) were evaluated. Post-TACE therapeutic assessment of HCC was done at 4 weeks. Patients with TACE done earlier and reporting with suspicion for recurrence were also included. Patients with hepatic masses seen on ultrasound were enrolled and subjected to CEUS, multiphase CT and magnetic resonance imaging (MRI). Hyperenhancing area at the tumor site on arterial phase of CEUS/multiphase CT/MRI was termed as residual disease (RD), the patterns of which were described on CEUS. Diagnostic accuracies of CEUS and MPCT were compared to that of MRI that was used as the reference standard.

RESULTS: CEUS detected RD in 43/70 HCCs (61%). RD had a heterogeneous pattern in 22/43 HCCs (51%). Sensitivities of CEUS and multiphase CT were 94% (34/36; 95% CI: 81-99%) and 50% (18/36; 95% CI: 33-67%) respectively. Significant difference in sensitivity was found between CEUS and multiphase CT ($P=0.0001$). CEUS and multiphase CT had 100% specificity (95% CI: 83-100%).

CONCLUSION: CEUS is a useful technique for detecting RD in HCC after TACE. For long term surveillance, CEUS should be complemented with multiphase CT/MRI for a comprehensive evaluation.

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DOI: 10.1016/j.diii.2016.09.002

PMID: 27692674

99: Pradhan P, Anant A, Venkatachalam VP. Comparison of Temporalis Fascia and Full-Thickness Cartilage Palisades in Type-I Underlay Tympanoplasty for Large/Subtotal Perforations. *Iran J Otorhinolaryngol*. 2017 Mar;29(91):63-68. PubMed PMID: 28393052; PubMed Central PMCID: PMC5380390.

INTRODUCTION: To demonstrate surgical techniques and to compare the anatomical

and functional outcomes between temporalis fascia and cartilage palisade grafting in type-I underlay tympanoplasty in patients with large/subtotal perforation. MATERIALS AND METHODS: Temporalis fascia and cartilage palisade grafting were conducted in Group A and Group B, respectively, each containing 30 patients with large/subtotal perforations. Pure tone audiogram (PTA) and speech reception thresholds (SRT) were performed preoperatively and at each postoperative visit; i.e. at the end of Month 1,3,6, and 24. A 10-dB closure of air bone gap (ABG) and a 10-dB improvement in SRT were considered significant.

RESULTS: The graft uptake rates were 80% and 96.7% in Group A and Group B, respectively, at the end of 24 months. In total, 90% of Group A and 88% in Group B had significant improvement in hearing (ABG \geq 10 dB). The mean improvement in SRT in the fascia and cartilage groups was 10 dB and 9 dB, respectively. Seventy-five percent of patients in Group A and 60% of patients in Group B had a significant gain in SRT.

CONCLUSION: Although both temporalis fascia and cartilage palisades can effectively be used for tympanic membrane (TM) grafting in difficult perforations, the latter is considered to be the better autograft, not only because of superior graft uptake but also because it results in a comparable hearing outcome.

PMCID: PMC5380390

PMID: 28393052

100: Purkait S, Miller CA, Kumar A, Sharma V, Pathak P, Jha P, Sharma MC, Suri V, Suri A, Sharma BS, Fulton RS, Kale SS, Dahiya S, Sarkar C. ATRX in Diffuse Gliomas With its Mosaic/Heterogeneous Expression in a Subset. *Brain Pathol.* 2017 Mar;27(2):138-145. doi: 10.1111/bpa.12364. Epub 2016 Jun 13. PubMed PMID: 26833422.

This study aims (1) to evaluate ATRX expression in different grades and subtypes of gliomas and correlate with other hallmark genetic alterations, (2) to identify and characterize mosaic/heterogeneous staining in gliomas in terms of mutation status. One hundred seventy six cases of glioma were assessed for ATRX immunohistochemistry and subdivided into positive, negative and mosaic/heterogeneous staining patterns. Five cases with heterogeneous staining were further subjected to next generation sequencing. Higher frequency of ATRX immune-negativity was detected in grade II/III astrocytic, oligoastrocytic tumors and secondary glioblastomas (GBMs), while infrequent in primary GBMs and rare in oligodendrogliomas. Loss of expression was significantly associated with IDH1 and/or TP53 mutation, while mutually exclusive with 1p/19q codeletion. Mosaic/heterogeneous staining was detected exclusively in GBMs (21.2%). Two different types of mosaic staining were identified (1) Admixture of positive and negative nuclei or intermixed mosaic and (2) Separate fragments with positive and negative/intermixed mosaic staining. ATRX mutation was identified in 2/5 (40%) cases with mosaic staining while one case showed DAXX mutation. All these cases were characterized by distinctly separate immune-negative and positive/intermixed foci. Hence, it is suggested that cases with heterogeneous staining (especially those with distinctly negative fragments) should be subjected to mutation analysis.

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DOI: 10.1111/bpa.12364

PMID: 26833422

101: Radhakrishnan V, Kapoor G, Arora B, Bansal D, Vora T, Prasad M, Chinnaswamy G, Laskar S, Agarwala S, Kaur T, Rath GK, Bakhshi S. Management of Hodgkins Lymphoma: ICMR Consensus Document. *Indian J Pediatr.* 2017 May;84(5):371-381. doi: 10.1007/s12098-017-2304-6. Epub 2017 Mar 30. Review. PubMed PMID: 28357582.

Pediatric Hodgkins lymphoma is a highly curable disease even in the developing world. Current treatment paradigms follow a risk and response based approach. The

goal is to minimise treatment related short and long-term toxicity while maintaining excellent survival. A confirmed histopathological diagnosis and full staging work-up are essential prior to embarking on treatment and guidelines for these are provided in the text. All patients require combination chemotherapy while radiotherapy is usually reserved for a select subgroup depending on the protocol used. It is important to follow these patients for relapse in the first five years and life-long for late effects as most of them will be cured.

DOI: 10.1007/s12098-017-2304-6

PMID: 28357582

102: Rajan D, Lakshmanan G, Gupta SK, Sivasubramanian R, Saxena A, Juneja R. Effect of Recorded Maternal Voice on Child's Cooperation During Cardiac Catheterization - A randomized controlled trial. *Indian Pediatr.* 2017 Mar 15;54(3):204-207. Epub 2017 Feb 2. PubMed PMID: 28159944.

OBJECTIVE: To assess the effect of recorded maternal voice on child's cooperation during cardiac catheterization.

DESIGN: Randomized placebo controlled trial.

Setting: Cardiac catheterization laboratory at a tertiary care hospital.

PARTICIPANTS: 90 children with congenital heart disease scheduled for cardiac catheterization between July 2014 and Dec 2014 randomized to maternal voice group and control group.

INTERVENTION: During cardiac catheterization, children in maternal voice group listened to a 3-min audio-recording of their mother's voice, played in loop, using head-phones. Children in the other group wore headphones without auditory stimuli.

MAIN OUTCOME MEASURES: Child's cooperation during cardiac catheterization as assessed by Child Emotional Manifestation Scale.

RESULTS: Children in the maternal voice group showed lower mean (SD) distress scores [13.2 (4.6) vs. 16 (5.6), $P=0.01$]. The requirement of sedative agents during the procedure was not different ($P=0.09$).

CONCLUSION: Allowing children to listen to recorded voice of their mother is an effective strategy to improve cooperation during cardiac catheterization.

PMID: 28159944 [Indexed for MEDLINE]

103: Rajesh Y, Pal I, Banik P, Chakraborty S, Borkar SA, Dey G, Mukherjee A, Mandal M. Insights into molecular therapy of glioma: current challenges and next generation blueprint. *Acta Pharmacol Sin.* 2017 May;38(5):591-613. doi: 10.1038/aps.2016.167. Epub 2017 Mar 20. Review. PubMed PMID: 28317871; PubMed Central PMCID: PMC5457688.

Glioma accounts for the majority of human brain tumors. With prevailing treatment regimens, the patients have poor survival rates. In spite of current development in mainstream glioma therapy, a cure for glioma appears to be out of reach. The infiltrative nature of glioma and acquired resistance substantially restrict the therapeutic options. Better elucidation of the complicated pathobiology of glioma and proteogenomic characterization might eventually open novel avenues for the design of more sophisticated and effective combination regimens. This could be accomplished by individually tailoring progressive neuroimaging techniques, terminating DNA synthesis with prodrug-activating genes, silencing gliomagenesis genes (gene therapy), targeting miRNA oncogenic activity (miRNA-mRNA interaction), combining Hedgehog-Gli/Akt inhibitors with stem cell therapy, employing tumor lysates as antigen sources for efficient depletion of tumor-specific cancer stem cells by cytotoxic T lymphocytes (dendritic cell vaccination), adoptive transfer of chimeric antigen receptor-modified T cells, and combining immune checkpoint inhibitors with conventional therapeutic modalities. Thus, the present review captures the latest trends associated with the molecular mechanisms involved in glial tumorigenesis as well as the limitations of surgery, radiation and chemotherapy. In this article we also critically discuss the next generation molecular therapeutic strategies and their

mechanisms for the successful treatment of glioma.

DOI: 10.1038/aps.2016.167

PMCID: PMC5457688

PMID: 28317871

104: Ramaiah A, Dai L, Contreras D, Sinha S, Sun R, Arumugaswami V. Comparative analysis of protein evolution in the genome of pre-epidemic and epidemic Zika virus. *Infect Genet Evol.* 2017 Jul;51:74-85. doi: 10.1016/j.meegid.2017.03.012. Epub 2017 Mar 14. PubMed PMID: 28315476.

