List of publications of AIIMS, New Delhi for the month of February, 2016 [Source: www.pubmed.com].

1: Agarwal B, Pandey S, Roychoudhury A. New technique for closure of an oroantral fistula using platelet-rich fibrin. Br J Oral Maxillofac Surg. 2016 Feb;54(2):e31-2. doi: 10.1016/j.bjoms.2015.09.039. Epub 2015 Dec 14. PubMed PMID: 26699819.

2: Agarwal H, Sebastian LJ, Gaikwad SB, Garg A, Mishra NK. Vein of Galen aneurysmal malformation-clinical and angiographic spectrum with management perspective: an institutional experience. J Neurointerv Surg. 2016 Feb 15. pii: neurintsurg-2015-012137. doi: 10.1136/neurintsurg-2015-012137. [Epub ahead of print] PubMed PMID: 26880722.

BACKGROUND AND PURPOSE: Vein of Galen aneurysmal malformation (VGAM) is a rare developmental intracranial vascular malformation. We analyzed the clinical presentations, imaging findings, angioarchitecture, management options, and outcome in a demographically heterogeneous set of VGAM patients.
METHODS: We retrospectively analyzed cases of VGAM from our departmental archive collected between 1988 and January 2015. Demographic, clinical, therapeutic, and follow-up details were obtained for each patient from the available records.
RESULTS: We identified 36 patients with VGAM including 6 neonates, 18 infants, 7 children aged 2-10 years, and 5 adults. Macrocrania was the commonest presenting feature. Type of fistulae was mural in 14 and choroidal in 18 patients while 4 had a thrombosed sac at presentation. In 3 cases the dilated venous sac had connection with the deep venous system. Bilateral jugular atresia and stenosis were seen in 9 and 6 patients, respectively. Giant venous sac (>4 cm) was significantly correlated with mural type (p=0.0001). Dural arterial recruitment was seen in 4 patients including 3 adults. Among the 23 patients treated by endovascular means, 14 had a good outcome, 5 had a poor outcome, and 4 died. A significant correlation was noted between jugular atresia and poor outcome (p=0.003).
CONCLUSIONS: We encountered a wide range of demographic, clinical, and angiographic features in VGAM. Mural type malformations were associated with giant venous sacs. Good outcome after embolization was seen in selected neonates and in most of the infants, children, and adults. Jugular atresia was significantly associated with poor outcome.

DOI: 10.1136/neurintsurg-2015-012137
PMID: 26880722 [PubMed - as supplied by publisher]

3: Agarwal S, George J, Padhan RK, Vadiraja PK, Behera S, Hasan A, Dhingra R, Shalimar, Garg PK. Reduction in mortality in severe acute pancreatitis: A time trend analysis over 16 years. Pancreatology. 2016 Mar-Apr;16(2):194-9. doi: 10.1016/j.pan.2016.01.012. Epub 2016 Feb 10. PubMed PMID: 26915280.

BACKGROUND: The trend in the outcome of patients with acute pancreatitis (AP) as a result of evolving management practices is not known.
OBJECTIVE: To study and compare the outcomes of patients with AP at a tertiary care academic center over a period of 16 years.
METHODS: In a retrospective study on a prospectively acquired database of patients with AP, we analyzed time trends of severity and mortality of AP. The influence of determinants of severity [APACHE II score, organ failure (OF), infected pancreatic necrosis (IPN)], and management strategy on the actual and predicted mortality was assessed. The actual mortality was adjusted for severity to analyze the severity-adjusted mortality at different times as a reflection of management practices over time.
RESULTS: A total of 1333 patients were studied. The number of patients hospitalized with AP has been increasing over time. The proportion of patients with severe AP also increased from 1997 to 2013 as shown by increasing incidence

of organ failure and IPN (Spearman's rank correlation coefficient (ρ): OF ρ(17) = 0.797, p < 0.01; IPN ρ(17) = 0.739, p < 0.001), indicating an increasing referral of sicker patients. Consequently, the overall mortality has been increasing (ρ(17) = 0.584; p = 0.014). However, despite increasing severity of AP, the mortality adjusted for OF has decreased significantly (ρ(17) = -0.55, p = 0.02).
CONCLUSION: Even with increasing proportion of patients with severe AP, there has been a significant decrease in organ failure adjusted mortality due to AP suggesting improved management over years.

DOI: 10.1016/j.pan.2016.01.012
PMID: 26915280 [PubMed - in process]

4: Aggarwal R, Gogtay N, Kumar R, Sahni P; Indian Association of Medical Journal Editors. The revised guidelines of the Medical Council of India for academic promotions: Need for a rethink. Indian J Gastroenterol. 2016 Jan;35(1):3-6. doi: 10.1007/s12664-015-0617-9. Epub 2016 Feb 5. PubMed PMID: 26846881.

Collaborators: Abbas Z, Abraham P, Aggarwal A, Bhaskar SB, Bhaumik S, Deepak KK, Desai C, Divakar MC, Goel A, Krishna VG, Grewal A, Gupta OP, Iyer P, Jain V, Jesani A, Kadri SM, Kapil A, Katoch VM, Kulkarni GK, Kumar A, Kumar S, Malik GM, Mallath MK, Mathur VP, Mishra S, Misra V, Mohan A, Nundy S, Pai SA, Patwardhan B, Prakash A, Ramakrishna BS, Raveenthiran V, Sachdev HP, Sarin YK, Shah C, Shah D, Rao PV, Suresh N, Thomas G, Yadav M.

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DOI: 10.1007/s12664-015-0617-9
PMID: 26846881 [PubMed - in process]

5: Ahuja V, Subodh S, Tuteja A, Mishra V, Garg SK, Gupta N, Makharia G, Acharya SK. Genome-wide gene expression analysis for target genes to differentiate patients with intestinal tuberculosis and Crohn's disease and discriminative value of FOXP3 mRNA expression. Gastroenterol Rep (Oxf). 2016 Feb;4(1):59-67. doi: 10.1093/gastro/gov015. Epub 2015 May 11. PubMed PMID: 25969456; PubMed Central PMCID: PMC4760064.

BACKGROUND AND AIMS: Crohn's disease (CD) and intestinal tuberculosis (ITB) are both chronic granulomatous conditions with similar phenotypic presentations. Hence, there is need for a biomarker to differentiate between both these two diseases. This study aimed at genome-wide gene expression analysis of colonic biopsies from confirmed cases of ITB and CD in comparison with controls. To evaluate the role of T regulatory cells, forkhead box P3 (FOXP3) mRNA expression was quantified in serum as well as in colonic biopsies from patients with ITB and with the controls.
METHODS: Paired samples, including serum and colonic biopsies, were taken from 33 study subjects (CD, ITB and controls), and total RNA was extracted. Human whole genome gene expression microarray analysis was performed using the Illumina HumanWG-6 BeadChip Kit with six total RNA samples of the three groups in duplicates. Real-time PCR for FOXP3 mRNA expression was analyzed in serum samples and colonic biopsy samples (4-CD, 5-ITB, 4-controls).
RESULTS: In CD and ITB there was 1.5-fold upregulation of 92 and 382 genes and 1.5-fold downregulation of 91 and 256 genes, respectively. Peroxisome proliferators via the PPARγ pathway were most significantly downregulated ($P<0.005$) in CD. Additionally, the IL4/5/6 signaling pathways and Toll-like receptor signaling pathway were identified as significantly differentially

regulated (P<0.005) at>2-fold change. In ITB, the complement activation pathway, specifically the classical pathway, was the most significantly upregulated. FOXP3 mRNA expression was significantly elevated in colonic biopsies obtained from ITB patients as compared with CD cases (4.70±2.21 vs 1.48±0.31, P=0.016).
CONCLUSIONS: FOXP3 mRNA expression in colonic mucosa could be a discriminatory marker between ITB and CD. Upregulation of the complement activation pathway in ITB suggests that pathogenetic mechanisms for ITB are similar to those of pulmonary tuberculosis. In CD, downregulation of PPARγ was seen in colonic tissue, suggesting that restoration of PPARγ-dependent anti-microbial barrier function may be a therapeutic target.

DOI: 10.1093/gastro/gov015
PMCID: PMC4760064
PMID: 25969456 [PubMed]

6: Arora G, Dubey P, Shukla J, Ghosh S, Bandopadhyaya G. Evaluation of cytotoxic and tumor targeting capability of (177)Lu-DOTATATE-nanoparticles: a trailblazing strategy in peptide receptor radionuclide therapy. Ann Nucl Med. 2016 Jun;30(5):334-45. doi: 10.1007/s12149-016-1067-x. Epub 2016 Feb 20. PubMed PMID: 26897009.

OBJECTIVE: We propose an innovative strategy of nanoparticle-mediated-peptide receptor radionuclide therapy (PRRT) employing PLGA-nanoparticles together with anti-β-hCG antibodies that can protect kidneys from radiation damage while simultaneously enhancing its tumor targeting and cytotoxic ability for somatostatin receptor (SSR) positive tumors.
METHODS: PEG-coated-(177)Lu-DOTATATE-PLGA-nanoparticles (PEG-LuD-NP) were formulated and characterized. In vitro toxicity of these particles was tested on human glioblastoma cell line U87MG over a radiation dose range of 19-78 Gy, using MTT assay and flow cytometry. To further enhance cytotoxicity and test the feasibility of active tumor targeting, apoptosis-inducing anti-β-hCG monoclonal antibodies were employed in vitro, after confirming expression of β-hCG on U87MG. In vivo tumor targeting ability of these particles, in comparison to uncoated particles and un-encapsulated (177)Lu-DOTATATE, was assessed by intravenous administration in tumor-induced wistar rats. Rats were first imaged in a gamma camera followed by euthanasia for organ extraction and counting in gamma counter.
RESULTS: The particles were spherical in shape with mean diameter of 300 nm. Highest cytotoxicity that could be achieved with PEG-LuD-NP, on radio-resistant U87MG cells, was 35.8 % due to complex cellular response triggered by ionizing radiation. Interestingly, synergistic action of antibodies and PEG-LuD-NP doubled the cytotoxicity (80 %). PEG-LuD-NP showed the highest tumor uptake (4.3 ± 0.46 % ID/g) as compared to (177)Lu-DOTATATE (3.5 ± 0.31 %) and uncoated-(177)Lu-DOTATATE-nanoparticles (3.4 ± 0.35 %) in tumor-inoculated wistar rats ($p < 0.001$). Renal uptake/retention was decreased 3-4 folds with these particles, resulting in the highest tumor-to-kidney ratio (8.58; $p < 0.01$) while tumor-to-liver and tumor-to-bone ratios were comparable to un-encapsulated-drug.
CONCLUSION: Nanocarrier-mediated-PRRT is an effective way of targeting SSR positive tumors for enhanced cytoxicity and reduced renal radiation dose associated with conventional PRRT. To our knowledge of literature, this is the first study to establish in vitro and in vivo efficacy profile of nanoparticles in PRRT providing a stepping-stone for undergoing and future research endeavors in the direction of abating associated radiation concerns of radionuclide therapy and may offer a paradigm shift in PRRT strategy.

DOI: 10.1007/s12149-016-1067-x
PMID: 26897009 [PubMed - in process]

7: Bagchi S, Singh G, Yadav R, Kalaivani M, Mahajan S, Bhowmik D, Dinda A, Agarwal SK. Clinical and histopathologic profile of patients with primary IgA

nephropathy seen in a tertiary hospital in India. Ren Fail. 2016;38(3):431-6. doi: 10.3109/0886022X.2016.1138817. Epub 2016 Feb 2. PubMed PMID: 26837482.

BACKGROUND: IgA nephropathy (IgAN) is known to have an aggressive course in Asians. There is a paucity of data regarding the Oxford classification pattern of Indian patients with IgAN. This study aims to characterize the clinical and histopathologic profile of these patients.
METHODS: All patients diagnosed to have primary IgAN by kidney biopsy in the nephrology department from July 2009 to July 2014 were included in this study. All kidney biopsies were reviewed and the MEST score was assigned as per the Oxford classification. The clinical features and Oxford classification score of patients were characterized.
RESULTS: Nephrotic range proteinuria (NRP) (65/103, 63.1%) with or without edema was the commonest presentation. 67.0% patients had eGFR ≥60 mL/min and 16.5% patients had eGFR <30 mL/min. Of the 103 patients, 80 (77.7%) had M1, 10 (9.7%) had E1, 45 (43.7%) had S1 and 41 (39.8%) had T1/T2 lesions by the Oxford criteria and 11 (10.7%) patients had crescents. 62 patients had eGFR ≥30 mL/min and follow up for at least 6 months (median -17.7 (6-65.1) months) of whom 52(83.9%) had received ACEi/ARBs and 38 (61.3%) had received immunosuppression. 11/62 (17.7%) patients developed renal worsening in this period of which 7 (11.3%) developed end stage kidney disease (ESKD).
CONCLUSION: Indian patients with primary IgA nephropathy have a unique profile. They commonly present with nephrotic range proteinuria. A significant proportion of these patients have normal renal function despite heavy proteinuria. Mesangial proliferative lesions are predominant with a paucity of endocapillary proliferation and crescents compared to other Asian populations. Immunosuppressive use is more common in Indian patients.

DOI: 10.3109/0886022X.2016.1138817
PMID: 26837482 [PubMed - in process]

8: Bansal M, Sarat Chandra K, Nair T, Iyengar SS, Gupta R, Manchanda SC, Mohanan PP, Dayasagar Rao V, Manjunath CN, Sawhney JP, Sinha N, Pancholia AK, Mishra S, Kasliwal RR, Kumar S, Krishnan U, Kalra S, Misra A, Shrivastava U, Gulati S. Consensus statement on the management of dyslipidemia in Indian subjects: Our perspective. Indian Heart J. 2016 Mar-Apr;68(2):238-41. doi: 10.1016/j.ihj.2016.02.003. Epub 2016 Feb 23. PubMed PMID: 27133351; PubMed Central PMCID: PMC4867022.

9: Bansal SK, Jaiswal D, Gupta N, Singh K, Dada R, Sankhwar SN, Gupta G, Rajender S. Gr/gr deletions on Y-chromosome correlate with male infertility: an original study, meta-analyses, and trial sequential analyses. Sci Rep. 2016 Feb 15;6:19798. doi: 10.1038/srep19798. PubMed PMID: 26876364; PubMed Central PMCID: PMC4753437.

We analyzed the AZFc region of the Y-chromosome for complete (b2/b4) and distinct partial deletions (gr/gr, b1/b3, b2/b3) in 822 infertile and 225 proven fertile men. We observed complete AZFc deletions in 0.97% and partial deletions in 6.20% of the cases. Among partial deletions, the frequency of gr/gr deletions was the highest (5.84%). The comparison of partial deletion data between cases and controls suggested a significant association of the gr/gr deletions with infertility (P = 0.0004); however, the other partial deletions did not correlate with infertility. In cohort analysis, men with gr/gr deletions had a relatively poor sperm count (54.20 ± 57.45 million/ml) in comparison to those without deletions (72.49 ± 60.06), though the difference was not statistically significant (p = 0.071). Meta-analysis also suggested that gr/gr deletions are significantly associated with male infertility risk (OR = 1.821, 95% CI = 1.39-2.37, p = 0.000). We also performed trial sequential analyses that strengthened the evidence for an overall significant association of gr/gr deletions with the risk of male infertility. Another meta-analysis suggested a significant association of the gr/gr deletions with low sperm count. In conclusion, the gr/gr deletions show a strong correlation with male infertility

risk and low sperm count, particularly in the Caucasian populations.

DOI: 10.1038/srep19798
PMCID: PMC4753437
PMID: 26876364 [PubMed - in process]

10: Batra A, Kumari M, Paul R, Patekar M, Dhawan D, Bakhshi S. Quality of Life Assessment in Retinoblastoma: A Cross-Sectional Study of 122 Survivors from India. Pediatr Blood Cancer. 2016 Feb;63(2):313-7. doi: 10.1002/pbc.25781. Epub 2015 Oct 21. PubMed PMID: 26488435.