Zika virus (ZIKV) causes microcephaly in congenital infection, neurological disorders, and poor pregnancy outcome and no vaccine is available for use in humans or approved. Although ZIKV was first discovered in 1947, the exact mechanism of virus replication and pathogenesis remains unknown. Recent outbreaks of Zika virus in the Americas clearly suggest a human-mosquito cycle or urban cycle of transmission. Understanding the conserved and adaptive features in the evolution of ZIKV genome will provide a hint on the mechanism of ZIKV adaptation to a new cycle of transmission. Here, we show comprehensive analysis of protein evolution of ZIKV strains including the current 2015-16 outbreak. To identify the constraints on ZIKV evolution, selection pressure at individual codons, immune epitopes and co-evolving sites were analyzed. Phylogenetic trees show that the ZIKV strains of the Asian genotype form distinct cluster and share a common ancestor with African genotype. The TMRCA (Time to the Most Recent Common Ancestor) for the Asian lineage and the subsequently evolved Asian human strains was calculated at 88 and 34 years ago, respectively. The proteome of current 2015/16 epidemic ZIKV strains of Asian genotype was found to be genetically conserved due to genome-wide negative selection, with limited positive selection. We identified a total of 16 amino acid substitutions in the epidemic and pre-epidemic strains from human, mosquito, and monkey hosts. Negatively selected amino acid sites of Envelope protein (E-protein) (positions 69, 166, and 174) and NS5 (292, 345, and 587) were located in central dimerization domains and C-terminal RNA-directed RNA polymerase regions, respectively. The predicted 137 (92 CD4 TCEs; 45 CD8 TCEs) immunogenic peptide chains comprising negatively selected amino acid sites can be considered as suitable target for sub-unit vaccine development, as these sites are less likely to generate immune-escape variants due to strong functional constraints operating on them. The targeted changes at the amino acid level may contribute to better adaptation of ZIKV strains to human-mosquito cycle or urban cycle of transmission.

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DOI: 10.1016/j.meegid.2017.03.012

PMID: 28315476

105: Ramalingam K, Vuthaluru S, Srivastava A, Dinda AK, Dhar A. Ultra structural changes occurring in duct ectasia and periductal mastitis and their significance in etiopathogenesis. *PLoS One.* 2017 Mar 8;12(3):e0173216. doi: 10.1371/journal.pone.0173216. eCollection 2017. PubMed PMID: 28273122; PubMed Central PMCID: PMC5342207.

INTRODUCTION: Duct ectasia (DE) and periductal mastitis (PDM) are the most common benign breast conditions seen in women. The etiopathogenesis of these entities is still not clear and most of the theories regarding the causation are based on the histological features as seen on light microscopy. The ultramicroscopic features associated with these conditions that may give more insight to the etiopathogenesis are unknown.

AIM: To study the ultrastructural changes occurring in mammary duct cones in patients with DE and PDM using Transmission Electron Microscopic (TEM).

METHOD: Major ducts removed by radical duct excision from 21 patients with final histopathological diagnosis of DE and PDM were subjected to TEM study with 2 normal duct samples as controls.

RESULTS: The TEM features of DE were denudation of the epithelial cells with

focal loss of microvilli, widening of the inter-epithelial junctions with focal disruption of the T bars, periductal collagenisation without inflammation, and features suggestive of Epithelial Mesenchymal Transition (EMT). PDM features are intact epithelial lining with proliferative epithelium and periductal collagenisation with inflammation.

CONCLUSIONS: Based on the TEM findings, we suggest that DE and PDM are two different entities. EMT a novel finding observed in DE in this study.

DOI: 10.1371/journal.pone.0173216

PMCID: PMC5342207

PMID: 28273122

106: Ramsuran V, Hernández-Sánchez PG, O'hUigin C, Sharma G, Spence N, Augusto DG, Gao X, García-Sepúlveda CA, Kaur G, Mehra NK, Carrington M. Sequence and Phylogenetic Analysis of the Untranslated Promoter Regions for HLA Class I Genes. *J Immunol*. 2017 Mar 15;198(6):2320-2329. doi: 10.4049/jimmunol.1601679. Epub 2017 Feb 1. PubMed PMID: 28148735; PubMed Central PMCID: PMC5340644.

Polymorphisms located within the MHC have been linked to many disease outcomes by mechanisms not yet fully understood in most cases. Variants located within untranslated regions of HLA genes are involved in allele-specific expression and may therefore underlie some of these disease associations. We determined sequences extending nearly 2 kb upstream of the transcription start site for 68 alleles from 57 major lineages of classical HLA class I genes. The nucleotide diversity within this promoter segment roughly follows that seen within the coding regions, with HLA-B showing the highest (~1.9%), followed by HLA-A (~1.8%), and HLA-C showing the lowest diversity (~0.9%). Despite its greater diversity, HLA-B mRNA expression levels determined in 178 European Americans do not vary in an allele- or lineage-specific manner, unlike the differential expression levels of HLA-A or HLA-C reported previously. Close proximity of promoter sequences in phylogenetic trees is roughly reflected by similarity of expression pattern for most HLA-A and -C loci. Although promoter sequence divergence might impact promoter activity, we observed no clear link between the phylogenetic structures as represented by pairwise nucleotide differences in the promoter regions with estimated differences in mRNA expression levels for the classical class I loci. Further, no pair of class I loci showed coordinated expression levels, suggesting that distinct mechanisms across loci determine their expression level under nonstimulated conditions. These data serve as a foundation for more in-depth analysis of the functional consequences of promoter region variation within the classical HLA class I loci.

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DOI: 10.4049/jimmunol.1601679

PMCID: PMC5340644 [Available on 2018-03-15]

PMID: 28148735

107: Rana M, Coshic P, Goswami R, Tyagi RK. Influence of a critical single nucleotide polymorphism on nuclear receptor PXR-promoter function. *Cell Biol Int*. 2017 May;41(5):570-576. doi: 10.1002/cbin.10744. Epub 2017 Mar 8. PubMed PMID: 28198586.

The Pregnane and Xenobiotic Receptor (PXR; NR1I2) is a ligand-modulated transcription factor that belongs to the nuclear receptor superfamily. It is expressed at higher levels primarily in liver and intestine as compared to the levels in several other organs. It is activated by a broad spectrum of xenobiotics and endobiotics. The primary function of PXR is to regulate the expression of drug metabolizing enzymes and transporters and prevent the accumulation of toxic chemicals in the body, thereby maintaining body's homeostasis. In this study, we identified a C/T single nucleotide polymorphism at position -831 from the transcriptional start site of the PXR gene promoter and examined the functional significance of this variant using both the luciferase

reporter gene assays and electrophoretic mobility shift assays (EMSA). Transient transfection experiments showed that the T-allele was associated with significantly greater transcriptional activity than the C-allele of SNP rs3814055. These results indicate that the -831C/T polymorphism has a direct effect on transcriptional regulation of PXR gene. This allelic variation may be a potential genetic marker that can help identify individuals at higher risk for Inflammatory Bowel Disease (IBD).

© 2017 International Federation for Cell Biology.

DOI: 10.1002/cbin.10744

PMID: 28198586 [Indexed for MEDLINE]

108: Ranjha R, Meena NK, Singh A, Ahuja V, Paul J. Association of miR-196a-2 and miR-499 variants with ulcerative colitis and their correlation with expression of respective miRNAs. PLoS One. 2017 Mar 16;12(3):e0173447. doi: 10.1371/journal.pone.0173447. eCollection 2017. PubMed PMID: 28301487; PubMed Central PMCID: PMC5354276.

BACKGROUND AND AIM: MicroRNAs are small non-coding RNAs that play an important role in regulating the gene expression of their target genes. SNP miR-196a-2 rs11614913 and miR-499 rs3746444 are reported to have association with the risk and prognosis of multiple-types of inflammatory diseases including IBD. This study was conducted to show if any association of SNP miR-196a-2rs11614913 and miR-499 rs3746444 exists with ulcerative colitis (UC) patients of north Indian population and how these polymorphisms modulate the expression profile of the respective miRNAs.

METHODS: A total of 638 participants including 197 UC patients and 441 controls were included in this study. Polymorphisms were genotyped by PCR-RFLP and the miRNA expression was measured using qRT-PCR. Genotypes and allele frequencies were calculated using SPSS 16 software.

RESULTS: MiR-196a-2 rs11614913 (C>T) and miR-499 rs3746444 (T>C) were found to be associated with UC. TT genotype of miR-196a-2 rs11614913 ($p = 0.03$) was negatively associated with UC whereas the heterozygous TC genotype of miR-499 rs3746444 ($p = 0.003$) was showing positive association with UC. Patients having a combination of both SNPs, developed disease at older age and they suffered from severe disease extent. Genotype that showed association with the disease also showed correlation with the changes in miRNA expression.

CONCLUSION: In this study we found miR-196a-2 rs11614913 and miR-499 rs3746444 were associated with UC in north Indian population. We found the genotype that showed association with UC also altered the expression of respective miRNA in the patient harboring the genotype. There was correlation between associated genotype and altered miRNA expression.

DOI: 10.1371/journal.pone.0173447

PMCID: PMC5354276

PMID: 28301487

109: Raza K, Singh S, Rani N, Mishra R, Mehta K, Kaler S. Anomalous Innervation of the Median Nerve in the Arm in the Absence of the Musculocutaneous Nerve. Sultan Qaboos Univ Med J. 2017 Feb;17(1):e106-e108. doi: 10.18295/squmj.2016.17.01.019. Epub 2017 Mar 30. PubMed PMID: 28417038; PubMed Central PMCID: PMC5380405.

The brachial plexus innervates the upper extremities. While variations in the formation of the brachial plexus and its terminal branches are quite common, it is uncommon for the median nerve to innervate the muscles of the arm. During the dissection of an elderly male cadaver at the Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India, in 2016, the coracobrachialis muscle was found to be supplied by a direct branch from the lateral root of the median nerve and the musculocutaneous nerve was absent. The branches of the median nerve supplied the biceps brachii and brachialis muscles and the last branch continued as the lateral cutaneous nerve of the forearm. These variations

may present atypically in cases of arm flexor paralysis or sensory loss on the lateral forearm. Knowledge of these variations is important in surgeries and during the administration of regional anaesthesia near the shoulder joint and upper arm.

DOI: 10.18295/squmj.2016.17.01.019
PMCID: PMC5380405
PMID: 28417038

110: Reeta KH, Singh D, Gupta YK. Chronic treatment with taurine after intracerebroventricular streptozotocin injection improves cognitive dysfunction in rats by modulating oxidative stress, cholinergic functions and neuroinflammation. *Neurochem Int.* 2017 Sep;108:146-156. doi: 10.1016/j.neuint.2017.03.006. Epub 2017 Mar 8. PubMed PMID: 28284975.

The present study investigated the neuroprotective effects of taurine, an essential amino acid for growth and development of central nervous system. Intracerebroventricular streptozotocin (ICV-STZ) model of cognitive impairment was used in male Wistar rats (270 ± 20 g). Morris water maze, elevated plus maze and passive avoidance paradigm were used to assess cognitive performance. Taurine (40, 60 and 120 mg/kg) was administered orally for 28 days following STZ administration on day 1. Oxidative stress parameters (malondialdehyde, glutathione, nitric oxide and superoxide dismutase) and cholinesterases (acetylcholinesterase and butyrylcholinesterase) activity were measured at end of the study in the cortex and hippocampus. Levels of TNF- α , IL-1 β , expression of rho kinase-II (ROCK-II), glycogen synthase kinase-3 β (GSK-3 β) and choline acetyltransferase (ChAT) were studied in cortex and hippocampus. STZ caused significant cognitive impairment as compared to normal control. Chronic administration of taurine attenuated STZ-induced cognitive impairment. Increased oxidative stress and increased levels of TNF- α , IL-1 β induced by STZ were also significantly attenuated by taurine. Taurine significantly ($p < 0.05$) decreased the STZ-induced increased expression of ROCK-II in cortex and hippocampus. Further, STZ-induced increased activity of cholinesterases was significantly ($p < 0.001$) mitigated by taurine. STZ decreased the expression of ChAT in hippocampus which was significantly ($p < 0.05$) reversed by taurine. However, GSK-3 β expression was not altered by either STZ or taurine. The present study indicates that taurine exerts a neuroprotective role against STZ-induced cognitive impairment in rats. This effect is probably mediated by modulating oxidative stress, cholinesterases, inflammatory cytokines and expression of ROCK-II. Thus, this study suggests a potential of chronic taurine administration in cognitive impairment of Alzheimer's type.

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DOI: 10.1016/j.neuint.2017.03.006
PMID: 28284975

111: Reeta KH, Singh D, Gupta YK. Edaravone attenuates intracerebroventricular streptozotocin-induced cognitive impairment in rats. *Eur J Neurosci.* 2017 Apr;45(7):987-997. doi: 10.1111/ejn.13543. Epub 2017 Mar 21. PubMed PMID: 28199036.

Alzheimer's disease is a major cause of dementia worldwide. Edaravone, a potent free radical scavenger, is reported to be neuroprotective. The present study was designed to investigate the effect of chronic edaravone administration on intracerebroventricular-streptozotocin (ICV-STZ) induced cognitive impairment in male Wistar rats. Cognitive impairment was developed by single ICV-STZ (3 mg/kg) injection bilaterally on day 1. Edaravone (1, 3 and 10 mg/kg, orally, once daily) was administered for 28 days. Morris water maze and passive avoidance tests were used to assess cognitive functions at baseline and on days 14 and 28. ICV-STZ caused cognitive impairment as evidenced by increased escape latency and decreased time spent in target quadrant in the Morris water maze test and reduced retention latency in the passive avoidance test. STZ caused increase in oxidative

stress, cholinesterases, inflammatory cytokines and protein expression of ROCK-II and decrease in protein expression of ChAT. Edaravone ameliorated the STZ-induced cognitive impairment. STZ-induced increase in oxidative stress and increased levels of pro-inflammatory cytokines (TNF- α , IL-1 β) were mitigated by edaravone. Edaravone also prevented STZ-induced increased protein expression of ROCK-II. Moreover, edaravone significantly prevented STZ-induced increased activity of cholinesterases in the cortex and hippocampus. The decreased expression of ChAT caused by STZ was brought towards normal by edaravone in the hippocampus. The results thus show that edaravone is protective against STZ-induced cognitive impairment, oxidative stress, cholinergic dysfunction and altered protein expressions. This study thus suggests the potential of edaravone as an adjuvant in the treatment of Alzheimer's disease.

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DOI: 10.1111/ejn.13543

PMID: 28199036

112: Roy S, Pathy S, Mohanti BK, Chander S, Biswas A. Adherence to Treatment, Response and Patterns of Failure in Pediatric Parameningeal Rhabdomyosarcoma: Experience From a Tertiary Cancer Care Center From India. *J Pediatr Hematol Oncol.* 2017 Mar;39(2):e62-e68. doi: 10.1097/MPH.0000000000000745. PubMed PMID: 28060113.

The study was aimed at evaluating adherence to treatment protocol and outcome in pediatric parameningeal rhabdomyosarcoma (PM-RMS). We analyzed the characteristics, treatment administered, outcomes and patterns of failure of pediatric PM-RMS, who were treated with multimodality therapy between January 2005 and December 2013. Univariate and multivariate analysis (MVA) was completed to evaluate the impact of various prognostic factors. Thirty-seven patients were treated at our institution. Majority of them had the primary disease in paranasal sinuses (n=13). Majority of the patients belonged to group III (n=30) and stage III (n=24). The overall response rate to treatment was 52.5% (n=21). At a mean follow-up of 19.1 months, 23 patients developed disease progression. The actuarial rates of failure-free survival and overall survival (OS) at 2 years were 40% and 67.5%, respectively. Patients who received >20 weeks of intended chemotherapy schedule (P=0.02) and had complete response to first-line treatment (P=0.0004) were found to have superior failure-free survival on MVA. Complete response was the lone determinant of superior OS on MVA (P=0.006). Majority of patients with PM-RMS present with advanced stage disease. Response to first-line treatment is a significant predictor of superior progression-free survival and OS in these patients.

DOI: 10.1097/MPH.0000000000000745

PMID: 28060113

113: Roy S, Gandhi AK, Devnani B, Singh L, Mohanti BK. Malignant peripheral nerve sheath tumor of the tongue with an unusual pattern of recurrence. *J Egypt Natl Canc Inst.* 2017 Jun;29(2):115-118. doi: 10.1016/j.jnci.2016.11.001. Epub 2017 Mar 1. PubMed PMID: 28258916.

Malignant peripheral nerve sheath tumor (MPNST) of oral cavity is an extremely uncommon malignancy. Less than 15 cases have been reported since 1973 though none of them describes a distant metastasis. We present a rare case of MPNST of the tongue who presented with features of hypoglossal nerve palsy. Incisional biopsy showed a malignant spindle cell tumor in the sub-epithelial connective tissue. The tumor cells were immune-positive for S-100. He underwent surgery followed by adjuvant chemo-radiation. Later the disease recurred in the form of isolated pelvic bone metastasis. Palliative chemotherapy was offered to him. With this case report we intend to refer to such unusual presentation and pattern of recurrence in a MPNST of tongue.

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114: Sharma JB, Kriplani A, Sharma E, Sharma S, Dharmendra S, Kumar S, Vanamail P, Sharma SK. Multi drug resistant female genital tuberculosis: A preliminary report. *Eur J Obstet Gynecol Reprod Biol.* 2017 Mar;210:108-115. doi: 10.1016/j.ejogrb.2016.12.009. Epub 2016 Dec 12. PubMed PMID: 28011331.

OBJECTIVE: Evaluation of 6 patients presenting with tubo-ovarian mass or infertility with multi drug resistant (MDR) female genital tuberculosis (FGTB).
STUDY DESIGN: It was an observational study in a tertiary referral centre, India on subjects with MDR FGTB on clinical examination and investigations. All patients were given category IV drugs using kanamycin (intramuscular), levofloxacin, pyrazinamide, cycloserine, ethionamide and ethambutol (or para aminosalicylic acid [PAS] for ethambutol resistant cases) for 6 months intensive phase followed by oral levofloxacin, cycloserine, ethionamide and ethambutol (or PAS for ethambutol resistant cases) for 18 months continuation phase. Patients were evaluated for primary end points (complete cure, partial response, no response, treatment completed) and secondary end points (recurrence rate, pregnancy rate) during treatment.

RESULTS: There were 2 (33.3%) primary MDR FGTB patients and 4 (66.6%) secondary MDR FGTB (three pulmonary MDR and one MDR lymphadenitis) patients. Mean age was 23.6 years. Presenting features were menstrual dysfunction in all patients (100%) especially oligomenorrhea in 3 (50%) patients, weight loss in all the patients (100%), cough with expectoration in three patients (50%), tubo-ovarian masses in five (83.3%) patients. Endometrial biopsy showed positive culture for AFB with rifampicin and isoniazid (INH) resistance in both primary MDR FGTB patients and in two secondary MDR FGTB patients who were sexually active. In secondary MDR FGTB, three pulmonary MDR patients had positive sputum AFB smear and culture, while the patient with MDR lymphadenitis had lymph node aspirate for AFB smear and culture positive with all showing resistance to rifampicin and isoniazid. Gene Xpert on endometrial biopsy or sputum was positive in 5 (83.3%) patients. Three (50%) patients (one primary and two secondary) have completed therapy while other 3 (50%) are in continuation phase. All patients are asymptomatic with one having 12 weeks ongoing successful pregnancy.

CONCLUSION: MDR FGTB should be thought of in women of FGTB with tubo- ovarian masses who are not responding to first line drugs. Gene Xpert can be used in early diagnosis of MDR FGTB.