BACKGROUND: With current modalities, cure rates of retinoblastoma are high and hence the number of survivors is increasing. However, data on quality of life (QOL) are minimal.
PROCEDURE: We analyzed QOL in 122 retinoblastoma survivors using the PedsQL(TM) 4.0 generic core scale. The self-reported questionnaire was filled by children of more than 5 years of age who had completed treatment for more than 12 months. The questionnaire consists of 23 questions on physical, social, emotional, and school domains on a scale from 0 to 4. This was converted to a scale from 0 to 100, where higher values represented better QOL. The QOL was compared with 50 siblings. Factors predicting the QOL were assessed.
RESULTS: The median age of retinoblastoma survivors was 98 months (range 60-247) and 68% were males. Overall QOL was significantly poorer in retinoblastoma survivors as compared with the controls. The emotional health domain of QOL was significantly affected. Difficulties in maintaining friendships and competing were reported in the social health domain. The school health domain showed significantly higher absenteeism. However, the physical health domain, including household work, exercise, and self-care, was similar in both the groups. Lower age at diagnosis (≤ 18 months) predicted better QOL (P = 0.05), whereas age at assessment, sex, IRSS stage, and previous surgery and radiotherapy were not predictive of poor QOL.
CONCLUSIONS: We found a significantly poorer QOL in retinoblastoma survivors with the psychosocial health domain being more affected than the physical domain. Age less than 18 months at diagnosis predicted better QOL.

DOI: 10.1002/pbc.25781
PMID: 26488435 [PubMed - indexed for MEDLINE]

11: Behera C, Sikary AK, Krishna K, Garg A, Chopra S, Gupta SK. Medico-legal autopsy of abandoned foetuses and newborns in India. Med Leg J. 2016 Jun;84(2):109-11. doi: 10.1177/0025817216631456. Epub 2016 Feb 8. PubMed PMID: 26857075.

Foeticide and the abandonment of newborns are important, albeit frequently neglected, issues. Concealment of childbirth is often seen in the setting of unwanted pregnancy which has been recognised as one of the most important factors in both cases. This study highlights the medico-legal autopsy findings of 238 abandoned foetuses and newborns over a period of 17 years (1996-2012) from the region of South Delhi, India. There was no sex predilection. The majority of the cases were full term. Nearly 35% of the foetuses were still born, about 29% were live born and the remainder were non-viable. Among the live born, death by homicide was more common than a natural death and most were left by the roadside. The abandoning and killing of newborns needs urgent attention, and strict measures are needed to save thousands of innocent lives.

DOI: 10.1177/0025817216631456
PMID: 26857075 [PubMed - in process]

12: Behera C, Chopra S, Garg A, Kumar R. Sulphuric acid marketed in water bottle in India: A cause for fatal accidental poisoning in an adult. Med Leg J. 2016 Jun;84(2):97-100. doi: 10.1177/0025817216629857. Epub 2016 Feb 2. PubMed PMID: 26837566.

Corrosive acid ingestion is a rare but serious health hazard with fatal complications. Cases of suicidal and accidental acid ingestion have been documented in the scientific literature. Accidental acid poisoning due to a mistaken identity of the bottle containing sulphuric acid is a matter of grave concern especially in a household set-up. We hereby report a fatal case of accidental sulphuric acid ingestion in an adult, who unsuspectingly swallowed about 50 ml of 'toilet-cleaner' at his residence. The bottle containing the acid was recently purchased from a local vendor and placed with water bottles in the kitchen. The autopsy and toxicological findings of this case are discussed in this paper with discussion of medico-legal issues on the sale and use of such corrosive acids in illegal bottles and its subsequent health hazards in India.

DOI: 10.1177/0025817216629857
PMID: 26837566 [PubMed - in process]

13: Bhagat M, Palanichamy JK, Ramalingam P, Mudassir M, Irshad K, Chosdol K, Sarkar C, Seth P, Goswami S, Sinha S, Chattopadhyay P. HIF-2Î± mediates a marked increase in migration and stemness characteristics in a subset of glioma cells under hypoxia by activating an Oct-4/Sox-2-Mena (INV) axis. Int J Biochem Cell Biol. 2016 May;74:60-71. doi: 10.1016/j.biocel.2016.02.017. Epub 2016 Feb 26. PubMed PMID: 26923292.

Hypoxia is a salient feature of most solid tumors and plays a central role in tumor progression owing to its multiple contributions to therapeutic resistance, metastasis, angiogenesis and stemness properties. Reports exist in literature about hypoxia increasing stemness characteristics and invasiveness potential of malignant cells. In order to delineate molecular crosstalk among factors driving glioma progression, we used knockdown and overexpression strategies. We have demonstrated that U87MG and A172 glioma cells inherently have a subset of cells with high migratory potential due to migration-inducing Mena transcripts. These cells also have elevated stemness markers (Sox-2 and Oct-4). There was a significant increase of number in this subset of migratory cells on exposure to hypoxia with corresponding elevation (over 1000 fold) in migration-inducing Mena transcripts. We were able to demonstrate that a HIF-2α-Sox-2/Oct-4-Mena (INV) axis that is strongly activated in hypoxia and markedly increases the migratory potential of the cells. Such cells also formed tumor spheres with greater efficiency. We have correlated our in-vitro results with human glioblastoma samples and found that hypoxia, invasiveness and stemness markers correlated well in native tumor samples. This study identifies a novel signaling mechanism mediated by HIF-2α in regulating invasiveness and stemness characteristics, suggesting that under hypoxic conditions, some tumor cells acquire more migratory potential by increased Pan Mena and Mena INV expression as a consequence of this HIF-2α mediated increase in Oct-4 and Sox-2. These properties would help the cells to form a new nidus after local invasion or metastasis.

DOI: 10.1016/j.biocel.2016.02.017
PMID: 26923292 [PubMed - in process]

14: Bhat A, Upadhyay A, Jaiswal V, Chawla D, Singh D, Kumar M, Yadav CP. Validity of non-invasive point-of-care hemoglobin estimation in healthy and sick children-a method comparison study. Eur J Pediatr. 2016 Feb;175(2):171-9. doi: 10.1007/s00431-015-2602-9. Epub 2015 Aug 19. PubMed PMID: 26286814.

This study was conducted at a tertiary care center in northern India to evaluate the validity of non-invasive transcutaneous hemoglobin estimation in healthy and sick children in comparison to hemoglobin estimation by traditional lab method. A method comparison study was conducted including 150 subjects. Enrolled patients included 80 neonates with average age of 3.9±2.1 days, and 70 children with average age of 5.8±2 years. Each population (newborn and children) comprised of almost equal numbers of healthy and critically ill patients with shock. Hemoglobin (Hb) was estimated on enrolment by transcutaneous spectrophotometry (SpHb) and traditional automated lab analyzer (Hb-Lab). Difference between Hb levels by the two methods (called bias) was measured and analyzed using Bland-Altman method. Out of 148 data pairs analyzed, bias between SpHb and Hb-Lab was -1.52±1.91 g/dl (mean ± SD). SpHb showed excellent positive correlation with Hb-Lab ($r=0.94$ ($p<0.001$)) and good visual agreement on Bland-Altman plots. Bias was higher in sick subjects with shock as compared to healthy ones in both neonatal and pediatric population (-2.31±2.21 g/dl versus -0.77±1.2 g/dl, respectively).CONCLUSIONS: SpHb showed good accuracy and correlated well with lab estimated Hb levels in healthy children. However, in children with impaired peripheral perfusion, its diagnostic accuracy was inadequate to justify routine use for quantification of severity of anemia and making transfusion decisions solely on non-invasive estimation of hemoglobin.
WHAT IS KNOWN: Non-invasive hemoglobin estimation is a relatively new and novel method which has given mixed results regarding its potential efficacy in adults. There is limited data regarding usefulness and accuracy of non-invasive Hb estimation by SpHb in sick neonates and children.
WHAT IS NEW: Non-invasive Hb estimation by SpHb monitor is reasonably accurate in healthy neonates and children. It can be used in critically ill children and neonates, but in conjunction with lab confirmation of Hb values.

DOI: 10.1007/s00431-015-2602-9
PMID: 26286814 [PubMed - in process]

15: Bhatia R, Kataria V, Vibha D, Kakkar A, Prasad K, Mathur S, Garg A, Bakhshi S. Mystery Case: Neurocutaneous melanosis with diffuse leptomeningeal malignant melanoma in an adult. Neurology. 2016 Feb 23;86(8):e75-9. doi: 10.1212/WNL.0000000000002396. PubMed PMID: 26903493.

16: Bhavani GS, Shah H, Shukla A, Gupta N, Gowrishankar K, Rao AP, Kabra M, Agarwal M, Ranganath P, Ekbote AV, Phadke SR, Kamath A, Dalal A, Girisha KM. Clinical and mutation profile of multicentric osteolysis nodulosis and arthropathy. Am J Med Genet A. 2016 Feb;170A(2):410-7. doi: 10.1002/ajmg.a.37447. Epub 2015 Nov 24. PubMed PMID: 26601801.

Multicentric osteolysis nodulosis and arthropathy (MONA) is an infrequently described autosomal recessive skeletal dysplasia characterized by progressive osteolysis and arthropathy. Inactivating mutations in MMP2, encoding matrix metalloproteinase-2, are known to cause this disorder. Fifteen families with mutations in MMP2 have been reported in literature. In this study we screened thirteen individuals from eleven families for MMP2 mutations and identified eight mutations (five novel and three known variants). We characterize the clinical, radiographic and molecular findings in all individuals with molecularly proven MONA from the present cohort and previous reports, and provide a comprehensive review of the MMP2 related disorders.

DOI: 10.1002/ajmg.a.37447
PMID: 26601801 [PubMed - in process]

17: Chawla B, Hasan F, Azad R, Seth R, Upadhyay AD, Pathy S, Pandey RM. Clinical presentation and survival of retinoblastoma in Indian children. Br J Ophthalmol. 2016 Feb;100(2):172-8. doi: 10.1136/bjophthalmol-2015-306672. Epub 2015 Jun 10. PubMed PMID: 26061162.

OBJECTIVE: To study the clinical presentation and survival among Indian children with retinoblastoma (RB) and to determine factors predictive of poor outcome.
METHODS: A retrospective review of children newly diagnosed with RB at a tertiary referral centre was undertaken. Demographic and clinical characteristics and treatment outcomes were studied.
RESULTS: A total of 600 patients (unilateral 67.6%, bilateral 32.4%) was studied. 61% was boys. The median age at presentation was 29 months (18 months vs 36 months in bilateral and unilateral cases, respectively, p<0.001). leukocoria was most common (83%), followed by proptosis (17%). Tumours were intraocular in 72.3% and extraocular in 27.7% cases. In the intraocular group, 78% were advanced Group D or E disease. Metastasis to the central nervous system was noted in 15.7% of extraocular cases. A statistically significant difference was seen between intraocular and extraocular groups in the median age (24 months vs 37.5 months, p<0.001) and median lag period (2.5 months vs 7 months, p<0.001). The Kaplan-Meier survival probability was 83%, 73% and 65% at 1 year, 2 years and 5 years, respectively. On univariate analysis, age >2 years (p=0.002), lag period >6 months (p=0.004) and extraocular stage (p<0.001) were associated with poor outcome. On multivariate analysis, extraocular invasion was predictive of low survival (HR 5.04, p<0.001).
CONCLUSIONS: Delayed presentation is a matter of concern. Improving awareness about the early signs and creating facilities for diagnosing and treating RB at the primary and secondary levels of healthcare are required to reduce mortality and morbidity, and lead to improved outcomes that are comparable with the developed nations.

DOI: 10.1136/bjophthalmol-2015-306672
PMID: 26061162 [PubMed - indexed for MEDLINE]

18: Das A, Bhalla AS, Sharma R, Kumar A, Sharma M, Gamanagatti S, Thakar A, Sharma S. Benign neck masses showing restricted diffusion: Is there a histological basis for discordant behavior? World J Radiol. 2016 Feb 28;8(2):174-82. doi: 10.4329/wjr.v8.i2.174. Review. PubMed PMID: 26981226; PubMed Central PMCID: PMC4770179.

Diffusion weighted imaging (DWI) evolved as a complementary tool to morphologic imaging by offering additional functional information about lesions. Although the technique utilizes movement of water molecules to characterize biological tissues in terms of their cellularity, there are other factors related to the histological constitution of lesions which can have a significant bearing on DWI. Benign lesions with atypical histology including presence of lymphoid stroma, inherently increased cellularity or abundant extracellular collagen can impede movement of water molecules similar to malignant tissues and thereby, show restricted diffusion. Knowledge of these atypical entities while interpreting DWI in clinical practice can avoid potential misdiagnosis. This review aims to present an imaging spectrum of such benign neck masses which, owing to their distinct histology, can show discordant behavior on DWI.

DOI: 10.4329/wjr.v8.i2.174
PMCID: PMC4770179
PMID: 26981226 [PubMed]

19: Das RR, Sankar J, Sankar MJ. Sick Neonate Score: Better than Others in Resource Restricted Settings? Indian J Pediatr. 2016 Feb;83(2):97-8. doi: 10.1007/s12098-015-2005-y. Epub 2016 Jan 9. PubMed PMID: 26747080.

20: Dash C, Gurjar H, Garg K, Sharma BS, Singla R. Massive life-threatening bifrontal epidural hematoma following placement of an external ventricular drain. Childs Nerv Syst. 2016 Feb;32(2):237-9. doi: 10.1007/s00381-015-2985-y. Epub 2016 Jan 6. PubMed PMID: 26738872.

21: Dhingra K, Vandana KL. Effectiveness of Azadirachta indica (neem) mouthrinse in plaque and gingivitis control: a systematic review. Int J Dent Hyg. 2016 Feb 15. doi: 10.1111/idh.12191. [Epub ahead of print] Review. PubMed PMID: 26876277.

OBJECTIVES: The aim of this systematic review was to evaluate the effectiveness of Azadirachta indica (neem)-based herbal mouthrinse in improving plaque control and gingival health.
METHODS: Literature search was accomplished using electronic databases (PubMed, Cochrane Central Register of Controlled Trials and EMBASE) and manual searching, up to February 2015, for randomized controlled trials (RCTs) presenting clinical data for efficacy of neem mouthrinses when used alone or as an adjunct to mechanical oral hygiene as compared to chlorhexidine mouthrinses for controlling plaque and gingival inflammation in patients with gingivitis.
RESULTS: Of the total 206 articles searched, three randomized controlled trials evaluating neem-based herbal mouthrinses were included. Due to marked heterogeneity observed in study characteristics, meta-analysis was not performed. These studies reported that neem mouthrinse was as effective as chlorhexidine mouthrinse when used as an adjunct to toothbrushing in reducing plaque and gingival inflammation in gingivitis patients. However, the quality of reporting and evidence along with methods of studies was generally flawed with unclear risk of bias.
CONCLUSION: Despite the promising results shown in existing randomized controlled trials, the evidence concerning the clinical use of neem mouthrinses is lacking and needs further reinforcement with high-quality randomized controlled trials based on the reporting guidelines of herbal CONSORT statement.

DOI: 10.1111/idh.12191
PMID: 26876277 [PubMed - as supplied by publisher]

22: Dhull VS, Khangembam BC, Sharma P, Rana N, Verma S, Sharma D, Shamim SA, Kumar S, Kumar R. Surgical Scar Site Recurrence in Patients With Cervical Cancer on 18F-FDG PET-CT: A Case-Control Study. Int J Gynecol Cancer. 2016 Feb;26(2):354-60. doi: 10.1097/IGC.0000000000000623. PubMed PMID: 26807566.

PURPOSE: The purpose of this study was to assess the role of fluorine 18 ((18)F)-fluorodeoxyglucose positron emission tomography-computed tomography ((18)F-FDG PET-CT) in evaluating various parameters in patients with surgical scar site recurrence in cervical carcinoma.
METHODS: Data of all patients with cervical cancer (n = 329) who underwent PET-CT at our institute between 2005 and 2013 was reviewed. Of these 329 patients, 132 patients who were surgically treated and underwent restaging/follow-up PET-CT were included in the present study for final analysis. Tumor recurrence at the abdominal surgical scar site was looked for. Abnormal uptakes suggestive of active disease at other sites were also noted. Maximum standardized uptake value was measured for all the lesions. Patients with scar site recurrence were taken as cases (n = 6), whereas the remaining patients served as controls (n = 126). Comparison with conventional imaging modalities was made wherever available. Histopathological examination was always sought for.
RESULTS: The incidence of scar site recurrence after surgery was found to be 4.5% (6/117). A total of 56 of 132 patients had recurrent disease, including 6 patients with scar site recurrence. All of the patients with scar site recurrence also had recurrent disease at other sites (local, nodal, or distant).