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115: Sharma SK, Mohan A. Miliary Tuberculosis. *Microbiol Spectr.* 2017 Mar;5(2). doi: 10.1128/microbiolspec.TNMI7-0013-2016. Review. PubMed PMID: 28281441.

Miliary tuberculosis (TB) results from a massive lymphohematogenous dissemination of *Mycobacterium tuberculosis* bacilli and is characterized by tiny tubercles evident on gross pathology resembling millet seeds in size and appearance. The global HIV/AIDS pandemic and widespread use of immunosuppressive drugs and biologicals have altered the epidemiology of miliary TB. Considered to be predominantly a disease of infants and children in the pre-antibiotic era, miliary TB is increasingly being encountered in adults as well. The clinical manifestations of miliary TB are protean and nonspecific. Atypical clinical presentation often delays the diagnosis. Clinicians, therefore, should have a low threshold for suspecting miliary TB. Focused, systematic physical examination helps in identifying the organ system(s) involved, particularly early in TB meningitis, as this has therapeutic significance. Fundus examination for

detecting choroid tubercles offers a valuable clinical clue for early diagnosis, as their presence is pathognomonic of miliary TB. Imaging modalities help in recognizing the miliary pattern, defining the extent of organ system involvement. Examination of sputum, body fluids, image-guided fine-needle aspiration cytology or biopsy from various organ sites, needle biopsy of the liver, bone marrow aspiration, and biopsy should be done to confirm the diagnosis. Cytopathological, histopathological, and molecular testing (e.g., Xpert MTB/RIF and line probe assay), mycobacterial culture, and drug susceptibility testing must be carried out as appropriate and feasible. Miliary TB is uniformly fatal if untreated; therefore, early initiation of specific anti-TB treatment can be lifesaving. Monitoring for complications, such as acute kidney injury, air leak syndromes, acute respiratory distress syndrome, adverse drug reactions such as drug-induced liver injury, and drug-drug interactions (especially in patients coinfecting with HIV/AIDS), is warranted.

DOI: 10.1128/microbiolspec.TNMI7-0013-2016

PMID: 28281441 [Indexed for MEDLINE]

116: Shergill S, Smyrk TC, Sweetser S. A Malignant Mimic. *Gastroenterology*. 2017 Apr;152(5):953-955. doi: 10.1053/j.gastro.2016.11.015. Epub 2017 Mar 1. PubMed PMID: 28259718.

117: Axshya SAMVAD Study Group, Shewade HD, Chadha SS, Gupta V, Tripathy JP, Satyanarayana S, Sagili K, Mohanty S, Bera OP, Pandey P, Rajeswaran P, Jayaraman G, Santhappan A, Bajpai UN, Mamatha AM, Maiser R, Naqvi AJ, Pandurangan S, Nath S, Ghule VH, Das A, Prasad BM, Biswas M, Singh G, Mallick G, Jeyakumar Jaisingh AJ, Rao R, Kumar AMV. Data collection using open access technology in multicentre operational research involving patient interviews. *Public Health Action*. 2017 Mar 21;7(1):74-77. doi: 10.5588/pha.15.0079. PubMed PMID: 28744430; PubMed Central PMCID: PMC5515255.

Conducting multicentre operational research is challenging due to issues related to the logistics of travel, training, supervision, monitoring and troubleshooting support. This is even more burdensome in resource-constrained settings and if the research includes patient interviews. In this article, we describe an innovative model that uses open access tools such as Dropbox, TeamViewer and CamScanner for efficient, quality-assured data collection in an ongoing multicentre operational research study involving record review and patient interviews. The tools used for data collection have been shared for adaptation and use by other researchers.

Publisher: Conduire des recherches opérationnelles multicentriques est un défi, particulièrement dans les contextes de ressources limitées, en tenant compte des questions de logistique de déplacement, de formation, de supervision, de suivi et de soutien à la résolution des problèmes; encore plus si cette recherche implique des entretiens avec des patients. Dans cet article, nous décrivons un modèle innovant qui utilise des outils à accès ouvert comme Dropbox, TeamViewer et CamScanner pour un recueil de données efficace et de qualité assurée dans le cadre d'une recherche opérationnelle continue multicentrique impliquant des revues de dossiers et des entretiens avec des patients. Les outils utilisés pour le recueil de données ont été partagés pour l'adaptation et l'utilisation par d'autres chercheurs. Publisher: La realización de investigaciones operativas multicéntricas puede ser problemática, sobre todo en los entornos con restricción de los recursos, habida cuenta de las dificultades en la organización de los desplazamientos, la capacitación, la supervisión, el seguimiento y el apoyo a la resolución de problemas; más aun, cuando la investigación precisa entrevistas a los pacientes. En el presente artículo se describe un modelo innovador que utiliza herramientas de libre acceso como las plataformas Dropbox, TeamViewer y CamScanner, con el fin de lograr una obtención de datos eficiente y de calidad garantizada, en una investigación operativa multicéntrica en curso que comporta el examen de las historias clínicas y entrevistas a los pacientes. Se comunican las herramientas utilizadas en la recogida de datos, con la finalidad de que otros investigadores puedan adaptarlas y las apliquen.

DOI: 10.5588/pha.15.0079
PMCID: PMC5515255
PMID: 28744430

118: Shruthi M, Gupta N, Jana M, Mridha AR, Kumar A, Agarwal R, Sharma R, Deka D, Gupta AK, Kabra M. Comparative study of conventional and virtual autopsy using postmortem MRI in the phenotypic characterization of stillbirths and malformed fetuses. *Ultrasound Obstet Gynecol.* 2017 Mar 13. doi: 10.1002/uog.17468. [Epub ahead of print] PubMed PMID: 28295775.

OBJECTIVE: To prospectively compare conventional and virtual autopsy using postmortem-MRI in the phenotypic characterization of stillbirths and malformed fetuses and their acceptability to parents.

METHODS: We performed whole body postmortem-MRI (1.5T) prior to conventional autopsy in 43 fetuses/still births (≥ 20 weeks of gestation) after excluding maternal causes of fetal death. With conventional autopsy as gold standard, postmortem-MRI findings were assessed and compared.

RESULTS: Malformations found in postmortem-MRI were compared with conventional autopsy. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of post-mortem MRI with 95% CI, taking conventional autopsy as gold standard respectively were, whole body [77.7% (72.4%-82.4%), 99.8% (99.6%-99.9%), 97.4% (94.4%-99.0%), 97.9% (97.4%-98.4%)], nervous system [93.1% (77.2%-99.15%), 99.0% (97.5%-99.7%), 87.1% (70.2%-96.4%), 99.5% (98.2%-99.9%)], cardiovascular system [60.9% (44.5%-75.8%), 100.0% (99.2%-100.0%), 100.0% (86.3%-100.0%), 96.7% (94.8%-98.1%)], pulmonary system [91.1% (80.4%-97.0%), 100.0% (98.5%-100.0%), 100.0% (93.0%-100.0%), 98.0% (95.4%-99.3%)], abdomen [80.6% (63.9%-91.8%), 99.8% (98.9%-100.0%), 96.7% (82.8%-99.9%), 98.7% (97.3%-99.5%)], renal system [96.1% (80.4%-99.9%), 99.7% (98.1%-99.9%), 96.1% (80.4%-99.9%), 99.7% (98.1%-99.9%)], and musculoskeletal system [66.8% (56.5%-75.8%), 100.0% (99.7%-100.0%), 100.0% (94.6%-100.0%), 97.2% (96.1%-98.1%)]. In 35 (81.4%) out of 43 cases, final diagnosis based on virtual autopsy using postmortem-MRI was concordant with that of conventional autopsy. Virtual autopsy was acceptable to 93.6% of families as compared to conventional autopsy in 82.5%.

CONCLUSION: Virtual autopsy using external examination of fetus, post-mortem MRI and other non-invasive/minimally invasive investigations can be an acceptable alternative to conventional autopsy when refused. Postmortem-MRI provides additional diagnostic information in brain and spinal cord malformations. Also post-mortem MRI is more acceptable to parents.

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DOI: 10.1002/uog.17468
PMID: 28295775

119: Sihota R. Treatment of primary angle-closure glaucoma: Does early lens extraction help? *Natl Med J India.* 2017 Mar-Apr;30(2):78-79. PubMed PMID: 28816215.

120: Singh A, Kumar Gupta A, Gopinath K, Sharma P, Singh S. Evaluation of 5 Novel protein biomarkers for the rapid diagnosis of pulmonary and extra-pulmonary tuberculosis: preliminary results. *Sci Rep.* 2017 Mar 24;7:44121. doi: 10.1038/srep44121. PubMed PMID: 28337993; PubMed Central PMCID: PMC5364505.

Improved methods are required for the early and accurate diagnosis of tuberculosis, especially in the patients with smear-negative disease. Several biomarkers have been tried but most have shown poor sensitivity or specificity. In present study we aimed to evaluate the diagnostic utility of five novel antigens identified earlier by us. This is an initial study conducted on 250 subjects. The five recombinant antigens, named as rSS1 (Rv2145c), rSS2 (Rv0164), rSS3 (Rv1437), rSS4 (Rv1827) and rSS5 (Rv2970c), were expressed in pQE-30 expression vector, purified and their sero-diagnostic efficacy was evaluated in

an unblinded manner using dot-blot and ELISA methods. The sensitivity and specificity of these novel antigens were compared with commercially available standard esat6 and 38kDa antigens. Bacteriologically confirmed TB patients, non-TB disease controls and healthy individuals were included. which are based on novel antigen or novel technology, Area under curve (AUC) of the selected antigens were 0.98 (0.98-0.99) for rSS1, 0.88 (0.84-0.92) for rSS2, 0.88 (0.84-0.92) for rSS3, 0.95 (0.93-0.98) for rSS4 and 0.99 (0.98-1.0) for rSS5. Receiver operative characteristic (ROC) curve showed highly significant difference between TB and healthy subjects ($p < 0.001$). These initial findings, show that the recombinant antigens rSS1, rSS4 and rSS5 could be used as highly potential biomarkers for the serological diagnosis of active TB.