Conventional imaging modalities were available in 4 of these 6 patients and detected scar site recurrence in 3 of those 4 patients. In patients with scar site recurrence, the mean ± SD time to scar site recurrence was 14.0 ± 10.9 months (median, 10 months; range, 7-36 months). Significant difference was seen between cases and control for International Federation of Genecology and Oncology stage (P = 0.001) and nodal recurrence (P = 0.007). Additionally, age, nodal recurrence, distant recurrence, and scar site recurrence were significantly associated with death.
CONCLUSIONS: Scar site recurrence carries a poor prognosis, and the incidence is much higher than previously known when PET-CT is used as a modality for its detection.

DOI: 10.1097/IGC.0000000000000623
PMID: 26807566 [PubMed - in process]

23: Dowlatshahi D, Yogendrakumar V, Aviv RI, Rodriguez-Luna D, Molina CA, Silva Y, Dzialowski I, Czlonkowska A, Boulanger JM, Lum C, Gubitz G, Padma V, Roy J, Kase CS, Bhatia R, Hill MD, Demchuk AM; PREDICT/Sunnybrook ICH CTA study group. Small intracerebral hemorrhages have a low spot sign prevalence and are less likely to expand. Int J Stroke. 2016 Feb;11(2):191-7. doi: 10.1177/1747493015616635. PubMed PMID: 26783310.

BACKGROUND: Hematoma expansion is a major predictor of morbidity and mortality after intracerebral hemorrhage (ICH). Both baseline hematoma volume and the CT-angiogram (CTA) spot sign predict hematoma expansion. Because the CTA spot sign may represent foci of active hemorrhage, we hypothesized that patients with smaller baseline hematoma volumes are less likely to be spot sign positive, and therefore less likely to expand.
AIM: We sought to validate our prior finding that small hematomas are unlikely to expand, and to determine the relationship between baseline hematoma volume, spot sign status, and risk of hematoma expansion.
METHODS: Data were from the prospective PREDICT ICH study. Patients presenting within 6 h of symptom onset with completed baseline CT, CTA, and follow-up CT were included. Baseline hematoma volume was categorized a priori (<3 mL, 3-10 mL, 10-20 mL, >20 mL). The primary outcome was significant hematoma expansion (≥6 mL, ≥12.5 mL or ≥33%) and secondary outcomes were early neurological worsening, good clinical outcome (modified Rankin Scale 0-3), and mortality at 90 days.
RESULTS: Among 315 patients meeting the inclusion criteria, baseline hematoma volume category predicted absolute hematoma expansion ($p < 0.001$), spot sign prevalence ($p < 0.001$), early neurologic worsening ($p = 0.002$), clinical outcome ($p < 0.001$), and mortality ($p < 0.001$). Very small hematomas (<3 mL) were unlikely to be spot positive (7.7%), unlikely to expand (2.6%), and were associated with a 73% chance of good clinical outcome. Spot sign appeared to be most predictive of expansion in the 3-10 mL baseline hematoma volume category.
CONCLUSION: Very small hematomas are unlikely to expand and have a low spot sign prevalence. Hemostatic therapy trials may be best targeted at hemorrhages >3 mL in volume.

DOI: 10.1177/1747493015616635
PMID: 26783310 [PubMed - in process]

24: Dubey R, Kaushik JS, Israni A, Saini L, Patel H, Chakrabarty B, Gulati S. Finger drop sign: Rare presentation of a common disorder. Brain Dev. 2016 Feb;38(2):250-2. doi: 10.1016/j.braindev.2015.08.004. Epub 2015 Aug 29. PubMed PMID: 26323550.

BACKGROUND: Guillain Barre syndrome (GBS) commonly presents with limb weakness and occasional cranial nerve, respiratory or autonomic involvement. Isolated or predominant bilateral finger drop as presenting feature has never been reported

CASE: A 9-year-old boy presented with deformity of both hands for 7 days and leg pain with difficulty in getting up from floor for 3 days. On examination he had bilateral clawing with subtle hip flexor weakness and hyporeflexia. His nerve conduction study revealed motor axonal neuropathy. His serum lead levels and autoimmune markers were within normal limits. His cerebrospinal fluid examination revealed albuminocytological dissociation. He was diagnosed as GBS and was given intravenous immunoglobulin. He improved completely over next 8 weeks.
CONCLUSIONS: GBS is one of the commonest causes of acquired neuropathy in the tropics. In resource limited setting, where electrophysiological facilities may not be available, identification of finger drop sign may help in correct management.

DOI: 10.1016/j.braindev.2015.08.004
PMID: 26323550 [PubMed - in process]

25: Faiq MA, Dada R, Qadri R, Dada T. CYP1B1-mediated Pathobiology of Primary Congenital Glaucoma. J Curr Glaucoma Pract. 2015 Sep-Dec;9(3):77-80. doi: 10.5005/jp-journals-10008-1189. Epub 2016 Feb 2. Review. PubMed PMID: 26997841; PubMed Central PMCID: PMC4779945.

CYP1B1 is a dioxin-inducible enzyme belonging to the cytochrome P450 superfamily. It has been observed to be important in a variety of developmental processes including in utero development of ocular structures. Owing to its role in the developmental biology of eye, its dysfunction can lead to ocular developmental defects. This has been found to be true and CYP1B1 mutations have been observed in a majority of primary congenital glaucoma (PCG) patients from all over the globe. Primary congenital glaucoma is an irreversibly blinding childhood disorder (onset at birth or early infancy) typified by anomalous development of trabecular meshwork (TM). How CYP1B1 causes PCG is not known; however, some basic investigations have been reported. Understanding the CYP1B1 mediated etiopathomechanism of PCG is very important to identify targets for therapy and preventive management. In this perspective, we will make an effort to reconstruct the pathomechanism of PCG in the light of already reported information about the disease and the CYP1B1 gene. How to cite this article: Faiq MA, Dada R, Qadri R, Dada T. CYP1 B1-mediated Pathobiology of Primary Congenital Glaucoma. J Curr Glaucoma Pract 2015;9(3):77-80.

DOI: 10.5005/jp-journals-10008-1189
PMCID: PMC4779945
PMID: 26997841 [PubMed]

26: Gandhi AK. Novel agents and treatment techniques to enhance radiotherapeutic outcomes in carcinoma of the uterine cervix. Ann Transl Med. 2016 Feb;4(3):49. doi: 10.3978/j.issn.2305-5839.2015.10.08. Review. PubMed PMID: 26904571; PubMed Central PMCID: PMC4740011.

BACKGROUND: Survival of patients with locally advanced carcinoma cervix (LACC) using the current standard of concurrent chemo-radiotherapy (CCRT) has reached a plateau over the last two decades. Loco-regional failure in first two years of treatment completion and distant metastasis in the subsequent years has put the survival curves at a halt. Strategies of induction and adjuvant chemotherapy have yielded little as has any advancement in techniques of delivery of radiation therapy. This article aims at discussing the current existing literature as well as promising novel strategies to enhance radiotherapeutic outcomes in carcinoma of the uterine cervix.
METHODS: The review of English literature included phase I-III trials evaluating either a novel agent, novel application/modifications of an existing treatment regimen or an innovative treatment technique. The studies have been divided in to subsections with summary of most important findings at the end of each section.
RESULTS: Despite CCRT being the 'gold standard' treatment, several issues like optimum drug combination, schedule of drug delivery, combination with molecular

targeted agents etc. remain undefined. Taxane, topoisomerase and gemcitabine based regimen needs to be further explored and compared with cisplatin based CCRT regimen. Several approaches like local delivery of cytotoxic agents, use of nano-medicine with CCRT are appearing on horizon with promises for the future. Therapies need to be designed based on the human papillomavirus titers of the patients and incorporation of radiosensitizers as an effective way of palliation with short course of radiotherapy may further enhance the radiotherapeutic outcomes.
CONCLUSIONS: The results of the studies with novel agents and treatment techniques appear promising. Further research in this arena including incorporation of cost-effectiveness analysis and quality of life issues in future trial designs are warranted.

DOI: 10.3978/j.issn.2305-5839.2015.10.08
PMCID: PMC4740011
PMID: 26904571 [PubMed]

27: Gandhi AK, Roy S, Biswas A, Raza MW, Saxena T, Bhasker S, Sharma A, Thakar A, Mohanti BK. Treatment of squamous cell carcinoma of external auditory canal: A tertiary cancer centre experience. Auris Nasus Larynx. 2016 Feb;43(1):45-9. doi: 10.1016/j.anl.2015.06.005. Epub 2015 Jul 9. PubMed PMID: 26165629.

OBJECTIVE: Carcinoma of external auditory canal (EAC) is a rare disease with variable management strategies and prognosis. We aimed to analyze treatment modalities, prognostic factors and survival outcomes in patients of squamous cell carcinoma of EAC treated at our institution.
METHODS: Forty-three patients of squamous cell carcinoma of EAC were analyzed for clinical presentation, stage, surgical procedures and radiotherapy (RT) modalities employed. Stell and McCormick staging system was used for staging of the patients. Progression free survival (PFS) was estimated by the use of Kaplan-Meier product-limit method. Log rank test was used to assess the impact of prognostic variables on PFS. Multivariate analysis was performed using the Cox hazard regression model. p value of <0.05 was considered significant for all statistical analysis.
RESULTS: Median age was 56 years (range: 12-84 years). Male to female ratio was 31:12. Stage was T1, T2 and T3 in 2, 17 and 18 patients respectively. Sixteen patients underwent surgery. Thirty-six patients received RT (14 received definitive RT, 11 had post-operative RT and 11 had RT with palliative intent). Eight patients (16%) received chemotherapy (5 received concurrent with RT, 2 had adjuvant and 1 had neo-adjuvant chemotherapy). Nine patients (of 11 patients) achieved a complete response (CR) and 2 achieved a partial response (PR) after surgery plus post-operative RT. Nine patients and 5 patients respectively achieved CR and PR after definitive RT (with or without concurrent chemotherapy). Of the 11 patients who received palliative RT, 2 had very good objective response (>50%) and 7 patients had PR to palliative RT. After a median follow-up of 16 months, median PFS for the entire cohort was 14 months. Two-year PFS rates were 85.7%, 46.9% and 0% for patients treated with surgery and post-operative RT, definitive RT and palliative RT respectively. On univariate analysis, higher stage (p=0.05) and facial nerve palsy at presentation (p=0.0008) were significant predictors of inferior PFS.
CONCLUSION: Patients with carcinoma of EAC present mostly in advanced stage at our centre. Combined higher stage (T3) and facial nerve palsy at presentation portend poorer outcome. Combined modality treatment with surgery and radiotherapy should be advocated and palliative RT remains a reasonable treatment option in patients with advanced incurable disease.

DOI: 10.1016/j.anl.2015.06.005
PMID: 26165629 [PubMed - in process]

28: Ganie MA, Marwaha RK, Dhingra A, Nisar S, Mani K, Masoodi S, Chakraborty S, Rashid A. Observation of phenotypic variation among Indian women with polycystic ovary syndrome (PCOS) from Delhi and Srinagar. Gynecol Endocrinol. 2016 Jul;32(7):566-70. doi: 10.3109/09513590.2016.1141879. Epub 2016 Feb 15. PubMed PMID: 26878496.

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder that demonstrates ethnic and regional differences. To assess the phenotypic variability among Indian PCOS women, we evaluated clinical, biochemical and hormonal parameters of these women being followed in two tertiary care institutions located in Delhi and Srinagar. A total of 299 (210 PCOS diagnosed by Rotterdam 2003 criteria and 89 healthy) women underwent estimation of T4, TSH, LH, FSH, total testosterone, prolactin, cortisol, 17OHP, and lipid profile, in addition to post OGTT, C-peptide, insulin, and glucose measurements. Among women with PCOS, mean age, age of menarche, height, systolic, diastolic blood pressure, and serum LH were comparable. PCOS women from Delhi had significantly higher BMI (26.99±5.38 versus 24.77±4.32 kg/m(2); P=0.01), glucose intolerance (36 versus 10%), insulin resistance as measured by HOMA-IR (4.20±3.39 versus 3.01±2.6; P=0.006) and QUICKI (0.140±0.013 versus 0.147±0.015; P=0.03) while PCOS from Srinagar had higher FG score (12.12±3.91 versus 10.32±2.22; P=0.01) and serum total testosterone levels (0.65±0.69 versus 0.86±0.41 ng/ml; P=0.01. Two clear phenotypes, i.e. obese hyperinsulinaemic dysglycemic women from Delhi and lean hyperandrogenic women from Srinagar are emerging. This is the first report on North Indian women with PCOS showing phenotypic differences in clinical, biochemical and hormonal parameters despite being in the same region.

DOI: 10.3109/09513590.2016.1141879
PMID: 26878496 [PubMed - in process]

29: Giri AK, Banerjee P, Chakraborty S, Kauser Y, Undru A, Roy S, Parekatt V, Ghosh S, Tandon N, Bharadwaj D. Genome wide association study of uric acid in Indian population and interaction of identified variants with Type 2 diabetes. Sci Rep. 2016 Feb 23;6:21440. doi: 10.1038/srep21440. PubMed PMID: 26902266; PubMed Central PMCID: PMC4763273.

Abnormal level of Serum Uric Acid (SUA) is an important marker and risk factor for complex diseases including Type 2 Diabetes. Since genetic determinant of uric acid in Indians is totally unexplored, we tried to identify common variants associated with SUA in Indians using Genome Wide Association Study (GWAS). Association of five known variants in SLC2A9 and SLC22A11 genes with SUA level in 4,834 normoglycemics (1,109 in discovery and 3,725 in validation phase) was revealed with different effect size in Indians compared to other major ethnic population of the world. Combined analysis of 1,077 T2DM subjects (772 in discovery and 305 in validation phase) and normoglycemics revealed additional GWAS signal in ABCG2 gene. Differences in effect sizes of ABCG2 and SLC2A9 gene variants were observed between normoglycemics and T2DM patients. We identified two novel variants near long non-coding RNA genes AL356739.1 and AC064865.1 with nearly genome wide significance level. Meta-analysis and in silico replication in 11,745 individuals from AUSTWIN consortium improved association for rs12206002 in AL356739.1 gene to sub-genome wide association level. Our results extends association of SLC2A9, SLC22A11 and ABCG2 genes with SUA level in Indians and enrich the assemblages of evidence for SUA level and T2DM interrelationship.

DOI: 10.1038/srep21440
PMCID: PMC4763273
PMID: 26902266 [PubMed - in process]

30: Goel A, Sharma S, Jain P, Kumar A, Aneja S. Concurrent Intramedullary and Intracerebral Tuberculoma. Indian J Pediatr. 2016 Feb;83(2):187-8. doi: 10.1007/s12098-015-1820-5. Epub 2015 Jul 5. PubMed PMID: 26141548.

31: Goyal M, Yu AY, Menon BK, Dippel DW, Hacke W, Davis SM, Fisher M, Yavagal DR, Turjman F, Ross J, Yoshimura S, Miao Z, Bhatia R, Almekhlafi M, Murayama Y, Sohn SI, Saver JL, Demchuk AM, Hill MD. Endovascular Therapy in Acute Ischemic Stroke: Challenges and Transition From Trials to Bedside. Stroke. 2016 Feb;47(2):548-53. doi: 10.1161/STROKEAHA.115.011426. Epub 2016 Jan 7. Review. PubMed PMID: 26742796.

32: Gupta P, Rath GP, Banik S, Mahajan C. Increased airway pressure due to superior mediastinal hematoma during endovascular coiling by transcarotid approach. J Clin Anesth. 2016 May;30:63-5. doi: 10.1016/j.jclinane.2015.12.039. Epub 2016 Feb 22. PubMed PMID: 27041267.