DOI: 10.1038/srep44121
PMCID: PMC5364505
PMID: 28337993

121: Singh A, Mankotia DS, Irshad M. A Single-step Multiplex Quantitative Real Time Polymerase Chain Reaction Assay for Hepatitis C Virus Genotypes. *J Transl Int Med.* 2017 Mar 31;5(1):34-42. doi: 10.1515/jtim-2017-0010. eCollection 2017 Mar. PubMed PMID: 28680837; PubMed Central PMCID: PMC5490960.

BACKGROUND AND OBJECTIVES: The variable response of hepatitis C virus (HCV) genotypes towards anti-viral treatment requires prior information on the genotype status before planning a therapeutic strategy. Although assays for typing or subtyping of HCV are available, however, a fast and reliable assay system is still needed. The present study was planned to develop a single-step multiplex quantitative real time polymerase chain reaction (qPCR) assay to determine HCV genotypes in patients' sera.

METHODS: The conserved sequences from 5' UTR, core and NS5b regions of HCV genome were used to design primers and hydrolysis probes labeled with fluorophores. Starting with the standardization of singleplex (qPCR) for each individual HCV-genotype, the experimental conditions were finally optimized for the development of multiplex assay. The sensitivity and specificity were assessed both for singleplex and multiplex assays. Using the template concentration of 10(2) copies per microliter, the value of quantification cycle (Cq) and the limit of detection (LOD) were also compared for both singleplex and multiplex assays. Similarly, the merit of multiplex assay was also compared with sequence analysis and restriction fragment length polymorphism (RFLP) techniques used for HCV genotyping. In order to find the application of multiplex qPCR assay, it was used for genotyping in a panel of 98 sera positive for HCV RNA after screening a total number of 239 patients with various liver diseases.

RESULTS: The results demonstrated the presence of genotype 1 in 26 of 98 (26.53%) sera, genotype 3 in 65 (66.32%) and genotype 4 in 2 (2.04%) sera samples, respectively. One sample showed mixed infection of genotype 1 and 3. Five samples could not show the presence of any genotype. Genotypes 2, 5 and 6 could not be detected in these sera samples. The analysis of sera by singleplex and RFLP indicated the results of multiplex to be comparable with singleplex and with clear merit of multiplex over RFLP. In addition, the results of multiplex assay were also found to be comparable with those from sequence analysis. The sensitivity, specificity, Cq values and LOD values were compared and found to be closely associated both for singleplex and multiplex assays.

CONCLUSION: The multiplex qPCR assay was found to be a fast, specific and sensitive method that can be used as a technique of choice for HCV genotyping in all routine laboratories.

DOI: 10.1515/jtim-2017-0010
PMCID: PMC5490960
PMID: 28680837

Conflict of interest statement: Conflict of Interest There is no conflict of interest among the authors.

122: Singh G, Kapil U, Sati HC. Physical Activity Level Amongst Rural Children

Aged 12-18 years in Kullu District, Himachal Pradesh. Indian J Pediatr. 2017 Jun;84(6):485-486. doi: 10.1007/s12098-017-2317-1. Epub 2017 Mar 9. PubMed PMID: 28281212.

123: Singh K, Shekhar S, Yadav Y, Xess I, Dey S. DS6: anticandidal, antibiofilm peptide against *Candida tropicalis* and exhibit synergy with commercial drug. J Pept Sci. 2017 Mar;23(3):228-235. doi: 10.1002/psc.2973. Epub 2017 Jan 25. PubMed PMID: 28120548.

Antifungal peptides have gained interest as therapeutic agents in recent years because of increased multidrug resistance against present antifungal drugs. This study designed, synthesized and characterized antifungal activity of a small peptide analogue, DS6. This peptide was designed using the template from the N-terminal part of the antifungal protein, *Aspergillus giganteus*. DS6 inhibited *Candida tropicalis* (ATCC 13803), as well as its clinical isolates. DS6 was found to be a fungicidal, killing the fungus very rapidly. DS6 is also non-toxic to human cells. Synergistic interactions of DS6 with amphotericin B and fluconazole were also evident. DS6 is membrane lytic and exhibits antibiofilm activity against *C. tropicalis*. In conclusion, DS6 may have utility as an alternative antifungal therapy for *C. tropicalis*. Copyright © 2017 European Peptide Society and John Wiley & Sons, Ltd.

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DOI: 10.1002/psc.2973
PMID: 28120548 [Indexed for MEDLINE]

124: Singh N, Rohatgi J, Kumar V. A Prospective Study of Anterior Segment Ocular Parameters in Anisometropia. Korean J Ophthalmol. 2017 Apr;31(2):165-171. doi: 10.3341/kjo.2017.31.2.165. Epub 2017 Mar 21. PubMed PMID: 28367046; PubMed Central PMCID: PMC5368091.

PURPOSE: The aim of this study was to investigate the differences in anterior segment ocular parameters in anisometropia >1 D.
METHODS: This study included 202 eyes of 101 subjects ranging from 10 to 40 years of age with anisometropia of 1 D or more. The subjects were divided into groups according to anisomyopia, anisoastigmatism, and anisohypermetropia. After providing informed consent, each patient underwent a detailed ophthalmological examination including cycloplegic refraction, best-corrected visual acuity, cover test, axial length (AL) measurement using A-scan ultrasound biometer, keratometry, anterior chamber depth, and central corneal thickness measurement. For each participant, the eye with greater refractive error was compared to the fellow eye via paired t-tests. Correlations between parameters were studied using the Pearson correlation coefficient.
RESULTS: The average age of subjects was 21.7 ± 9.3 years. Of 101 subjects, 31 had anisomyopia; 42 had anisohypermetropia; and 28 had anisoastigmatism. A predisposition toward greater myopia in right eyes was noted in anisomyopia (24 of 31 subjects, 77%). The inter-ocular acuity difference was significant in all three groups ($p < 0.01$). As the degree of anisometropia increased, there was significant positive correlation in the difference in AL in myopes ($r = 0.863$, $p < 0.01$) and hypermetropes ($r = 0.669$, $p < 0.01$) and the difference in corneal curvature in anisoastigmatism ($r = 0.564$, $p = 0.002$) and hypermetropes ($r = 0.376$, $p = 0.014$). A significant positive correlation was also present between the anterior chamber depth difference and refractive difference in hypermetropes ($r = 0.359$, $p = 0.020$).
CONCLUSIONS: This study showed that anisomyopia is correlated only with anterior chamber differences. Anisohypermetropia is correlated with AL differences as well as corneal curvature difference and anterior chamber depth difference. The amount of anisoastigmatism correlates only with corneal curvature difference.

DOI: 10.3341/kjo.2017.31.2.165
PMCID: PMC5368091

Conflict of interest statement: Conflict of Interest: No potential conflict of interest relevant to this article was reported.

125: Singh PK, Sirohi HV, Iqbal N, Tiwari P, Kaur P, Sharma S, Singh TP. Structure of bovine lactoperoxidase with a partially linked heme moiety at 1.98Å resolution. *Biochim Biophys Acta*. 2017 Mar;1865(3):329-335. doi: 10.1016/j.bbapap.2016.12.006. Epub 2016 Dec 13. PubMed PMID: 27986533.

Lactoperoxidase (LPO) is a member of mammalian heme peroxidase superfamily whose other members are myeloperoxidase (MPO), eosinophil peroxidase (EPO) and thyroid peroxidase (TPO). In these enzymes, the heme moiety is linked to protein through two or three covalent bonds. In the mature LPO, the heme moiety is linked to protein through two ester bonds with highly conserved glutamate and aspartate residues. The previously reported structures of LPO have confirmed the formation of two covalent linkages involving Glu258 and Asp108 with 1-methyl and 5-methyl groups of pyrrole rings A and C respectively. We report here a new form of structure of LPO where the covalent bond between Glu258 and 1-methyl group of pyrrole ring A is present only in a fraction of protein molecules. In this case, the side chain of Glu258 occupies two distinct positions, each of which has a 0.5 occupancy. In one position, it forms a normal ester covalent linkage while in the second position, the side chain of Glu258 is located in the middle of the substrate binding site on the distal heme side. In this position, the atom of the side chain of Glu258 forms several contacts with atoms of other residues and heme moiety. Out of the two observed positions of the side chain of Glu258, the former contributes to the stabilization of heme position and improved catalytic action of LPO while the latter is responsible for the reduced stability of the heme position as well as it blocks the substrate binding site.

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DOI: 10.1016/j.bbapap.2016.12.006
PMID: 27986533

126: Singh PM, Panwar R, Borle A, Mulier JP, Sinha A, Goudra B. Perioperative analgesic profile of dexmedetomidine infusions in morbidly obese undergoing bariatric surgery: a meta-analysis and trial sequential analysis. *Surg Obes Relat Dis*. 2017 Mar 10. pii: S1550-7289(17)30110-7. doi: 10.1016/j.soard.2017.02.025. [Epub ahead of print] PubMed PMID: 28396128.

BACKGROUND: Opioid-sparing analgesia for bariatric surgery in morbidly obese can potentially prevent catastrophic airway complications. Our meta-analysis attempts to consolidate the evidence on dexmedetomidine evaluating its analgesic and safety profile.

METHODS: Trails comparing perioperative dexmedetomidine infusion to conventional analgesic regimens for bariatric surgery were searched. Comparisons were made for 24-hour and postanesthesia care unit (PACU) morphine consumed, PACU pain scores, postoperative nausea and vomiting pain scores, and heartrate. Meta-regression was performed for length of stay to evaluate various analgesic control subgroups.

RESULTS: Six trials were included in the final analysis. Dexmedetomidine infusion (reported in 5 intraoperative subgroups and 2 postoperative subgroups) decreased 24-hour morphine by 18.13±6.11 mg (random effects: $P < .001$, $I(2) = 95.48\%$). Despite the small number of included studies, the sample size for avoiding a false positive result was adequate as the trial sequential analysis found the present sample size (362) to be well past the required "sample size" ($n = 312$) for 85% power. Meta-regression for infusion dose on morphine consumption difference found a predictability of 49% (coefficient = 39.93, random-effects, $Tau(2) = 396.08$), and predictability of the model improved to 68% on inclusion of time of initiation of infusion. The dexmedetomidine group had lower PACU morphine consumption (by 6.91±1.19, $I(2) = 34.37\%$), lower pain scores (scale of 0-10±2.27, $I(2) = 88.14\%$), lower postoperative nausea and vomiting incidence (odds ratio =±0.26, $I(2) = 0\%$), and lower heart rate (73.25 versus. 83.50) (mean difference

=±10.15 I(2) = 94.04%). No adverse events were reported across trials.
CONCLUSION: Perioperative dexmedetomidine infusion in obese patients undergoing bariatric surgery is a promising and safe alternative. Both intraoperative or postoperative infusions lead to significant opioid sparing in early and extend postoperative recovery phase. Morbidly obese patients receiving perioperative dexmedetomidine infusions have overall better pain control and lower incidence of postoperative nausea-vomiting. All the aforementioned merits come with a stable hemodynamic profile and without any reported major adverse events.

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DOI: 10.1016/j.soard.2017.02.025

PMID: 28396128

127: Singh S, Collins BF, Sharma BB, Joshi JM, Talwar D, Katiyar S, Singh N, Ho L, Samaria JK, Bhattacharya P, Gupta R, Chaudhari S, Singh T, Moond V, Pipavath S, Ahuja J, Chetambath R, Ghoshal AG, Jain NK, Devi HJ, Kant S, Koul P, Dhar R, Swarnakar R, Sharma SK, Roy DJ, Sarmah KR, Jankharia B, Schmidt R, Katiyar SK, Jindal A, Mangal DK, Singh V, Raghu G. Interstitial Lung Disease in India. Results of a Prospective Registry. *Am J Respir Crit Care Med*. 2017 Mar 15;195(6):801-813. doi: 10.1164/rccm.201607-1484OC. PubMed PMID: 27684041.

RATIONALE: Interstitial lung disease (ILD) is a heterogeneous group of acute and chronic inflammatory and fibrotic lung diseases. Existing ILD registries have had variable findings. Little is known about the clinical profile of ILDs in India. OBJECTIVES: To characterize new-onset ILDs in India by creating a prospective ILD using multidisciplinary discussion (MDD) to validate diagnoses.

METHODS: Adult patients of Indian origin living in India with new-onset ILD (27 centers, 19 Indian cities, March 2012-June 2015) without malignancy or infection were included. All had connective tissue disease (CTD) serologies, spirometry, and high-resolution computed tomography chest. ILD pattern was defined by high-resolution computed tomography images. Three groups independently made diagnoses after review of clinical data including that from prompted case report forms: local site investigators, ILD experts at the National Data Coordinating Center (NDCC; Jaipur, India) with MDD, and experienced ILD experts at the Center for ILD (CILD; Seattle, WA) with MDD. Cohen's κ was used to assess reliability of interobserver agreement.

MEASUREMENTS AND MAIN RESULTS: A total of 1,084 patients were recruited. Final diagnosis: hypersensitivity pneumonitis in 47.3% (n=513; exposure, 48.1% air coolers), CTD-ILD in 13.9%, and idiopathic pulmonary fibrosis in 13.7%. Cohen's κ : 0.351 site investigator/CILD, 0.519 site investigator/NDCC, and 0.618 NDCC/CILD.

CONCLUSIONS: Hypersensitivity pneumonitis was the most common new-onset ILD in India, followed by CTD-ILD and idiopathic pulmonary fibrosis; diagnoses varied between site investigators and CILD experts, emphasizing the value of MDD in ILD diagnosis. Prompted case report forms including environmental exposures in prospective registries will likely provide further insight into the etiology and management of ILD worldwide.

DOI: 10.1164/rccm.201607-1484OC

PMID: 27684041 [Indexed for MEDLINE]

128: Singh SK, Mankotia DS, Borkar SA, Gupta UD. Multiple mirror image cervical neurofibromas in neurofibromatosis type 1. *Neurol India*. 2017 Mar-Apr;65(2):428-429. doi: 10.4103/neuroindia.NI_1370_15. PubMed PMID: 28290428.

129: Singh SK, Raheja AA, Jagdevan AK, Singh PK, Purkait S, Suri VA. Malignant temporal muscle myofibroblastoma with an early recurrence in a child. *Neurol India*. 2017 Mar-Apr;65(2):408-410. doi: 10.4103/neuroindia.NI_1241_15. PubMed PMID: 28290416.

130: Singh T, Modi JN, Kumar V, Dhaliwal U, Gupta P, Sood R. Admission to Undergraduate and Postgraduate Medical Courses: Looking Beyond Single Entrance Examinations. *Indian Pediatr.* 2017 Mar 15;54(3):231-238. Epub 2017 Feb 2. PubMed PMID: 28159948.

In India, a single national level entrance examination for admission to undergraduate and postgraduate medical courses has been introduced. This is largely an effort towards alleviating financial corruption in admission process, improving logistics and ease of examination for students, and resource-efficacy in conduct of examination. Unfortunately, the possible educational impact of such single high-stakes examination has not been overtly discussed. A major handicap in doing so is the lack of documentation and analysis of our own experience with multiple entrance examinations over many years. One adverse aspect of a single high-stakes examination, especially the Postgraduate entrance examination, is that the students' learning priorities get redefined to being 'examination-oriented' rather than 'competency-development oriented'. Hence, we must draw lessons from admission processes in other countries that have gone through similar course. Two key effective practices in these countries include giving weightage to prior academic performance, and use of a combination of some form of cognitive testing, aptitude testing and non-cognitive assessment, for taking selection decisions. It is prudent to modify our existent examination processes utilizing the same principles. There is a need to improve the formative assessments and the end-of-training certification examinations, and possibly also include them as inputs for the admission process.

PMID: 28159948 [Indexed for MEDLINE]

131: Sinha A, Gupta A, Kalaivani M, Hari P, Dinda AK, Bagga A. Mycophenolate mofetil is inferior to tacrolimus in sustaining remission in children with idiopathic steroid-resistant nephrotic syndrome. *Kidney Int.* 2017 Jul;92(1):248-257. doi: 10.1016/j.kint.2017.01.019. Epub 2017 Mar 18. PubMed PMID: 28318625.

Studies of nephrotic syndrome show that substitution of calcineurin inhibitors by mycophenolate mofetil (MMF) enables sustained remission and corticosteroid sparing and avoids therapy associated adverse effects. However, controlled studies in patients with steroid resistance are lacking. Here we examined the effect of switching from therapy with tacrolimus to MMF on disease course in an open-label, one-to-one randomized, controlled trial on children (one to 18 years old), recently diagnosed with steroid-resistant nephrotic syndrome, at a referral center in India. Following six months of therapy with tacrolimus, patients with complete or partial remission were randomly assigned such that 29 received MMF while 31 received tacrolimus along with tapering prednisolone on alternate days for 12 months. On intention-to-treat analyses, the proportion of patients with a favorable outcome (sustained remission, infrequent relapses) at one year was significantly lower (44.8%) in the MMF group than in the tacrolimus group (90.3%). The incidence of relapses was significantly higher for patients treated with MMF than tacrolimus (mean difference: 1.05 relapses per person-year). While there was no difference in the proportion of patients with sustained remission, the risk of recurrence of steroid resistance was significantly higher for patients receiving MMF compared to tacrolimus (mean difference: 20.7%). Compared to tacrolimus, patients receiving MMF had a significantly (71%) lower likelihood of a favorable outcome and significantly increased risk of treatment failure (frequent relapses, steroid resistance). Thus, replacing tacrolimus with MMF after six months of tacrolimus therapy for steroid-resistant nephrotic syndrome in children is associated with significant risk of frequent relapses or recurrence of resistance. These findings have implications for guiding the duration of therapy with tacrolimus for steroid-resistant nephrotic syndrome.

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DOI: 10.1016/j.kint.2017.01.019
PMID: 28318625

132: Sokhal N, Rath GP, Chaturvedi A, Singh M, Dash HH. Comparison of 20% mannitol and 3% hypertonic saline on intracranial pressure and systemic hemodynamics. *J Clin Neurosci*. 2017 Aug;42:148-154. doi: 10.1016/j.jocn.2017.03.016. Epub 2017 Mar 22. PubMed PMID: 28342705.

Mannitol and hypertonic saline (HS) are most commonly used hyperosmotic agents for intraoperative brain relaxation. We compared the changes in ICP and systemic hemodynamics after infusion of equiosmolar solutions of both agents in patients undergoing craniotomy for supratentorial tumors. Forty enrolled adults underwent a standard anesthetic induction. Apart from routine monitoring parameters, subdural ICP with Codmann catheter and cardiac indices by Vigileo monitor, were recorded. The patients were randomized to receive equiosmolar solutions of either 20% mannitol (5ml/kg) or 3% HS (5.35ml/kg) for brain relaxation. The time of placement of ICP catheter was marked as T0 and baseline ICP and systemic hemodynamic variables were noted; it was followed by recording of the same parameters every 5min till 45min (Study Period). After the completion of study period, brain relaxation score as assessed by the neurosurgeon was recorded. Arterial blood gas (ABG) was analysed every 30min starting from T0 upto one and half hours (T90), and values of various parameters were recorded. Data was analysed using appropriate statistical methods. Both mannitol and HS significantly reduced the ICP; the values were comparable in between the two groups at most of the times. The brain relaxation score was comparable in both the groups. Urine output was significantly higher with mannitol. The perioperative complications, overall hospital stay, and Glasgow outcome score at discharge were comparable in between the two groups. To conclude, both mannitol and hypertonic saline in equiosmolar concentrations produced comparable effects on ICP reduction, brain relaxation, and systemic hemodynamics.