An elderly woman with subarachanoid hemorrhage presented to our interventional neuroradiology suite for coil embolization of multiple intracranial aneurysms. The patient had difficult vascular access for the passage of microcatheter; hence, the embolization procedure was carried out with direct puncture of the left common carotid artery. During the procedure, the patient developed thromboembolism which was treated by administration of an antiplatelet agent, abciximab. At the end of procedure, she developed airway compromise due to extension of a local neck hematoma into the superior mediastinum. The management issues in such a scenario have been discussed.

DOI: 10.1016/j.jclinane.2015.12.039
PMID: 27041267 [PubMed - in process]

33: Gupta S, Sinha G, Sharma R, Nayak B, Patil B, Kashyap B, Shameer A, Dada T. Agreement between diurnal variations of intraocular pressure by Tono-Pen and Goldmann applanation tonometer in patients on topical anti-glaucoma medication. Int Ophthalmol. 2016 Feb;36(1):9-15. doi: 10.1007/s10792-015-0067-5. Epub 2015 Mar 28. PubMed PMID: 25820518.

To estimate agreement in diurnal variations of intraocular pressure (IOP) by Tono-Pen (TP) and Goldmann applanation tonometer (GAT) in glaucoma patients on topical anti-glaucoma medication(s). IOP was measured at every 3 h from 7 a.m. to 10 a.m. in 50 eyes of glaucoma patients on topical medication(s). Diurnal fluctuation of IOP by each method was calculated as maximum-minimum IOP in a day. Central corneal thickness (CCT) was measured by ultrasonic pachymeter. There was good correlation between TP and GAT at all times during a day, minimum, and maximum IOPs during a day (Correlation coefficient, 0.706 at 7 a.m., 0.624 at 10 a.m., 0.682 at 1 p.m., 0.814 at 4 p.m., 0.652 at 7 p.m., 0.572 at 10 p.m., 0.668 minimum IOP, 0.689 maximum IOP). Mean IOPs by TP were always higher than GAT at all times during a day. Bland-Altman plots suggested a close relationship between the two sets of readings, and that this relationship was consistent at different times in a day, in maximum IOPs, minimum IOPs and also in fluctuation of IOPs. Linear regression analysis between the differences of diurnal fluctuation (diurnal fluctuation by GAT-diurnal fluctuation by TP) and CCT showed strong association ($R^2 = 0.857$, $p < 0.001$). The mean change in difference of diurnal fluctuation (GAT-TP) for a 10-micron increase in CCT was 0.69 mmHg. TP can be considered a reliable alternative to GAT in glaucoma patients for knowing the diurnal control of IOP; however these two methods should not be used interchangeably. Difference of diurnal fluctuation between two methods is dependent on CCT.

DOI: 10.1007/s10792-015-0067-5
PMID: 25820518 [PubMed - in process]

34: Gupta SK, Bakhshi S, Kumar L, Seth R, Kumar R. IKZF1 (IKAROS) deletions in B-ALL and its clinical correlation: A prospective study from a tertiary care centre in Northern India. Leuk Res. 2016 Feb;41:7-11. doi: 10.1016/j.leukres.2015.07.010. Epub 2015 Jul 31. PubMed PMID: 26704074.

INTRODUCTION: IKZF1 deletions have been reported with variable frequency in B-ALL. This study was carried out to find the prevalence and profile of IKZF1 deletions and their correlation in B-ALL.
METHODS: The untreated B-ALL cases were prospectively analyzed for IKZF1 deletions over a period of eleven months using multiplex ligation dependent probe amplification (MLPA). The IKZF1 deletions were classified into three functional groups-dominant negative, haploinsufficiency and others. The response to induction chemotherapy was correlated with the IKZF1 deletion status.
RESULTS: The median age of 101 cases was 7 years (1-67) with 82 pediatric (<18 years) cases. Fifteen cases were positive for BCR-ABL. The IKZF1 deletions were detected in 29 (28.7%) cases; 53% BCR-ABL positive, 24% BCR-ABL negative, 47% adult and 24% pediatric cases. Out of the 29 deletions, 19 (66%) were haploinsufficiency, 8 (28%) were dominant negative and 2 others. The IKZF1 deleted cases had higher induction failure rates compared to the cases without IKZF1 deletions.
CONCLUSIONS: The IKZF1 deletions were detected in 28.7% B-ALL patients. These were more common in BCR-ABL positive and adult B-ALL compared to the BCR-ABL negative and pediatric cases, respectively. The haploinsufficiency was commoner than dominant negative IKZF1 deletions. IKZF1 deletions correlated with higher induction failure.

DOI: 10.1016/j.leukres.2015.07.010
PMID: 26704074 [PubMed - indexed for MEDLINE]

35: Gupta V, Bhatia R, Sondhi P, Mahajan R. 'Ring-within-a-ring' appearance: morphological clue to topical steroid abuse in dermatophytosis. J Eur Acad Dermatol Venereol. 2016 Feb 9. doi: 10.1111/jdv.13576. [Epub ahead of print] PubMed PMID: 26856975.

36: Jagadish N, Parashar D, Gupta N, Agarwal S, Sharma A, Fatima R, Suri V, Kumar R, Gupta A, Lohiya NK, Suri A. A novel cancer testis antigen target A-kinase anchor protein (AKAP4) for the early diagnosis and immunotherapy of colon cancer. Oncoimmunology. 2016 Feb 9;5(2):e1078965. eCollection 2016 Feb. PubMed PMID: 27057472; PubMed Central PMCID: PMC4801464.

Colorectal cancer (CRC) is mainly a disease of developed countries and a major cause of death worldwide. The present study was undertaken to investigate the association of novel cancer testis (CT) antigen, A-kinase anchor protein (AKAP4) with CRC. AKAP4 gene and protein was examined by RT-PCR, in situ hybridization and immunohistochemistry (IHC) in 200 clinical specimens of different stages and grades. In addition, humoral response against AKAP4 was detected by enzyme-linked immunosorbent assay and Western blotting in 172 available sera samples of CRC patients. We observed that majority of CRC patients demonstrated AKAP4 expression and elicited immune response. AKAP4 protein expression, based on immunoreactivity score (IRS) predicted presence of CRC with 84% sensitivity, 100% specificity, 100% of positive predictive value (PPV) and 83.33% negative predictive value (NPV). Humoral response against AKAP4 protein was generated in 82% of the CRC patients. Further, statistical analysis revealed that antibodies found against AKAP4 in CRC patients predicted presence of malignancy with 81.98% sensitivity, 100% specificity, 100% PPV, and 63.53% NPV. Collectively, our data suggests that the majority of CRC cases show significant difference of AKAP4 expression among stages and grades and also generated antibodies against AKAP4 protein. Therefore, AKAP4 may be potential candidate molecule for developing as a biomarker for early diagnosis and immunotherapy of CRC.

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PMCID: PMC4801464 [Available on 2017-02-09]
PMID: 27057472 [PubMed]

37: Jain P, Sharma S, Dua T, Barbui C, Das RR, Aneja S. Efficacy and safety of anti-epileptic drugs in patients with active convulsive seizures when no IV access is available: Systematic review and meta-analysis. Epilepsy Res. 2016 May;122:47-55. doi: 10.1016/j.eplepsyres.2016.02.006. Epub 2016 Feb 16. Review. PubMed PMID: 26922313.

OBJECTIVES: To explore the existing evidence for anti-convulsant drugs and their routes of administration in treating acute seizures in children and adults when intravenous access is not available.
METHODS: All major databases including Medline via Ovid, PubMed, Cochrane CENTRAL, Embase, and Google Scholar were searched till May 2015. Randomized and quasi-randomized controlled trials comparing two anti-convulsant drugs (at least one comparator being administered through non-intravenous route) for treatment of acute seizures were included.
OUTCOME MEASURES: Primary outcome measure was proportion of children with clinical seizure cessation within 10min of drug administration. Secondary outcome measures were time taken to clinical seizure cessation from the time of admission and from the time of drug administration, and incidence of significant adverse effects.
RESULTS: Out of the 19,165 citations, 26 studies were finally included. Regarding the primary outcome measure, the quality of evidence was 'moderate' for following 3 comparisons: buccal midazolam being superior to per-rectal diazepam (RR 1.14; 95% CI, 1.06-1.24), intra-nasal lorazepam being same as intravenous lorazepam (RR 1.04; 95% CI, 0.89-1.22) and intramuscular paraldehyde (RR 1.22; 95% CI, 0.99-1.52). The quality of evidence was 'very-low' for 1 comparison: per-rectal lorazepam being superior to per-rectal diazepam (RR 3.17; 95% CI, 1.63-6.14). The quality of evidence was 'low' for following 2 comparisons: sub-lingual lorazepam being inferior to rectal diazepam (RR 0.71; 95% CI, 0.62-0.81), and intranasal midazolam being superior to per-rectal diazepam (RR 1.14; 95% CI, 1.05-1.25). The rest of the comparisons did not show any difference, but the quality of evidence was 'low' to 'very low'. The time to seizure cessation after drug administration was lower in the intravenous group. However, time to seizure cessation after presentation (includes time for drug administration) was lower in the non-intravenous group. Significant adverse effects were infrequently reported and when present, were similar in both the groups.
CONCLUSIONS: When intravenous access is not available, non-intravenous routes of administration of benzodiazepines should be considered for the control of acute seizures in children/adults. The preference may be guided by availability, expertise and social preference. [PROSPERO No: CRD42015019012].

DOI: 10.1016/j.eplepsyres.2016.02.006
PMID: 26922313 [PubMed - in process]

38: Jamaluddin MA, Kataria K. Management of Acute Necrotizing Pancreatitis. Indian J Surg. 2016 Apr;78(2):168-9. doi: 10.1007/s12262-016-1458-1. Epub 2016 Feb 17. PubMed PMID: 27303134; PubMed Central PMCID: PMC4875911.

39: Jayaraj P, Sen S, Bhattacharya T, Arora J, Yadav S, Chhoker V, Kumar A, Dhanaraj PS, Yadavilli KS, Verma M. Clinical relevance of cyclooxygenase 2 and peroxisome proliferator-activated receptor Î³ in eyelid sebaceous gland carcinoma.
Histopathology. 2016 Aug;69(2):268-75. doi: 10.1111/his.12932. Epub 2016 Feb 26. PubMed PMID: 26791964.

AIMS: Sebaceous gland carcinoma (SGC) is a malignancy associated with the pilosebaceous unit, and occurs at ocular or non-ocular sites. Cyclooxygenases

(COXs) are enzymes that are crucial for lipid metabolism. COX-2 is overexpressed in various cancers, and its inhibition by non-steroidal anti-inflammatory drugs is known to reduce the risk of many cancers. Peroxisome proliferator-activated receptor (PPAR)-γ is a transcription factor involved in adipogenesis. PPAR-γ is a potential therapeutic target for the treatment of malignant tumours, including colon carcinoma. The aim of this study was to explore the status of COX-2 and PPAR-γ as prognostic markers in human eyelid SGC.
METHODS AND RESULTS: The immunohistochemical expression of COX-2 and PPAR-γ was evaluated in 31 SGC cases. Cytoplasmic expression of COX-2 was detected in 80% of the SGC cases, and nuclear expression of PPAR-γ in 87%. There were significant correlations of PPAR-γ expression with well-differentiated SGC [19/21 (90%)] and of COX-2 overexpression with reduced disease-free survival (P = 0.0441, log rank analysis). COX-2 expression [odds ratio (OR) 3.82, 95% confidence interval (CI) 1.02-14.33, P = 0.046] and lymph node metastasis (OR 0.17, 95% CI 0.04-0.65, P = 0.009) emerged as significant risk factors in the univariate analysis. However, COX-2 expression did not emerge as a significant independent prognostic factor in multivariate analysis.
CONCLUSIONS: COX-2 is a potential marker for identifying high-risk SGC patients. Expression of PPAR-γ in eyelid SGC cases reflects terminal sebaceous differentiation. Inhibitors of COX-2 signalling and PPAR-γ agonists are both prospective novel therapeutic targets in the management of eyelid SGC patients.

DOI: 10.1111/his.12932
PMID: 26791964 [PubMed - in process]

40: Jha AK, Gharde P, Chauhan S, Kiran U, Malhotra Kapoor P. Echocardiographic Assessment of the Alterations in Pulmonary Blood Flow Associated with Ketamine and Etomidate Administration in Children with Tetralogy of Fallot. Echocardiography. 2016 Feb;33(2):307-13. doi: 10.1111/echo.13014. Epub 2015 Jul 19. PubMed PMID: 26190746.

BACKGROUND: Despite widespread uses of ketamine, the clinical studies determining its effect on pulmonary blood flow in children with tetralogy of Fallot (TOF) are lacking. Furthermore, the quantification of pulmonary blood flow is not possible in these patients, because pulmonary artery catheter is contraindicated. Therefore, the purpose of this study was to evaluate the changes in pulmonary blood flow by intra-operative transesophageal echocardiography after ketamine or etomidate administration in children with TOF.
METHODS: Eleven children each in the two clinical variants of TOF (group A-moderate to severe cyanosis; group B-mild to minimal cyanosis) undergoing intracardiac repair were prospectively studied after endotracheal intubation. A single bolus dose of ketamine (2 mg/kg) and etomidate (0.3 mg/kg) was administered in a random order after 15 minute interval. Hemodynamic, arterial blood gas, and echocardiographic measurements were obtained at 7 consecutive times (T) points (baseline, 1, 2, 4, 6, 8, and 15 minutes after drug administration).
RESULTS: Ketamine produced a significant reduction in VTI-T (velocity time integrals total of left upper pulmonary vein), RVOT-PG (right ventricular outflow tract peak gradient), and MG (mean gradient) in group A while those in group B had a significant increase in VTI-T, RVOT-PG, and RVOT-MG at time (T1, T2, T4, and T6; P = 0.00). This divergent behavior, however, was not observed with etomidate.
CONCLUSION: Etomidate does not change pulmonary blood flow. However, ketamine produces divergent effects; it increases pulmonary blood flow in children with minimal cyanosis and decreases pulmonary blood flow in children with moderate to severe cyanosis.

DOI: 10.1111/echo.13014
PMID: 26190746 [PubMed - in process]

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Repetitive transcranial magnetic stimulation (rTMS) has emerged as a potential treatment in treatment resistant major depressive disorder (MDD). However, there is no consensus about the exact site of stimulation for rTMS. Single-photon emission computed tomography (SPECT) offers a potential technique in deciding the site of stimulation. The present study was conducted to assess the difference in outcome of brain SPECT assisted rTMS versus standard protocol of twenty sessions of high frequency rTMS as add on treatment in 20 patients with treatment resistant MDD, given over a period of 4 weeks. Thirteen subjects (group I) received high frequency rTMS over an area of hypoperfusion in the prefrontal cortex, as identified on SPECT, whereas 7 subjects (group II) were administered rTMS in the left dorsoslateral prefrontal cortex (DLPFC) area. Improvement was monitored using standardized instruments. Patients in the group I showed a significantly better response compared to those in the group II. In group I, 46% of the subjects were responders on MADRS, 38% on BDI and 77% on CGI. The parallel figures of responders in Group II were 0% on MADRS, 14% on BDI and 43% on CGI. There were no remitters in the study. No significant untoward side effects were noticed. The study had limitations of a small sample size and non-controlled design, and all the subjects were also receiving the standard antidepressant therapy. Administration of rTMS over brain SPECT specified area of hypoperfusion may have a better clinical outcome compared to the standard protocol.

DOI: 10.1016/j.ajp.2016.02.003
PMID: 27208445 [PubMed - in process]

42: Joshi S, Gupta N, Khan R, Kumar R, Sharma M, Kumar L, Sharma A. Interrelationship between angiogenesis, inflammation and oxidative stress in Indian patients with multiple myeloma. Clin Transl Oncol. 2016 Feb;18(2):132-7. doi: 10.1007/s12094-015-1344-5. Epub 2015 Jul 14. PubMed PMID: 26169214.

BACKGROUND: Multiple myeloma (MM) is a B-cell malignancy characterized by the accumulation of clonal population of plasma cells in the bone marrow (BM). A variety of angiogenic factors, proteases, reactive oxygen species and inflammatory cytokines induce the formation of an extensive and suitable BM microenvironment. Previous studies have established the importance of angiogenic factors, inflammatory molecules and oxidative stress in MM but their interplay and effect on each other are not being taken together.
METHODS: Circulatory levels of VEGF, angiopoietin-2 (Ang-2), IL-6 and TNF-α along with the activity of superoxide dismutase (SOD) and glutathione peroxidase (GPx) were investigated in 112 subjects including 62 MM patients and 50 healthy controls. Inter-stage analysis was done to evaluate the association of these molecules with the severity of disease. Pearson correlation was determined to find interrelationship, if any, between these molecules.
RESULTS: We have observed elevated levels of VEGF, Ang-2, IL-6, TNF-α and decreased activity of SOD, GPx in MM patients in comparison to controls. All these molecules also showed a trend with the severity of disease. We have found strong association between these factors upon their correlation and regression analysis.
CONCLUSION: This study is a step toward understanding the indepth contribution of angiogenesis, inflammation and oxidative stress together in making BM microenvironment suitable for growth, survival and proliferation of malignant plasma cells in MM.

DOI: 10.1007/s12094-015-1344-5
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43: Kahr PC, Kahr MK, Dabral H, Agarwal R, Kothari SS, Saxena A, Ramakrishnan S. Changes in Myocardial Contractility and Electromechanical Interval During the First Month of Life in Healthy Neonates. Pediatr Cardiol. 2016 Feb;37(2):409-18. doi: 10.1007/s00246-015-1292-4. Epub 2015 Oct 24. PubMed PMID: 26499358.

This study aims at documenting the changes in ventricular tissue velocities, longitudinal strain and electromechanical coupling during the first month of life. During the neonatal period, when the ventricular myocardium is not yet fully maturated, the heart is subjected to significant hemodynamic changes. We studied the ventricular performance of 16 healthy neonates at three time points over the first month of life: on days 2 (IQR [2;2]), 13 [12;14] and 27 [25;29]. We found that systolic and diastolic tissue velocities increased significantly in both left and right ventricle (by 1.2-1.7 times, $p < 0.001$). Congruently, we found that peak systolic longitudinal strain of the right and left ventricles increased significantly. However, no significant changes in longitudinal strain rate were observed. Finally, QS-intervals shortened during the neonatal period: being measured at 12 points throughout the left ventricle, time to peak systolic velocity decreased on average to 89 % in the second and to 80 % in the fourth week of life (22.3 ± 0.2 vs. 19.8 ± 0.3 vs. 17.8 ± 0.5 ms, $r = -0.564$, $p < 0.001$). When comparing opposing walls of the left ventricle, no dyssynchrony in left ventricular contraction was found. In addition to increasing systolic and diastolic tissue velocities during the first month of life, the time to peak systolic contraction shortens in the neonatal heart, which may reflect an increasing efficiency of the excitation-contraction coupling in the maturing myocardium. While there appears to be no dyssynchrony in ventricular contraction, these findings may extend our appreciation of the immature neonatal heart and certain disease states.

DOI: 10.1007/s00246-015-1292-4
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Rhabdoid meningioma is a rare meningioma variant, classified as WHO grade III. Although this tumor is known for its aggressive behavior and poor prognosis, extracranial metastasis is rare. We report the rare case of a 31-year-old patient with rhabdoid meningioma which recurred several times despite gross total resection, radiation therapy, and gamma knife radiosurgery, and the last recurrence was associated with metastases to lungs, lymph node and bone. The patient showed no response to paclitaxel-carboplatin, or vincristine-cyclophosphamide-adriamycin chemotherapy, and succumbed to the disease. Metastases from rhabdoid meningioma prove to be a diagnostic challenge, and treatment for metastatic meningiomas is not optimized, thus necessitating documentation and interdisciplinary consensus on management protocols.

DOI: 10.1007/s10014-016-0250-z
PMID: 26875176 [PubMed - in process]

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Magnetic resonance imaging (MRI) is a radiation-free imaging modality with excellent contrast resolution and multiplanar capabilities. Since ionizing radiation is an important concern in the pediatric population, MRI serves as a useful alternative to computed tomography (CT) and also provides additional clues to diagnosis, not discernible on other investigations. Magnetic resonance cholangiopancreatography (MRCP), urography, angiography, enterography, dynamic multiphasic imaging and diffusion-weighted imaging provide wealth of information. The main limitations include, long scan time, need for sedation/anesthesia, cost

and lack of widespread availability. With the emergence of newer sequences and variety of contrast agents, MRI has become a robust modality and may serve as a one-stop shop for both anatomical and functional information.

DOI: 10.1007/s12098-015-1978-x
PMID: 26916887 [PubMed - in process]

46: Kapil U, Sareen N, Nambiar VS, Khenduja P, Sofi NY. Iodine Nutritional Status among Adolescent Girls in Uttarakhand, India. J Trop Pediatr. 2016 Feb;62(1):81-2. doi: 10.1093/tropej/fmv069. Epub 2015 Oct 17. PubMed PMID: 26477042; PubMed Central PMCID: PMC4892387.

INTRODUCTION: Uttarakhand (UK) state is a known endemic region for Iodine deficiency.
OBJECTIVE: To assess iodine nutritional status among adolescent girls in districts: Udham Singh Nagar (USN), Nainital (N) and Pauri (P) of UK state.
METHODS: In each district, 30 clusters (schools) were identified by using population proportionate to size cluster sampling. In each school, 60 girls (12-18 years) attending the schools were included. Total of 5430 girls from USN (1823), N (1811) and P (1796) were studied. Clinical examination of thyroid of each girl was conducted. From each cluster, spot urine and salt samples were collected.
RESULTS: Total goiter rate was found to be 6.8% (USN), 8.2% (N) and 5.6% (P). Median urinary iodine concentration levels were 250 µg/l (USN), 200 µg/l (N) and 183 µg/l (P).
CONCLUSION: Findings of the study documented that adolescent girls had adequate iodine nutritional status in the three districts of UK.

DOI: 10.1093/tropej/fmv069
PMCID: PMC4892387 [Available on 2017-02-01]
PMID: 26477042 [PubMed - indexed for MEDLINE]

47: Khandelwal P, Murugan V, Hari S, Lakshmy R, Sinha A, Hari P, Bagga A. Dyslipidemia, carotid intima-media thickness and endothelial dysfunction in children with chronic kidney disease. Pediatr Nephrol. 2016 Aug;31(8):1313-20. doi: 10.1007/s00467-016-3350-4. Epub 2016 Feb 26. PubMed PMID: 26921213.

BACKGROUND: Chronic kidney disease (CKD) predisposes to accelerated atherosclerosis that is measured by carotid artery intima-media thickness (cIMT) and brachial artery flow-mediated dilation (FMD). Information on the association of these parameters with dyslipidemia in pre-dialysis pediatric CKD is limited.
METHODS: Eighty patients aged 9.9±3.2 years, with estimated glomerular filtration rate of 38.8±10.8 ml/1.73 m(2)/min, and 42 pediatric controls underwent cross-sectional analysis of lipid profile, cIMT, and brachial artery FMD. Significant differences in these parameters between patients and controls were analyzed using Student's t test. Predictors of cIMT and dyslipidemia were assessed using linear and logistic regression respectively.
RESULTS: Patients had elevated blood levels of triglyceride and of total and LDL cholesterol than controls ($P \leq 0.001$); 73.8 % were dyslipidemic. Mean cIMT was higher (0.421±0.054 mm vs 0.388±0.036 mm, $P = 0.001$) and brachial artery FMD was reduced (10.6±4.9 % vs 18.9±4.1 %, $P < 0.0001$) in patients compared with controls. On multivariate analysis, hypertension (OR 3.68, $P = 0.044$) and male gender (OR 10.21, $P = 0.004$) were associated with dyslipidemia; cIMT was significantly associated with LDL cholesterol ($\beta = 28.36$, $P = 0.033$).
CONCLUSION: Dyslipidemia was prevalent and cIMT significantly elevated in pre-dialysis pediatric CKD, indicating increased cardiovascular risk. Elevated LDL cholesterol predicted increased cIMT, strengthening the association between dyslipidemia and atherosclerosis in early CKD.

DOI: 10.1007/s00467-016-3350-4
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BACKGROUND & OBJECTIVES: Chronic obstructive pulmonary disease (COPD) is characterized by slowly progressive airflow limitaion, chronic lung inflammation and associated systemic manifestations. The objective of this preliminary study was to investigate the levels of high sensitivity C reactive protein (hs CRP) and tumour necrosis factor-α (TNF-α) as markers of systemic inflammation and assessment of systemic vascular reactivity that may play an important role in development of cardiovascular disease in COPD patients.
METHODS: Systemic vascular reactivity was assessed non-invasively by measuring peripheral pulse waveform changes during reactive hyperemia (RH) in 16 COPD patients and 14 controls by photoplethysmography technique (PPG). Parameters measured were pulse wave amplitude (PWA), slope and pulse transit time (PTT). Tumour necrosis factor-α (TNF-α) and hs CRP were measured as markers of inflammation.
RESULTS: PWA during the 1 st , 2 nd and 3 rd minutes post release of occlusion were significantly higher than the baseline means in controls, whereas in the patient group there was no significant change in the PWA during any of the observed time periods following release of occlusion, in comparison to the baseline means. Similar results were observed in slope values for patients and controls. Maximum percentage change in PWA during RH with reference to baseline was significantly lower in patients as compared to controls (26.78±20.19 vs 57.20±19.80%, p<0.001). Maximum percentage change in slope during RH with reference to baseline was significantly lower in patients as compared to controls (19.77±10.73 vs 39.25±13.49%, P<0.001). A vascular tone response as represented by PTT was also impaired in the 3 rd minute of RH as compared to baseline mean values in COPD patients only.
INTERPRETATION & CONCLUSIONS: Our findings showed raised hs CRP levels and impaired systemic vascular reactivity in COPD patients. Whether these may increase the risk of cardiovascular disease in COPD patients need to be confirmed in future studies with large sample size and appropriate study design.

DOI: 10.4103/0971-5916.180209
PMCID: PMC4859129
PMID: 27121518 [PubMed - in process]

50: Kuchay MS, Kudyar RP, Gupta A, Pandita KK, Ganie MA. Gender differences in insulin and C-peptide concentrations at birth using cord blood collection. Arch Endocrinol Metab. 2016 Feb 23;60(3):264-6. doi: 10.1590/2359-3997000000148. PubMed PMID: 26910627.

OBJECTIVE: To study gender differences in insulin and C-peptide concentrations at birth using cord blood collection.
SUBJECTS AND METHODS: This study was conducted in a maternity hospital, in Jammu province of Jammu and Kashmir, India. All women with pregnancy who were hospitalized for delivery were followed. All pregnant ladies who had no medical condition affecting insulin levels, as per history and routine antenatal blood testing, were included in the study. The test for cord plasma insulin and C-peptide was done in 60 (30 males) full-term (≥ 37 completed weeks) normal delivery babies within 4 hours of the collection of samples using the electro-chemiluminescence immunoassay (ECLIA) on Roche elecsys module immunoassay

analyzer. Weight of the babies was taken immediately after birth using digital scales.
RESULTS: Cord plasma insulin and C-peptide measured in EDTA were compared between boys and girls and also related to birth weight. Girls were lighter (2,830 ± 37 vs. 3,236 ± 46 g; p = < 0.001) but had higher cord insulin (16.48 ± 4.88 vs. 10.53 ± 4.04 µU/mL; p = < 0.001), and C-peptide (2.47 ± 0.66 vs. 0.834 ± 0.26 ng/mL; p = < 0.001) concentrations than newborn boys.
CONCLUSION: Female newborn babies have higher cord plasma insulin and C-peptide concentrations than male newborns, despite being smaller, suggesting intrinsic insulin resistance in girls.

DOI: 10.1590/2359-3997000000148
PMID: 26910627 [PubMed - in process]

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Blunt pancreatic trauma is an uncommon injury but has high morbidity and mortality. In modern era of trauma care, pancreatic trauma remains a persistent challenge to radiologists and surgeons alike. Early detection of pancreatic trauma is essential to prevent subsequent complications. However early pancreatic injury is often subtle on computed tomography (CT) and can be missed unless specifically looked for. Signs of pancreatic injury on CT include laceration, transection, bulky pancreas, heterogeneous enhancement, peripancreatic fluid and signs of pancreatitis. Pan-creatic ductal injury is a vital decision-making parameter as ductal injury is an indication for laparotomy. While lacerations involving more than half of pancreatic parenchyma are suggestive of ductal injury on CT, ductal injuries can be directly assessed on magnetic resonance imaging (MRI) or encoscopic retrograde cholangio-pancreatography. Pancreatic trauma also shows temporal evolution with increase in extent of injury with time. Hence early CT scans may underestimate the extent of injures and sequential imaging with CT or MRI is important in pancreatic trauma. Sequential imaging is also needed for successful non-operative management of pancreatic injury. Accurate early detection on initial CT and adopting a multimodality and sequential imaging strategy can improve outcome in pancreatic trauma.

DOI: 10.4329/wjr.v8.i2.159
PMCID: PMC4770178
PMID: 26981225 [PubMed]

52: Kumar A, Mohanty S, Nandy SB, Gupta S, Khaitan BK, Sharma S, Bhargava B, Airan B. Hair & skin derived progenitor cells: In search of a candidate cell for regenerative medicine. Indian J Med Res. 2016 Feb;143(2):175-83. doi: 10.4103/0971-5916.180205. PubMed PMID: 27121515; PubMed Central PMCID: PMC4859126.

BACKGROUND & OBJECTIVES: Skin is an established tissue source for cell based therapy. The hair follicle has been introduced later as a tissue source for cell based therapy. The ease of tissue harvest and multipotent nature of the resident stem cells in skin and hair follicle has promoted basic and clinical research in this area. This study was conducted to evaluate skin stem cells (SSCs) and hair follicle stem cells (HFSCs) as candidate cells appropriate for neuronal and melanocyte lineage differentiation.
METHODS: In this study, SSCs and hair follicle stem cells (HFSCs) were expanded in vitro by explant culture method and were compared in terms of proliferative potential and stemness; differentiation potential into melanocytes and neuronal lineage.
RESULTS: SSCs were found to be more proliferative in comparison to HFSCs, however, telomerase activity was more in HFSCs in comparison to SSCs. Capacity to differentiate into two lineages of ectoderm origin (neuronal and melanocyte) was found to be different. HFSCs cells showed more propensities towards melanocyte

lineage, whereas SSCs were more inclined towards neuronal lineage.
INTERPRETATION & CONCLUSIONS: The study showed that SSCs had differential advantage over the HFSCs for neuronal cell differentiation, whereas, the HFSCs were better source for melanocytic differentiation.

DOI: 10.4103/0971-5916.180205
PMCID: PMC4859126
PMID: 27121515 [PubMed - in process]

53: Kumar A, Sharma AK, Mittal S, Kumar G. The Relationship Between Body Mass Index and Bone Mineral Density in Premenopausal and Postmenopausal North Indian Women. J Obstet Gynaecol India. 2016 Feb;66(1):52-6. doi: 10.1007/s13224-014-0629-x. Epub 2014 Oct 29. PubMed PMID: 26924908; PubMed Central PMCID: PMC4755946.