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DOI: 10.1016/j.jocn.2017.03.016
PMID: 28342705

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134: Srivastava R, Batra A, Dhawan D, Bakhshi S. Association of energy intake and expenditure with obesity: A cross-sectional study of 150 pediatric patients following treatment for leukemia. *Pediatr Hematol Oncol*. 2017 Feb;34(1):29-35. doi: 10.1080/08880018.2016.1272025. Epub 2017 Mar 13. PubMed PMID: 28287332.

Increased obesity in leukemia survivors has been attributed to chemotherapy and radiation. Data on total energy intake (TEI) and total energy expenditure (TEE) are lacking in obese childhood leukemia patients after completion of therapy from India. We conducted a cross-sectional study in pediatric acute leukemia patients after completion of therapy wherein energy intake was assessed by 24-hour recall method. TEE was calculated using Harris-Benedict equation, by assessing the physical activity level using Physical Activity Questionnaire for children and basal metabolic rate by World Health Organization equation. Indian Academy of Pediatrics 2015 guidelines for BMI were used for defining overweight and obesity. Nutritional status was assessed in 150 leukemia patients after completion of therapy. Twenty-five percent of leukemia patients after completion of therapy were overweight and obese versus 11% of healthy controls ($p = 0.042$). The mean ratio of TEI/required energy intake (REI), TEE/required energy expenditure (REE), and (TEI:REI)/(TEE:REE) were significantly higher in overweight and obese group versus nonobese survivors ($p < 0.001$, $p = 0.091$, $p < 0.001$, respectively).

Multivariate analysis showed higher income (HR-2.3, p = 0.04), increased TEI/REI (HR-4, p = 0.049) and higher (TEI:REI)/(TEE:REE) (HR-3.1, p = 0.039) to be significant factors predicting obesity. Obesity in leukemia patients after completion of therapy is associated with increased energy intake, causing imbalance between energy intake and TEE in these patients.

DOI: 10.1080/08880018.2016.1272025
PMID: 28287332 [Indexed for MEDLINE]

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Suicide by inhalation of carbon monoxide is not uncommon and usually involves car exhausts or burning charcoal or defective boilers. We report a case of a 25-year-old man, who committed suicide by inhaling carbon monoxide gas inside a polythene bag in a bathroom. The open carbon monoxide cylinder found inside the polythene bag was purchased online by the deceased a few days earlier. He had stated that the gas would be used for his experiment on the environment. A suicide note recovered from his trouser pocket revealed his intention for a painless death.

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PMID: 27620849 [Indexed for MEDLINE]

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138: Tandon V, Raheja A, Suri A, Chandra PS, Kale SS, Kumar R, Garg A, Kalaivani M, Pandey RM, Sharma BS. Randomized trial for superiority of high field strength intra-operative magnetic resonance imaging guided resection in pituitary surgery. *J Clin Neurosci*. 2017 Mar;37:96-103. doi: 10.1016/j.jocn.2016.10.044. Epub 2016 Nov 18. PubMed PMID: 27876186.

Till date there are no randomized trials to suggest the superiority of intra-operative magnetic resonance imaging (IOMRI) guided trans-sphenoidal pituitary resection over two dimensional fluoroscopic (2D-F) guided resections. We conducted this trial to establish the superiority of IOMRI in pituitary surgery. Primary objective was to compare extent of tumor resection between the two study arms. It was a prospective, randomized, outcome assessor and statistician blinded, two arm (A: IOMRI, n=25 and B: 2D-F, n=25), parallel group clinical trial. 4 patients from IOMRI group cross-over to 2D-F group and were consequently analyzed in latter group, based on modified intent to treat method. A total of 50 patients were enrolled till completion of trial (n=25 in each study arm). Demographic profile and baseline parameters were comparable among the two arms (p>0.05) except for higher number of endoscopic procedures and experienced neurosurgeons (>10years) in arm B (p=0.02, 0.002 respectively). Extent of resection was similar in both study arms (A, 94.9% vs B, 93.6%; p=0.78), despite adjusting for experience of operating surgeon and use of microscope/endoscope for surgical resection. We observed that use of IOMRI helped optimize the extent of resection in 5/20 patients (25%) for pituitary tumor resection in-group A. Present study failed to observe superiority of IOMRI over conventional 2D-F guided resection in pituitary macroadenoma surgery. By use of this technology, younger surgeons could validate their results intra-operatively and hence could increase EOR without causing any increase in complications.

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DOI: 10.1016/j.jocn.2016.10.044
PMID: 27876186 [Indexed for MEDLINE]

139: Tarique M, Saini C, Naqvi RA, Khanna N, Sharma A, Rao DN. IL-12 and IL-23 modulate plasticity of FoxP3(+) regulatory T cells in human Leprosy. *Mol Immunol.* 2017 Mar;83:72-81. doi: 10.1016/j.molimm.2017.01.008. Epub 2017 Jan 19. PubMed PMID: 28110210.

Leprosy is a bacterial disease caused by *M. leprae*. Its clinical spectrum reflects the host's immune response to the *M. leprae* and provide an ideal model to investigate the host pathogen interaction and immunological dysregulation. Tregs are high in leprosy patients and responsible for immune suppression of the host by producing IL-10 and TGF- β cytokines. In leprosy, plasticity of Tregs remain unstudied. This is the first study describing the conversion of Tregs into Th1-like and Th17-like cells using in vitro cytokine therapy in leprosy patients. Peripheral blood mononuclear cells from leprosy patients were isolated and stimulated with *M. leprae* antigen (MLCwA), rIL-12 and rIL-23 for 48h. Expression of FoxP3 in CD4(+)CD25(+) Tregs, intracellular cytokines IFN- γ , TGF- β , IL-10 and IL-17 in Tregs cells were evaluated by flow cytometry (FACS) after stimulation. rIL-12 treatment increases the levels of pStat4 in Tregs and IFN- γ production. In the presence of rIL-23, pStat3(+) and IL-17A(+) cells increase. rIL-12 and r-IL-23 treatment downregulated the FoxP3 expression, IL-10 and TGF- β production by Tregs and enhances the expression of co-stimulatory molecules (CD80, CD86). In conclusion rIL-12 converts Tregs into IFN- γ producing cells through STAT-4 signaling while rIL-23 converts Tregs into IL-17 producing cells through STAT-3 signaling in leprosy patients. This study may helpful to provide a new avenue to overcome the immunosuppression in leprosy patients using in vitro cytokine.

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DOI: 10.1016/j.molimm.2017.01.008
PMID: 28110210

140: Tarique M, Saini C, Naqvi RA, Khanna N, Rao DN. Increased IL-35 producing Tregs and CD19(+)IL-35(+) cells are associated with disease progression in leprosy patients. *Cytokine.* 2017 Mar;91:82-88. doi: 10.1016/j.cyto.2016.12.011. Epub 2016 Dec 27. PubMed PMID: 28038394.

BACKGROUND: The clinical forms of leprosy consist of a spectrum that reflects the host's immune response to the *M. leprae*; it provides an ideal model to study the host pathogen interaction and immunological dysregulation in humans. IL-10 and TGF- β producing Tregs are high in leprosy patients and responsible for immune suppression and *M. leprae* specific T cells anergy. In leprosy, involvement of IL-35 producing Tregs and Bregs remain unstudied.

OBJECTIVE: To study the role of IL-35 producing Tregs and Bregs in the human leprosy.

METHODS: Peripheral blood mononuclear cells from leprosy patients were isolated and stimulated with *M. leprae* antigen (MLCwA) for 48h. Intracellular cytokine IL-35 was evaluated in CD4(+)CD25(+) Tregs, CD19(+) cells by FACS. Expression of PD-1 on CD4(+)CD25(+) Tregs, CD19(+) cells and its ligand (PD-L1) on B cells, CD11c cells were evaluated by flow cytometry (FACS). Serum IL-35 level was estimated by ELISA.

RESULTS: The frequency of IL-35 producing Tregs and Bregs cells were found to be high in leprosy patients ($p < 0.0001$) as compared to healthy controls. These cells produced suppressive cytokine IL-35 which showed positive correlation with bacteriological index (BI) and TGF- β producing Tregs, indicating its suppressive nature. We found higher expression of PD-1 on Tregs, B cell and its ligand (PD-L1) on antigen presenting cells in leprosy patients.

CONCLUSION: This study point out a shift in our understanding of the

immunological features that mediate and regulate the immune suppression and the disease progression in leprosy patients with a new paradigm (IL-35 producing Tregs and Bregs) that is beyond TGF- β and IL-10 producing Treg cells.

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DOI: 10.1016/j.cyto.2016.12.011
PMID: 28038394

141: Tejwani N, Tyagi S, Dass J. Multiple Auer Rod Like Inclusions in Multiple Myeloma. *Indian J Hematol Blood Transfus.* 2017 Mar;33(1):121-122. doi: 10.1007/s12288-016-0744-1. Epub 2016 Nov 5. PubMed PMID: 28194068; PubMed Central PMCID: PMC5280870.

Conflict of interest statement: The authors state that there is no conflict of interest present. Informed Consent Informed consent was taken before bone marrow procedure.

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143: Tiwari A, Gupta VG, Bakhshi S. Newer medical therapies for metastatic soft tissue sarcoma. *Expert Rev Anticancer Ther.* 2017 Mar;17(3):257-270. doi: 10.1080/14737140.2017.1285229. Epub 2017 Feb 6. Review. PubMed PMID: 28103739.