PURPOSE: Present study aims to examine the relationship of the bone mineral density (BMD) with body mass index (BMI) in an apparently healthy premenopausal and postmenopausal north Indian female population.
METHODS: Two hundred and fifty-five apparently healthy women were evaluated by a detailed questionnaire including all possible factors that could affect the BMD. The height and weight of all the subjects were recorded and BMI was calculated. Bone mineral density was measured by DXA (Dual Electron X-ray Absorptiometry) at L1-L4 Lumbar spine (LS) and femur neck (FN) by using the Prodigy DXA system (software version:8.50) manufactured by GE medical systems LUNAR.
RESULTS: The population was divided into pre and postmenopausal groups. The BMD at all sites increased with BMI in both groups. In a multiple regression model, the attributability of BMI and age to variation in LSBMD and FNBMD was 10.3 and 13.9 %, respectively. In postmenopausal women, age, BMI, and a previous history of fracture together attributed to a variance in BMI of 40.1 and 27.6 % at lumbar spine and femur neck, respectively. BMI was found to be significantly associated with low BMD at both sites in premenopausal women, while the association was lost in postmenopausal females.
CONCLUSION: BMI is an important determinant of BMD in Indian females. However, the association is not present in postmenopausal women with osteopenia. In addition, the effect of increase in BMI on BMD has a ceiling effect, and moderate to morbid obesity might not actually be a preventive factor for osteopenia.

DOI: 10.1007/s13224-014-0629-x
PMCID: PMC4755946 [Available on 2017-02-01]
PMID: 26924908 [PubMed]

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Vaccine hesitancy is an emerging term in the socio-medical literature which describes an approach to vaccine decision making. It recognizes that there is a continuum between full acceptance and outright refusal of some or all vaccines and challenges the previous understanding of individuals or groups, as being either anti-vaccine or pro-vaccine. The behaviours responsible for vaccine hesitancy can be related to confidence, convenience and complacency. The causes of vaccine hesitancy can be described by the epidemiological triad i.e. the complex interaction of environmental- (i.e. external), agent- (i.e. vaccine) and host (or parent)- specific factors. Vaccine hesitancy is a complex and dynamic issue; future vaccination programs need to reflect and address these context-specific factors in both their design and evaluation. Many experts are of

the view that it is best to counter vaccine hesitancy at the population level. They believe that it can be done by introducing more transparency into policy decision-making before immunization programs, providing up-to-date information to the public and health providers about the rigorous procedures undertaken before introduction of new vaccines, and through diversified post-marketing surveillance of vaccine-related events.

DOI: 10.1186/s13584-016-0062-y
PMCID: PMC4736490
PMID: 26839681 [PubMed]

56: Kumar MV, Choudhary SK, Talwar S, Gharde P, Sahu M, Kumar S, Chandra D, Saxena R, Kumar L, Airan B. Extraanatomic Bypass to Supraceliac Abdominal Aorta for Complex Thoracic Aortic Obstruction. Ann Thorac Surg. 2016 Apr;101(4):1552-7. doi: 10.1016/j.athoracsur.2015.10.080. Epub 2016 Feb 6. PubMed PMID: 26857636.

BACKGROUND: The standard surgical treatment of coarctation of the aorta is through a left posterolateral thoracotomy. However, when a concomitant cardiac procedure is required or the conventional approach is not possible or is hazardous, extraanatomic bypass to the supraceliac abdominal aorta may be advantageous. We discuss our technique and report the long-term results.
METHODS: Between January 1986 and January 2015, 25 patients (16 males, 9 females) underwent extraanatomic bypass to the supraceliac abdominal aorta for various lesions of the arch and the descending thoracic aorta. Extraanatomic bypass to the supraceliac abdominal aorta was performed for patients in whom balloon dilatation was not feasible due to associated arch hypoplasia (n = 9), long-segment thoracic aorta narrowing due to nonspecific aortoarteritis (n = 3), or isolated long-segment coarctation of the aorta (n = 3). Patients who needed concomitant cardiac procedures, such as aortic valve replacement (n = 4), ascending aortic aneurysm repair (n = 2), or coronary artery bypass grafting (n = 1), and in whom balloon dilatation had failed, also underwent extraanatomic bypass to the supraceliac abdominal aorta. Extraanatomic bypass was also performed in 3 patients with recurrent coarctation after surgical repair and in whom balloon dilation was not feasible or unsuccessful.
RESULTS: There were no early or late deaths. The peak-to-peak gradients between the upper limb and the lower limb decreased from 59.3 ± 16.3 mm Hg to 2.0 ± 2.8 mm Hg ($p < 0.0001$). The mean follow-up was 96.6 ± 92.6 months (range, 1 to 240 months; median, 54 months). Doppler interrogation of the lower limb arterial system after a mean follow-up of 86.4 ± 85.2 months showed an unobstructed flow pattern. The ankle-brachial pressure index improved from a preoperative value of 0.60 ± 0.07 to 1.04 ± 0.11 ($p < 0.0001$). Systolic blood pressure decreased significantly compared with preoperative values (153.9 ± 18.9 vs 122.8 ± 10.2, $p < 0.0001$). Three patients continued to receive antihypertensive medication due to persistent mild hypertension.
CONCLUSIONS: Extraanatomic bypass to the supraceliac abdominal aorta provides effective palliation for complex aortic obstructions. It is easy and quick to perform, avoids fatal complications, and is well tolerated in all age groups.

DOI: 10.1016/j.athoracsur.2015.10.080
PMID: 26857636 [PubMed - indexed for MEDLINE]

57: Kumar N, Padma Srivastava MV, Verma R, Sharma H, Modak T. Can low-frequency repetitive transcranial magnetic stimulation precipitate a late-onset seizure in a stroke patient? Clin Neurophysiol. 2016 Feb;127(2):1734-6. doi: 10.1016/j.clinph.2015.06.033. Epub 2015 Jul 26. PubMed PMID: 26306660.

58: Kumar P, Kumar A, Sagar R, Misra S, Faruq M, Suroliya V, Vivekanandhan S, Kumar Srivastava A, Prasad K. Association between interleukin-6 (G174C and C572G) promoter gene polymorphisms and risk of ischemic stroke in North Indian population: a case-control study. Neurol Res. 2016 Jan;38(1):69-74. doi: 10.1080/01616412.2015.1133028. Epub 2016 Feb 18. PubMed PMID: 26883819.

BACKGROUND: Polymorphisms of G174C and C572G in the interleukin-6 (IL-6) promoter gene can affect both transcription and secretion of IL-6 and may be involved in inflammation related to and pathogenesis of ischemic stroke (IS). Whether these IL-6 gene polymorphisms are risk factors for IS or not, remains controversial.
OBJECTIVE: The aim of this study was to determine the association between IL-6 G174C and C572G gene polymorphisms and susceptibility to ischemic stroke in North Indian Population.
METHODS: Two hundred and fifty IS patients and 250 age- and sex-matched controls were studied. Genotyping was performed using SNaPshot method. Stroke was classified using Trial of Org 10172 in acute stroke treatment classification. Conditional logistic regression analysis was used to calculate the strength of association between IL-6 (G174C and C572G) polymorphisms and risk of IS.
RESULTS: Hypertension, diabetes, dyslipidemia, alcohol, smoking, family history of stroke, sedentary life style and low socioeconomic status were found to be associated with the risk of IS. Conditional logistic regression analysis showed a significant association of IL-6 G174C with the risk of IS under dominant model (OR, 1.61; 95%CI, 1.0-2.4; P value 0.02) and allelic model (OR, 1.5; 95%CI, 1.0-2.1; P value 0.02). For IL-6 C572G, multivariate adjusted analysis showed a significant association with the risk of IS under dominant model for overall IS (OR, 1.81; 95%CI, 1.04-3.15; P value 0.03) and small vessel disease subtype of IS (OR, 2.8; 95%CI, 1.3-6.0; P value 0.006).
CONCLUSION: Our results suggest that IL-6 (G174C) polymorphism is significantly associated with the risk of IS in North Indian population. However, IL-6 (C572G) polymorphism is found significantly associated with the risk of IS after adjusting the demographic and risk factors variables. Prospective studies with large sample size are required for independent validation. Our findings could be helpful in identifying individuals at increased risk for developing IS.

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PMID: 26883819 [PubMed - in process]

59: Kumar P, Kumar A, Misra S, Sagar R, Faruq M, Suroliya V, Vivekanandhan S, Srivastava AK, Prasad K. Tumor necrosis factor-alpha (-Â 308G/A, +Â 488G/A, -Â 857C/T and -1031Â T/C) gene polymorphisms and risk of ischemic stroke in north Indian population: A hospital based case-control study. Meta Gene. 2015 Nov 17;7:34-9. doi: 10.1016/j.mgene.2015.11.003. eCollection 2016 Feb. PubMed PMID: 26862479; PubMed Central PMCID: PMC4707245.

BACKGROUND: Genetic factors may play a role in the susceptibility of Ischemic stroke (IS). Previous studies have shown that Tumour necrosis factor-α (TNF-α) gene polymorphisms were associated with the risk of IS in multiple ethnicities. The present case-control study tested the hypothesis that genetic polymorphisms of the TNF-α gene may affect the risk of IS in North Indian population. We investigated the association of four single nucleotide polymorphisms (- 308G/A, + 488G/A, - 857C/T and -1031 T/C) within TNF-α gene promoter and their haplotypes with the risk of IS.
METHODS: IS was classified using the Trial of Org 10,172 in Acute Stroke Treatment (TOAST) classification. Genotyping was performed for 250 IS patients and 250 age- and sex-matched IS free controls by using SNaPshot technique. Multivariate logistic regression was used to control the confounding effects of demographic and risk factor variables. Haplotype analyses were done by using PHASE software and Linkage disequilibrium (LD) analyses were done by using Haploview version 4.2 software.
RESULTS: An independent association between TNF-α + 488G/A (OR = 2.59; 95%CI 1.46 to 4.60; p = 0.001) and -857C/T (OR = 1.77; 95%CI 1.01 to 3.11; p < 0.04) and risk of IS was observed under dominant model. However, no significant association between -308G/A and -1031 T/C gene polymorphisms and risk of IS was observed.

Haplotype analysis showed that A308-G488-C857-T1031 haplotypes were significantly associated with the increased risk of IS [OR = 1.66; 95%CI 1.02 to 2.71; p = 0.003]. Strong linkage disequilibrium (LD) was observed for + 488G/A and -857C/T (D' = 0.41, r(2) = 0.004).
CONCLUSIONS: Two SNPs (+ 488G/A and -857C/T) of TNF-α gene and their haplotypes are significantly associated with the risk of IS in the population enrolled from North India. Our findings indicate that polymorphisms and haplotypes of TNF-α gene may be used as a genetic marker for identifying individuals at increased risk for developing IS.

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PMCID: PMC4707245
PMID: 26862479 [PubMed]

60: Kumar P, Kumar A, Sagar R, Misra S, Faruq M, Suroliya V, Vivekanandhan S, Srivastava AK, Prasad K. Association between Interleukin-10 -1082G/A Gene Polymorphism and Risk of Stroke in the North Indian Population: A Case-Control Study. J Stroke Cerebrovasc Dis. 2016 Feb;25(2):461-8. doi: 10.1016/j.jstrokecerebrovasdis.2015.10.020. Epub 2015 Dec 1. PubMed PMID: 26654671.

BACKGROUND: Anti-inflammatory interleukin-10 (IL-10) cytokine and its genetic variations may play an important role in the pathogenesis of various human diseases including stroke.
OBJECTIVE: The aim of this present case-control study was to determine the association between IL-10 -1082G/A (rs1800896) gene polymorphism and risk of stroke in the North Indian population.
METHODS: Genotyping was carried out by using SNaPshot method (Applied Biosystems, Foster City, California, United States) for 250 ischemic stroke (IS) patients, 250 age- and sex-matched IS free controls, 100 intracerebral hemorrhage (ICH) patients, and 100 age- and sex-matched ICH free controls. IS was classified using the Trial of Org 10172 in Acute Stroke Treatment classification. Conditional logistic regression analysis with adjustment for multiple demographic and risk factor variables was used to calculate the strength of association between IL-10 (-1082G/A) polymorphism and risk of stroke.
RESULTS: Conditional logistic regression analysis showed an independent association between IL-10 -1082G/A and risk of IS under a dominant model (odds ratio [OR] = 2.39, 95% confidence interval [CI] = 1.34-4.27, P = .003) and an allelic model (OR = 2.49, 95% CI 1.71-3.63, P < .001). An independent association between IL-10 -1082G/A, under the dominant model (OR = 6.8, 95% CI 2.2-20.7, P < .001) and the allelic model (OR = 3.4, 95% CI 1.8-6.3, P < .001), and the risk of ICH was also observed.
CONCLUSION: Our results suggest that IL-10 -1082G/A gene polymorphism is an independent risk factor for the risk of IS and ICH in the North Indian population. Our findings indicate that IL-10 -1082G/A polymorphism may be used as a genetic marker for identifying individuals at increased risk of developing stroke.

DOI: 10.1016/j.jstrokecerebrovasdis.2015.10.020
PMID: 26654671 [PubMed - in process]

61: Kumar P, Misra S, Kumar A, Pandit AK, Chakravarty K, Prasad K. Association between Tumor Necrosis Factor-Î± (-238G/A and -308G/A) Gene Polymorphisms and Risk
of Ischemic Stroke: A Meta-Analysis. Pulse (Basel). 2016 Apr;3(3-4):217-28. doi: 10.1159/000443770. Epub 2016 Feb 17. Review. PubMed PMID: 27195243; PubMed Central PMCID: PMC4865080.

Tumor necrosis factor-α (TNF-α) is a proinflammatory pleiotropic cytokine which may contribute to the initiation and progression of ischemic stroke (IS). Thus

far, numerous studies have been performed to examine the association between -238G/A (rs361525) and -308G/A (rs1800629) polymorphisms in the promoter regions of the TNF-α gene and susceptibility to IS, but results are still conflicting. The aim of this meta-analysis is to provide a relatively comprehensive account of the association between TNF-α -238G/A and -308G/A gene polymorphisms and susceptibility to IS. A literature search for eligible candidate gene studies published before April 20, 2015, was conducted in the PubMed, Medline, EMBASE and Google Scholar databases. The following combinations of main keywords were used: ('Tumor Necrosis Factor-Alpha' or 'TNF-α') and ('ischemic stroke' or 'cerebral infarction' or 'IS') and ('genetic polymorphism' or 'single nucleotide polymorphisms' or 'SNP'). Fixed- or random-effect models were used to estimate the pooled odds ratio (OR) and 95% confidence interval (CI). Meta-analysis was carried out by using RevMan 5.3 software. For TNF-α -238G/A gene polymorphism, 7 case-control studies with a total of 1,846 IS patients and 1,905 controls showed a significant association with susceptibility to IS under a dominant model (AA + GA vs. GG; OR, 1.40; 95% CI, 1.11-1.76; p value 0.004). For TNF-α -308G/A gene polymorphism, 16 case-control studies with a total of 5,651 IS patients and 5,792 controls showed a significant protective association with susceptibility to IS under a dominant model (AA + GA vs. GG; OR, 0.78, 95% CI, 0.63-0.97; p value 0.03). Our meta-analysis shows that TNF-α -238G/A gene polymorphism is more likely to be associated with the risk of IS in Caucasian populations as compared to Asian populations. However, TNF-α -308G/A gene polymorphism is more likely to be protective against IS in Asian populations as compared to Caucasian populations. Further large, well-designed prospective epidemiological studies are needed to confirm these findings.

DOI: 10.1159/000443770
PMCID: PMC4865080
PMID: 27195243 [PubMed]

62: Kumar R, Kumar R, Kumar V, Malhotra R. Comparative analysis of dual-phase 18F-fluoride PET/CT and three phase bone scintigraphy in the evaluation of septic (or painful) hip prostheses: A prospective study. J Orthop Sci. 2016 Mar;21(2):205-10. doi: 10.1016/j.jos.2015.12.018. Epub 2016 Feb 2. PubMed PMID: 26850923.

BACKGROUND: The preoperative differentiation of aseptic and septic loosening of hip prostheses remains a diagnostic challenge for clinicians and many molecular imaging techniques have been evaluated. The objective of current study was to establish the clinical utility of dual phase 18F-fluoride PET/CT (DPFP) in diagnosing implant loosening, differentiation between septic and aseptic loosening and to compare the diagnostic accuracy of DPFP and three-phase bone scan (TPBS).
METHODS: In this prospective study, we evaluated 57 hip components in 45 patients (bilateral prostheses in 12 patients, 45 painful and 12 asymptomatic contralateral hip components) with dual phase fluoride PET/CT and TPBS. Findings of skeletal scintigraphy and PET/CT were evaluated by two expert nuclear medicine physicians, blinded with clinical findings and final diagnosis. The patterns of tracer uptake and maximum standardized uptake value (SUVmax) were noted for each joint. The final diagnosis was based on intraoperative findings, histopathological or microbiological examinations.
RESULTS: Out of twelve non-painful hips, DPFP correctly identified no loosening in 11 hips while TPBS detected in 10 hips. In the remaining 45 hips with radiological proven loosening to rule out sepsis, DPFP had a sensitivity, specificity, PPV, NPV and accuracy of 75%, 97%, 92%, 88% and 88% respectively while TPBS revealed 81%, 86%, 76%, 89% and 82% respectively. DPFP had shown a higher specificity and PPV as compared to the TPBS in the evaluation of painful hip prostheses. The pattern of tracer uptake may help in the differentiation between the two entities. We also noted a significant difference between SUVmax values of septic and aseptic loosening.
CONCLUSIONS: The results suggested that DPFP has considerable potential in differentiating septic from aseptic loosening of hip prostheses and more specific to rule out sepsis than TPBS. It may be employed before revision arthroplasty to

evaluate implant for loosening and sepsis in loosened implant.

DOI: 10.1016/j.jos.2015.12.018
PMID: 26850923 [PubMed - in process]

63: Kumar S, Malik MA, Goswami S, Sihota R, Kaur J. Candidate genes involved in the susceptibility of primary open angle glaucoma. Gene. 2016 Feb 15;577(2):119-31. doi: 10.1016/j.gene.2015.11.032. Epub 2015 Nov 24. Review. PubMed PMID: 26621382.

PURPOSE: Glaucoma is a common disease often identified by high intraocular pressure, characteristic optic neuropathy and vision loss. It is currently a leading cause of blindness worldwide with no known cure. Primary open angle glaucoma (POAG) is the most common type of glaucoma worldwide. It is a multifactorial disease where both genetic as well as environmental factors are involved in the pathogenesis.
RESULTS: Till date, at least 29 genetic loci have been found to be linked to POAG. However, the role of only three underlying genes Myocilin (MYOC), Optineurin (OPTN) and WD repeat Domain 36, (WDR36) is well established. Also, the role of Cytochrome P450, family 1, subfamily B, polypeptide 1 (CYP1B1), Glutathione S-transferase mu 1 (GSTM1) and Neurotrophin (NTF4) has been fairly identified. Association studies have found that 66 loci with 76 genes associated to POAG till date, but even more studies are required to confirm their role in the disease pathology. Gene mutations in various populations have been identified by genetic studies to establish that about 5% of POAG is currently attributed to single-gene or Mendelian forms of glaucoma and others caused by the combined effects of many genetic and environmental risk factors, each of which do not act alone to cause glaucoma.
CONCLUSION: Although the clinical progression of the disease is well defined, the molecular events responsible for glaucoma are poorly understood and thus the etiology of POAG remains a mystery. Despite strong genetic influence in POAG pathogenesis, only a small part of the disease can be explained in terms of genetic aberration. This review is an overview and update on the latest research and progress of genetic studies associated with POAG.

DOI: 10.1016/j.gene.2015.11.032
PMID: 26621382 [PubMed - indexed for MEDLINE]

64: Lalwani S, Rajkumari N, Mathur P, Sharma V, Trikha V. Sepsis in fatal pelvic trauma patients: report from a level-1 Indian Trauma Centre. Eur J Trauma Emerg Surg. 2016 Feb;42(1):43-5. doi: 10.1007/s00068-015-0496-x. Epub 2015 Feb 20. PubMed PMID: 26038017.

65: Lohani N, Singh HN, Moganty RR. Structural aspects of the interaction of anticancer drug Actinomycin-D to the GC rich region of hmgb1 gene. Int J Biol Macromol. 2016 Jun;87:433-42. doi: 10.1016/j.ijbiomac.2016.02.060. Epub 2016 Feb 26. PubMed PMID: 26923673.

The high mobility group box 1 protein has been identified as a key player in chromatin homeostasis including transcription regulation, recombination, repair, and chromatin remodeling. Emerging findings indicate HMGB1 protein over expression in nearly all types of human cancers and inflammatory disorders. Thus it is considered as a potential therapeutic target for treating various malignancies. We screened the promoter region of hmgb1 gene and selected a positive regulatory element of 25 base pair duplex (25RY) (-165 to -183) as a potential target for chemotherapeutic intervention. The molecular interaction of actinomycin (ACT) with the regulatory region of hmgb1 gene was characterized by

spectroscopic, calorimetric and molecular docking studies. The hypochromic and bathochromic shift in the absorption spectrum, stabilization of 25RY duplex against thermal denaturation, perturbation of CD spectrum of duplex and enhancement of fluorescence intensity of actinomycin indicate strong binding of actinomycin to the hmgb1 promoter region (25RY).The energetics was characterized to be endothermic and entropy driven. All these results are in good agreement with in silico investigation that suggest minor groove binding with effective intercalation at GC bases of actinomycin to 25RY. This study identifies hmgb1 gene promoter region a potential target for the anticancer therapautiucs.

66: Lohani N, Rajeswari MR. Dichotomous life of DNA Binding High Mobility Group box1 Protein in human health and disease. Curr Protein Pept Sci. 2016 Feb 26. [Epub ahead of print] PubMed PMID: 26916160.

The High mobility box 1 (HMGB1) protein is an extremely versatile, highly conserved nuclear protein, with its unique intracellular and extracellular functions mediated by its relatively simple domain structure. Within the nucleus, HMGB1 binds to DNA minor groove in a non-specific manner and causes bends in the double helix thus helps in recruiting a number of DNA binding protein and transcription factors, to facilitate transcription of various genes. HMGB1 also helps in DNA repair, chromatin remodeling, V (D) J recombination, and assembly of nucleosome on the chromatin. On contrary, under pathological conditions HMGB1 displays inflammatory response by interaction with specific cell surface receptors like RAGE, TLR-4, TLR9, and TLR2 and activates NF-kB downstream signaling pathways. The upregulation of HMGB1 is directly associated with the pathogenesis of cancer, sepsis, ischemia, hemorrhagic shock, anorexia, rheumatic disease, periodontal disease etc. Therefore, HMGB1 has been considered as a promising target in the treatment of various human diseases. The interest in HMGB1 is evident and reflected in the exponential increase in the recent publications, and therefore there is a need for an update on the understanding of the role of HMGB1 in pathogenesis and its potential application of HMGB1 as a therapeutic target in a number of human diseases.

67: Mahajan C, Rath GP, Bithal PK, Mahapatra AK. Perioperative Management of Children With Giant Encephalocele: A Clinical Report of 29 Cases. J Neurosurg Anesthesiol. 2016 Feb 2. [Epub ahead of print] PubMed PMID: 26841351.

BACKGROUND: Giant encephalocele, a rare entity, makes anesthesiologists wary of challenging anesthetic course. Apart from inherent challenges of pediatric anesthesia, the anesthesiologist has to deal with unusual positioning, difficult tracheal intubation, and associated anomalies during the perioperative course.
MATERIALS AND METHODS: Medical records of 29 children with giant encephalocele, who underwent excision and repair, during a period of 13 years, were retrospectively analyzed. Data pertaining to anesthetic management, perioperative complications, and outcome at discharge were reviewed.
RESULTS: The average age at admission was 164 days. Hydrocephalus and delayed milestones were present in 19 (65.5%) and 7 (24.1%) children, respectively. Difficulty in tracheal intubation was encountered, in 15 (51.7%) children. Tracheal intubation was attempted with direct laryngoscopy, most often, in lateral position (24 [82.8%]). Intraoperative hemodynamic and respiratory complications were observed in 9 (31.0%) and 5 (17.2%) children, respectively. Intraoperative hypothermia was observed in 4 (13.8%) children. The average stay in the intensive care unit was 2.7 days and average hospital stay was 11.5 days. The condition at discharge remained same as the preoperative period in 24 children (82.7%), deteriorated in 2 (6.9%), and 3 children (10.3%) died.
CONCLUSIONS: Management of children with giant encephalocele requires the updated knowledge on possible difficulties encountered during the perioperative period. They need specialized anesthetic care for dealing with difficult tracheal intubation, associated congenital anomalies, unusual positioning, electrolyte abnormalities, hypothermia, and cardiorespiratory disturbances. For securing the airway, we suggest the practice of direct laryngoscopy in lateral position after

inhalational induction. Muscle relaxant should be administered only after visualization of the glottis.

DOI: 10.1097/ANA.0000000000000282
PMID: 26841351 [PubMed - as supplied by publisher]

68: Mahalangikar R, Kumar A, Sharma BS. Transorbital Penetrating Intracranial Injury with an Umbrella Wire Causing Cavernous Internal Carotid Artery Injury and Thrombosis. World Neurosurg. 2016 Feb;86:513.e15-8. doi: 10.1016/j.wneu.2015.09.033. Epub 2015 Sep 25. PubMed PMID: 26407931.

BACKGROUND: Transorbital penetrating intracranial injuries, though rare, can have serious consequences. Intracranial penetration can be present even if orbital trauma is trivial.
CASE DESCRIPTION: We report an unusual case of transorbital penetrating intracranial injury with umbrella wire, sustained while opening an umbrella, leading to internal carotid artery injury and thrombosis. The patient sustained only ipsilateral third nerve palsy that completely recovered during followup.
CONCLUSION: Trivial orbital injuries can be associated with significant intracranial injury in a neurologically intact patient. This case emphasizes the potentially injury-prone opening mechanism of conventional umbrellas. A high index of suspicion is important while evaluating such patients.

69: Mahapatra A, Sharma P. Internet snapshot survey: A novel methodology to monitor novel psychotropic substances and its need in Asia. Asian J Psychiatr. 2016 Jun;21:7-8. doi: 10.1016/j.ajp.2016.01.014. Epub 2016 Feb 21. PubMed PMID: 27208446.

Recently there has been upsurge in the use of novel psychoactive substances, commonly known as legal highs. There is limited data available on the use and availability of these substances. Internet snapshot methodology has been successfully used in Europe and America to understand rapidly adapting internet based drug market but no data is available from Asian region. Hence there is need of application of similar methodology in Asia to explore and gauge the problem statement about these substances.

DOI: 10.1016/j.ajp.2016.01.014
PMID: 27208446 [PubMed - in process]

70: Mal G, Vyas S, Srinivasan A, Patil NV, Pathak KM. Studies on Liquefaction Time and Proteins Involved in the Improvement of Seminal Characteristics in Dromedary Camels (Camelus dromedarius). Scientifica (Cairo). 2016;2016:4659358. doi: 10.1155/2016/4659358. Epub 2016 Feb 18. PubMed PMID: 27022505; PubMed Central PMCID: PMC4775800.

Semen was collected from six dromedary camels using artificial vagina during rutting season. Liquefaction of the viscous semen occurred in 23.89 ± 1.49 h. During liquefaction, proteins with molecular masses of 24.55 kDa and 22.07 kDa appeared in conjunction with the disappearance of intact 26.00 kDa protein after 18-24 h. These proteins were identified as β-nerve growth factors (β-NGFs) in liquefied camel semen. Guanidine-HCL improves the rheological characteristics of dromedary camel semen along with significant ($P < 0.01$) increase in sperm motility. No significant differences were found in viability of spermatozoa indicating no visible detrimental effects on spermatozoa. The cause of semen viscosity, as well as proteins that are present in liquefied dromedary camel seminal plasma, is described for the first time.

71: Maulik SK, Wilson V, Seth S, Bhargava B, Dua P, Ramakrishnan S, Katiyar CK. Clinical efficacy of water extract of stem bark of Terminalia arjuna (Roxb. ex DC.) Wight & Arn. in patients of chronic heart failure: a double-blind, randomized controlled trial. Phytomedicine. 2016 Oct 15;23(11):1211-9. doi: 10.1016/j.phymed.2016.02.007. Epub 2016 Feb 23. PubMed PMID: 26988798.

BACKGROUND: The stem bark of Terminalia arjuna (Roxb. ex DC.) Wight and Arn. (Arjuna) is used in Indian system of medicine (Ayurveda) for treatment of various cardiac diseases, including heart failure. However, well designed clinical trials exploring its efficacy and safety in chronic heart failure (CHF) are lacking.
PURPOSE: To ascertain the add-on efficacy and safety of a standardized water extract of stem bark of Arjuna (Arjuna extract) in CHF patients on standard pharmacotherapy.
STUDY DESIGN: Double-blind, parallel, randomized, placebo-controlled add-on clinical trial.
METHODS: After approval of institutional ethics committee, 100 patients of CHF of New York Heart Association (NYHA) functional class II on standard pharmacotherapy having an echocardiographic left ventricular ejection fraction (LVEF) ≤ 40% were consecutively recruited with informed consent and randomized 1:1 to Arjuna extract 750 mg or matching placebo twice daily. The primary outcome measure was change in LVEF at 12 weeks. Secondary outcome measures included changes in (i) NYHA functional class, (ii) distance covered in 6 min walk test (6MWT), (iii) quality of life (QoL), as determined by the Kansas City Cardiomyopathy Questionnaire (KCCQ), (iv) plasma brain natriuretic peptide, (v) plasma cytokines (interleukin-6, high sensitivity C-reactive protein and tumour necrosis factor-α) and (vi) oxidative stress markers [serum thiobarbituric acid reactive substances (TBARS), red blood cell (RBC) superoxide dismutase (SOD), RBC catalase and RBC glutathione (GSH)] at 6 and 12 weeks. Safety assessment was done by adverse event monitoring and laboratory investigations. Results were expressed as mean ± SD or median (interquartile range) and analysed with intention-to- treat principle using appropriate two-sided statistical tests. A p-value < 0.05 was considered significant.
RESULTS: Arjuna extract was well-tolerated, but did not change LVEF (24.3 ± 7.1 versus 25.5 ± 7.7%; p = 0.4) or secondary outcome measures except preservation of RBC catalase activity [1275(104, 10350) versus 1243.5(104, 10350) U/g haemoglobin; p = 0.01] compared to placebo. Significantly greater percentage increases occurred in distance covered in 6 MWT, RBC-SOD, RBC catalase, RBC GSH and in symptom severity and stability domains of KCCQ in patients on Arjuna extract versus those on placebo, on a post-hoc analysis, between subgroups of patients who improved in these outcomes.
CONCLUSION: Arjuna extract did not improve LVEF in CHF patients over 12 weeks, although there was improvement in functional capacity, antioxidant reserves and symptom-related QoL domains in some patients.

DOI: 10.1016/j.phymed.2016.02.007
PMID: 26988798 [PubMed - in process]

72: Mitra A, Bajpai M. Impacted Sharp Oesophageal Foreign Bodies--A Novel Technique of Removal with the Paediatric Bronchoscope. J Trop Pediatr. 2016 Apr;62(2):161-4. doi: 10.1093/tropej/fmv075. Epub 2016 Feb 6. PubMed PMID: 26851436; PubMed Central PMCID: PMC4886110.

Sharp foreign bodies in the oesophagus may present as an entirely asymptomatic child with only radiological evidence but require emergent surgical management. Safety pins, razor blades and needles are a few of the commonly ingested sharp objects in developing countries. The open safety pin is a particularly interesting clinical problem, as the management depends on its location and orientation. Many methods and instruments have been used over the years to remove them from the upper digestive tract. We present a novel method using the rigid paediatric bronchoscope and alligator forceps for the extraction of this unusual foreign body from the oesophagus of a 6 year old girl.

DOI: 10.1093/tropej/fmv075
PMCID: PMC4886110 [Available on 2017-04-01]
PMID: 26851436 [PubMed - in process]

73: Mohan I, Gupta R, Misra A, Sharma KK, Agrawal A, Vikram NK, Sharma V, Shrivastava U, Pandey RM. Disparities in Prevalence of Cardiometablic Risk Factors in Rural, Urban-Poor, and Urban-Middle Class Women in India. PLoS One. 2016 Feb 16;11(2):e0149437. doi: 10.1371/journal.pone.0149437. eCollection 2016. PubMed PMID: 26881429; PubMed Central PMCID: PMC4755555.