INTRODUCTION: Metastatic/advanced soft tissue sarcoma has a poor prognosis conventionally, treatment options have been limited. In recent years, this area has been a rich ground for research with many new drugs being approved and several more in the pipeline. With multiple new treatment options available, it is vital to keep up pace with this rapidly changing field. Areas covered: Recent data regarding use of novel agents in advanced soft tissue sarcoma is reviewed with a focus on clinical applicability. The goal is to guide the clinician into choosing appropriate lines of therapy for the individual patient in light of recent availability of multiple new treatment options. Expert commentary: Patients with advanced soft tissue sarcoma can expect to receive several lines of therapy in the modern era. Tumor histology should ideally guide the choice of therapy. The new FDA approved second line drugs viz, trabectedin, pazopanib and eribulin should be considered first after failure of doxorubicin-based chemotherapy. Additional options have become available, such as antiangiogenic agents, mTOR inhibitors, and several new molecules targeting specific oncogenic pathways. All these agents have a role in treating soft tissue sarcoma, and careful individualization of therapy can help achieve optimal outcomes in these challenging patients.

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PMID: 28103739 [Indexed for MEDLINE]

144: Tiwari D, Nayak B, Seth A. Good response of an aggressive rare variant of signet ring cell carcinoma of prostate with hormonal therapy. *BMJ Case Rep.* 2017 Mar 8;2017. pii: bcr2016217567. doi: 10.1136/bcr-2016-217567. PubMed PMID: 28275015.

Primary signet ring cell carcinoma (SRCC) of the prostate is a rare entity, characterised by its aggressive nature and dismal prognosis. We report a case of an advanced SRCC of the prostate presenting as a large pelvic mass with obstructive uropathy and rectal involvement managed by complete androgen blockade. At 24 months follow-up, the patient has no evidence of progression or metastasis. Aggressive management with multimodality approach combining surgery, radiation and hormonal ablation can result in long disease-free survival in some patients, despite the aggressive nature of this disease.

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INTRODUCTION: Cancer of the uterine cervix is the fourth most common cancer worldwide among women. However, there is limited data about elderly patients with cervical cancer and gross underrepresentation of elderly patients in clinical trials. Hence, the optimal therapy of such patients is not well formulated. **METHODOLOGY:** We conducted this systematic review of evidence to assess patterns of care in elderly patients with cervical cancer. **RESULTS:** A total of 17,338 publications are reported in PubMed until July, 2016 pertaining to cervical cancer. Out of these, only 24 publications (full length papers or meeting proceedings) reported about clinical outcomes of elderly patients with cervical carcinoma. These publications report data from as early as 1949 to the present. In these publications, out of 14,479 patients aged ≥ 60 years of age, 11,279 (77.89%) received external beam radiation. Concurrent chemotherapy has been used in 11 publications. Brachytherapy usage has been reported in 19 publications. In a few studies, brachytherapy was not used because of fear of toxicity. Overall, low dose rate (LDR) was the most common modality, followed by high dose rate (HDR). The authors have showed technical reasons (48.7%), comorbidities (69.4%) and patient refusal (38.3%) as causes for not delivering brachytherapy. Five-year overall survival (OS) has been found to be inferior to the non-elderly cohort and ranges from 27%-69% for elderly patients compared to 58%-75% in the non-elderly population. An 11% 5year OS has been reported for patients treated with suboptimal radiation dose compared to 74% in those treated with chemo radiotherapy followed by brachytherapy. **CONCLUSION:** Gross underrepresentation of patients above 65years in clinical trials has resulted in treatment dilemmas in the elderly. Newer advances like immunotherapy, hypoxic modifiers, image guided radiation, image guided brachytherapy are promising approaches to reduce treatment complications and optimize outcome in elderly patients in cervical cancer.

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148: Verma G, Vishnoi K, Tyagi A, Jadli M, Singh T, Goel A, Sharma A, Agarwal K, Prasad SC, Pandey D, Sharma S, Mehrotra R, Singh SM, Bharti AC. Characterization of key transcription factors as molecular signatures of HPV-positive and HPV-negative oral cancers. *Cancer Med.* 2017 Mar;6(3):591-604. doi: 10.1002/cam4.983. Epub 2017 Feb 3. PubMed PMID: 28155253; PubMed Central PMCID: PMC5345654.

in oral cancer. Differential expression/activation of specific members of these transcription factors has been documented in HPV-positive oral lesions that respond better to therapy. We performed a comprehensive analysis of differentially expressed, transcriptionally active members of these pivotal signaling mediators to develop specific signatures of HPV-positive and HPV-negative oral lesions by immunohistochemical method that is applicable in low-resource settings. We examined a total of 31 prospective and 30 formalin-fixed, paraffin-embedded tissues from treatment-naïve, histopathologically and clinically confirmed cases diagnosed as oral or oropharyngeal squamous cell carcinoma (OSCC/OPSCC). Following determination of their HPV status by GP5 + /GP6 + PCR, the sequential sections of the tissues were evaluated for expression of JunB, JunD, c-Fos, p50, p65, STAT3, and pSTAT3(Y705), along with two key regulatory proteins pEGFR and p16 by IHC. Independent analysis of JunB and p65 showed direct correlation with HPV positivity, whereas STAT3 and pSTAT3 were inversely correlated. A combined analysis of transcription factors revealed a more restrictive combination, characterized by the presence of AP-1 and NF-κB lacking involvement of STAT3 that strongly correlated with HPV-positive tumors. Presence of STAT3/pSTAT3 with NF-κB irrespective of the presence or absence of AP-1 members was present in HPV-negative lesions. Expression of pSTAT3 strongly correlated with all the AP-1/NF-κB members (except JunD), its upstream activator pEGFR(Y)(1092) , and HPV infection-related negative regulator p16. Overall, we show a simple combination of AP-1, NF-κB, and STAT3 members' expression that may serve as molecular signature of HPV-positive lesions or more broadly the tumors that show better prognosis.

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DOI: 10.1002/cam4.983
PMCID: PMC5345654
PMID: 28155253

149: Yadav HK, Saini GK, Chhabra HS, Panwar PS. Endodontic Management of a Maxillary First Molar with Seven Root Canals Using Spiral Computed Tomography. J Dent (Shiraz). 2017 Mar;18(1):65-69. PubMed PMID: 28293666; PubMed Central PMCID: PMC5338178.

The main objective of this case report is to present a rare root canal configuration of maxillary molar with seven root canals; three mesiobuccal, two palatal and two distobuccal canals diagnosed during treatment procedure confirmed by spiral computed tomography. A thorough knowledge of root canal morphology, proper clinical and radiographic examination, and use of dental operating microscopes are necessary for successful clinical outcomes. This article highlights the variations in the morphology of maxillary first molar and use of the latest techniques in successful diagnosis and negotiation of the additional canals.

PMCID: PMC5338178
PMID: 28293666

Conflict of interest statement: Conflict of interests: The authors deny any conflict of interest that could influence their work.

150: Yadav S, Singh P, Nayak B, Dogra PN. Unusual cause of renal stone following robotic pyeloplasty. BMJ Case Rep. 2017 Mar 13;2017. pii: bcr2017219374. doi: 10.1136/bcr-2017-219374. PubMed PMID: 28289002.

Non-absorbable Hem-o-Lok clips are commonly used for vascular pedicle control or suture stabilisation during laparoscopic or robotic reconstructive procedures. As they are placed close to suture line and with tension, these clips have a propensity to migrate. We report a case of a 22-year-old man with history of bilateral robotic pyeloplasty presenting with left inferior calyceal stone. He

underwent left mini percutaneous nephrolithotomy which revealed an encrusted migrated Hem-o-Lok clip that was used to close the mesenteric window formed during transmesocolic pyeloplasty. Thus, these clips should be used sparingly and only at places where other effective alternatives are unavailable.

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DOI: 10.1136/bcr-2017-219374

PMID: 28289002 [Indexed for MEDLINE]

151: Yadav S, Khandelwal M, Seth A, Saini AK, Dogra PN, Sharma A. Serum microRNA Expression Profiling: Potential Diagnostic Implications of a Panel of Serum microRNAs for Clear Cell Renal Cell Cancer. *Urology*. 2017 Jun;104:64-69. doi: 10.1016/j.urology.2017.03.013. Epub 2017 Mar 20. PubMed PMID: 28336290.

OBJECTIVE: To study the expression profiles of 5 microRNAs in tissue and serum of patients with clear cell renal cell cancer (ccRCC) and evaluate their diagnostic and prognostic potential.

MATERIALS AND METHODS: We prospectively analyzed 30 patients of histologically proven ccRCC and collected 3mL of serum preoperatively and small pieces of tumor and adjacent non-tumor renal tissue intraoperatively. Control serum samples were obtained from 15 patients of non-renal benign diseases. We analyzed 5 miRNAs-miR-34a, miR-141, miR-200c, miR-1233, and miR-21-2. Freshly collected samples were immediately frozen in liquid nitrogen and total RNA was extracted. cDNA was synthesized by reverse transcription, and quantitative polymerase chain reaction was performed to determine relative miRNA expression.

RESULTS: In the renal tissue and serum samples, 3 out of 5 miRNAs were differentially expressed; that is, the expression levels of miR-34a and miR-141 were significantly decreased, whereas that of miR-1233 was significantly increased. Serum miR-34a, miR-141, and miR-1233 were able to diagnose ccRCC with a sensitivity of 80.76%, 75%, and 93.33%, and specificity of 80%, 73.33%, and 100%, respectively, as compared to histopathology. Using a panel of 2 serum miRNAs (miR-141 and miR-1233) ccRCC can be diagnosed with 100% sensitivity and 73.3% specificity.

CONCLUSION: miRNAs are differentially expressed in serum of patients with ccRCC and can be used to diagnose ccRCC with high sensitivity and specificity. Diagnostic sensitivity can be further improved by using a panel of miRNAs and has the potential to serve as novel diagnostic markers of ccRCC.

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DOI: 10.1016/j.urology.2017.03.013

PMID: 28336290