OBJECTIVE: Urbanization is an important determinant of cardiovascular disease (CVD) risk. To determine location-based differences in CVD risk factors in India we performed studies among women in rural, urban-poor and urban middle-class locations.
METHODS: Population-based cross-sectional studies in rural, urban-poor, and urban-middle class women (35-70 y) were performed at multiple sites. We evaluated 6853 women (rural 2616, 5 sites; urban-poor 2008, 4 sites; urban middle-class 2229, 11 sites) for socioeconomic, lifestyle, anthropometric and biochemical risk factors. Descriptive statistics are reported.
RESULTS: Mean levels of body mass index (BMI), waist circumference, waist-hip ratio (WHR), systolic BP, fasting glucose and cholesterol in rural, urban-poor and urban-middle class women showed significantly increasing trends (ANOVAtrend, p <0.001). Age-adjusted prevalence of diabetes and risk factors among rural, urban-poor and urban-middle class women, respectively was, diabetes (2.2, 9.3, 17.7%), overweight BMI ≥25 kg/m2 (22.5, 45.6, 57.4%), waist >80 cm (28.3, 63.4, 61.9%), waist >90 cm (8.4, 31.4, 38.2%), waist hip ratio (WHR) >0.8 (60.4, 90.7, 88.5), WHR>0.9 (13.0, 44.3, 56.1%), hypertension (31.6, 48.2, 59.0%) and hypercholesterolemia (13.5, 27.7, 37.4%) (Mantel Haenszel X2 ptrend <0.01). Inverse trend was observed for tobacco use (41.6, 19.6, 9.4%). There was significant association of hypertension, hypercholesterolemia and diabetes with overweight and obesity (adjusted R2 0.89-0.99).
CONCLUSIONS: There are significant location based differences in cardiometabolic risk factors in India. The urban-middle class women have the highest risk compared to urban-poor and rural.

74: Mondal K, Chakravarti S, Ghosh AK, Kumar S, Nayak B, Nandi S, Sarkar U, Deb R, De A, Biswas J. Novel identification of Factor XI deficiency in Indian Sahiwal (Bos indicus) cattle. Mol Biol Rep. 2016 Apr;43(4):213-9. doi: 10.1007/s11033-016-3955-5. Epub 2016 Feb 18. PubMed PMID: 26892783.

Factor-XI deficiency (FXID) is inherited as autosomal lethal recessive disorder of carrier Holstein-Friesian bulls. A 76 base pair segment insertion into exon 12 in Factor-XI gene causes FXID in cattle. Keeping this in view the present study was conducted to screen breeding bulls of both indigenous and exotic breeds for mutation in Factor-XI gene and to find out the frequency of FXID carrier animals in breeding bulls. A total of 120 bulls of different age group maintained at Frozen Semen Bull Station, India were randomly selected from different cattle breeds to screen presence of FXID syndrome in breeding sires. Genomic DNA was isolated from blood of the selected bulls. PCR parameters were standardized to obtain 244 and 320 bp amplicons. The results showed that 2 Sahiwal bulls out of 120 animals were carrier for FXID. Amplicons of the carrier animals were sequenced and annoted, which confirms a 76 bp insertion in the exon 12. Bleeding and clotting time showed considerable discrepancy in the carrier animals as compared to the normal animals. The findings of relative mRNA expression of Factor XI transcript revealed identical tendency in the carrier. The frequency of carrier animals and mutant allele was 2.5 % and 0.025 respectively. This study recommends for screening of breeding at AI bull centers in the country for FXID. The study also stands a merit for identification of FXID carrier in Bos indicus for the first time.

75: Naz F, Koul V, Srivastava A, Gupta YK, Dinda AK. Biokinetics of ultrafine gold nanoparticles (AuNPs) relating to redistribution and urinary excretion: a long-term in vivo study. J Drug Target. 2016 Sep;24(8):720-9. doi: 10.3109/1061186X.2016.1144758. Epub 2016 Feb 26. PubMed PMID: 26837799.

Gold nanoparticles (AuNPs) of ultrafine size have drawn attention for their use in drug delivery systems. Tissue toxicity may be an issue when AuNPs are used for such applications. We investigated the long-term biokinetics (90 d), redistribution, and urinary excretion of three different-sized (2 ± 0.5 nm, 5 ± 1 nm, and 10 ± 2 nm) AuNPs after a single intravenous (i.v.) administration of 1250 µg/kg dose in mice. ICP-AES analysis of lungs, liver, spleen, heart, kidney, brain, blood, and urine revealed highest accumulation of gold in spleen around 15 d after injection. A low concentration was detected in brain after 1 d without any residual AuNPs after 30 d. Ultrastructural study of brain tissue also showed few AuNPs in lysosome with no changes in cellular architecture. Renal retention of AuNPs was limited indicating low nephrotoxic potential. AuNPs were detectable in urine till 30 d after single injection indicating slow excretion from the body. No evidence of significant toxicity was observed in hemogram, serum biochemistry, and tissue histology. No mortality, changes in behavior, hair color, weight, and food intake was observed as compared to control mice. Therefore, we conclude that the ultrafine AuNPs are predominantly excreted in urine without any systemic toxicity following i.v. administration and are hence safe for use in drug delivery systems.

76: Neogi SB, Negandhi H, Kar R, Bhattacharya M, Sen R, Varma N, Bharti P, Sharma J, Bhushan H, Zodpey S, Saxena R. Diagnostic accuracy of haemoglobin colour strip (HCS-HLL), a digital haemoglobinometer (TrueHb) and a non-invasive device (TouchHb) for screening patients with anaemia. J Clin Pathol. 2016 Feb;69(2):164-70. doi: 10.1136/jclinpath-2015-203135. Epub 2015 Aug 14. PubMed PMID: 26280783.

AIM: Estimation of haemoglobin (Hb) remains a challenge, particularly in outreach settings. There is a need to have a simple and cost-effective device to detect anaemia. Three devices (haemoglobin colour scale (HCS)-HLL (Hindustan Lifecare Limited), TrueHb V.1.1, TouchHb Alpha 1.1- non-invasive) have been developed in India recently. This study aimed to determine the diagnostic accuracy of these tests (index) for the screening of anaemia against haematological autoanalyzer (reference).
METHODS: The study was conducted in four medical colleges of India. All consenting adult patients (>18 years of age) undergoing routine investigations were included. Each patient underwent the reference test and at least one index test. Outcome assessors for the index tests were blinded to the results of the reference test. Diagnostic accuracy was calculated using cut-offs proposed by WHO.
RESULTS: A total of 5244 patients underwent the reference test while HCS-HLL, TrueHb and TouchHb tests were conducted on 2745, 2331 and 2874 patients respectively. The positive likelihood ratio of HCS-HLL using capillary blood (1.2), venous blood (1.7) and TouchHb (1.5) was lower than TrueHb capillary (3.7; 95% CI 3.3 to 4.2) and venous blood (5.7; 95% CI 4.9 to 6.6). TrueHb had a sensitivity of 74.4% (95% CI 71.9% to 76.8%) for venous and 82.0% (95% CI 79.8% to 89.2%) for capillary samples. The specificity was high (>75.0%). The area under receiver operating characteristic was close to 80.0%. Consistent results were seen for detection of severe anaemia.
CONCLUSIONS: The digital method (TrueHb) emerged as a better diagnostic method for screening anaemia. Its effectiveness should be established in outreach settings before further recommendation.

DOI: 10.1136/jclinpath-2015-203135

PMID: 26280783 [PubMed - indexed for MEDLINE]

77: Pahwa R, Kumar U, Das N. Modulation of PBMC-decay accelerating factor (PBMC-DAF) and cytokines in rheumatoid arthritis. Mol Cell Biochem. 2016 Mar;414(1-2):85-94. doi: 10.1007/s11010-016-2661-x. Epub 2016 Feb 23. PubMed PMID: 26906204.

Studies have suggested that abnormal expression of complement regulatory proteins and cytokines contribute significantly to the path-physiology of rheumatoid arthritis. In this context, Decay accelerating factor (DAF) a complement regulatory protein is gaining increased attention. With the notion that immune effecter mechanisms are all interlinked and circulating peripheral blood mononuclear cells (PBMCs) should have a role in a systemic disease like rheumatoid arthritis, we studied the modulation and significance of PBMC-DAF and cytokines in RA. Seventy-five RA patients and 75 healthy controls were recruited. Expression of DAF and cytokines (IFN-γ, IL-17A and IL-10) in the PBMCs of patients and controls was determined. Correlations among DAF, cytokines, and disease activity were evaluated by standard statistical methods. The effect of IFN-γ, IL-17A, and IL-10 on the expression of DAF in patients and controls was studied in vitro. Expression of PBMC-DAF declined in patients both at mRNA and surface level and correlated negatively with the disease activity. Expression of IFN-γ also declined in patients but correlated positively with DAF and negatively with disease activity. Expression of IL-17A and IL-10 was higher in patients. The levels correlated positively with disease activity and negatively with DAF both in patients and controls. In vitro studies indicated that IFN-γ up-regulated DAF expression in PBMCs, whereas IL-17A and IL-10 had negative effect on the same. The decline in the PBMC-DAF is a contributing factor in manifestations of RA. Cytokine environment contributes to this decline. These findings brought novel insights into the complement-cytokine axis in the path-physiology of RA.

DOI: 10.1007/s11010-016-2661-x
PMID: 26906204 [PubMed - in process]

78: Pal A, Parmar A. Forensic issues of involuntary admissions: The Achilles heel of psychiatry residency in general hospital psychiatry unit in India. Asian J Psychiatr. 2016 Apr;20:30-1. doi: 10.1016/j.ajp.2016.01.011. Epub 2016 Feb 6. PubMed PMID: 27025468.

79: Panda S, Sikka K, Punj J, Sharma SC. Bilateral congenital alveolar synechiae-a rare cause of trismus. Maxillofac Plast Reconstr Surg. 2016 Feb 19;38(1):8. eCollection 2016 Dec. PubMed PMID: 26942163; PubMed Central PMCID: PMC4760995.

Congenital alveolar synechiae is a rare anomaly mostly presenting in association with cleft palate. Owing to reduced mouth opening, feeding difficulties, and compromised airway in extreme cases along with presentation in early neonatal period, these patients present unique challenges to the surgeon as well as the anesthetist. Here, we discuss the surgical and anesthetic management of this entity in a 12-month-old female child.

DOI: 10.1186/s40902-016-0056-2
PMCID: PMC4760995
PMID: 26942163 [PubMed]

80: Parmeswaran GG, Kalaivani M, Gupta SK, Goswami AK, Nongkynrih B. Assessment of home hazards for childhood injuries in an urban population in New Delhi. Child Care Health Dev. 2016 Jul;42(4):473-7. doi: 10.1111/cch.12328. Epub 2016 Feb 19. PubMed PMID: 26892878.

BACKGROUND: Childhood injuries, especially the unintentional category of injuries, occur most commonly in the environment inside a child's home. The primary objective of the present study was to assess the presence of home hazards

for childhood injuries in households in an urban resettlement colony in New Delhi.
METHODS: A community-based cross-sectional study was carried out in an urban resettlement colony in Delhi. A hazards assessment tool was used to check the presence of hazards in the houses.
RESULTS: A total of 225 households were included. It was seen that121 (53.7%) had a cooking stove within the reach of the child, and 190 (84.3%) had the gas pipe within reach. Fire hazard was seen in 84% of houses. About 78% of households did not have locked storage for chemicals.
CONCLUSION: The study revealed a significant burden of hazards for childhood injuries within their own homes, thus emphasizing the need for injury prevention interventions to reduce the number of hazards.

DOI: 10.1111/cch.12328
PMID: 26892878 [PubMed - in process]

81: Patnaik U, Sikka K, Agarwal S, Kumar R, Thakar A, Sharma SC. Cochlear re-implantation: lessons learnt and the way ahead. Acta Otolaryngol. 2016 Jun;136(6):564-7. doi: 10.3109/00016489.2015.1136430. Epub 2016 Feb 22. PubMed PMID: 26898701.

Conclusion A cochlear re-implantation procedure is undesirable; however, the cochlear implant surgeon may have to perform a re-implantation procedure occasionally for various reasons. Following standard techniques, implant performance comparable with primary implantation may be achieved. Objective To study the causes and outcomes of cochlear re-implantation in an Asian Indian population. Study design Retrospective analysis of clinical charts over an 18-year period with prospective follow-up of patients. Methods The charts of 534 patients, who underwent cochlear implant, at an Otorhinolaryngology institutional Centre, from January 1997 to January 2015 were studied. Of these, the charts of 18 patients who underwent cochlear re-implantation were studied. The causes and audiological and speech outcomes were analysed. Results Eighteen patients (3.4%) underwent cochlear re-implantation for various reasons. The commonest indication was device failure in seven patients (39%), followed by electrode extrusion in five (28%), trauma in three (11%), electrode migration in two (11%) and improper electrode placement in one (6%) patient. The audiological performance tests and speech tests either remained the same or improved from those achieved for patients undergoing primary implantation, in 87% patients.

DOI: 10.3109/00016489.2015.1136430
PMID: 26898701 [PubMed - in process]

82: Pattnaik B, Bodas M, Bhatraju NK, Ahmad T, Pant R, Guleria R, Ghosh B, Agrawal A. IL-4 promotes asymmetric dimethylarginine accumulation, oxo-nitrative stress, and hypoxic response-induced mitochondrial loss in airway epithelial cells. J Allergy Clin Immunol. 2016 Jul;138(1):130-141.e9. doi: 10.1016/j.jaci.2015.11.036. Epub 2016 Feb 23. PubMed PMID: 26915676.
BACKGROUND: Obesity is known to increase asthma risk and severity. Increased levels of asymmetric dimethylarginine (ADMA), an endogenous nitric oxide synthase inhibitor, are associated with mitochondrial toxicity, asthma, and metabolic syndrome. IL-4 upregulates the expression of protein arginine methyltransferases, which are essential for ADMA formation. Importantly, cross-talk between IL-4, ADMA, and mitochondrial dysfunction could explain how obesity and IL-4 can synergize to exacerbate allergic inflammation.
OBJECTIVE: We sought to investigate how IL-4, a key asthma-associated cytokine, can influence ADMA-related effects on lungs.
METHODS: BEAS2B (bronchial epithelial) cells were treated with IL-4 followed by ADMA and investigated for oxo-nitrative stress and resultant mitochondrial toxicity after 48 hours by using flow cytometry, confocal imaging, immunoblotting, and fluorimetric assays.
RESULTS: IL-4–induced mitotoxicity in BEAS2B cells was significantly higher in

the presence of exogenous ADMA. IL-4 treatment led to proteolytic degradation of dimethylarginine dimethylaminohydrolase 2, which catabolizes ADMA. IL-4 pretreatment was associated with increased intracellular ADMA accumulation and increased ADMA-induced mitotoxicity. Airway epithelial cells treated with IL-4 followed by ADMA showed exaggerated oxo-nitrative stress and potent induction of the cellular hypoxic response, despite normoxic conditions. The hypoxic response was associated with reduced mitochondrial function but was reversible by overexpression of the mitochondrial biogenesis factor, mitochondrial transcription factor A.
CONCLUSION: We conclude that IL-4 promotes intracellular ADMA accumulation, leading to mitochondrial loss through oxo-nitrative stress and hypoxic response. This provides a novel understanding of how obesity, with high ADMA levels, and asthma, with high IL-4 levels, might potentiate each other and highlights the potential of mitochondrial-targeted therapeutics in obese subjects with asthma.

DOI: 10.1016/j.jaci.2015.11.036
PMID: 26915676 [PubMed - in process]

83: Paul VK. Participatory women's groups: time for integration into programmes. Lancet Glob Health. 2016 Feb;4(2):e74-5. doi: 10.1016/S2214-109X(16)00010-3. PubMed PMID: 26823216.

84: Prabhakar H, Singh GP, Ali Z, Kalaivani M, Smith MA. Pharmacological and non-pharmacological interventions for reducing rocuronium bromide induced pain on injection in children and adults. Cochrane Database Syst Rev. 2016 Feb 12;2:CD009346. doi: 10.1002/14651858.CD009346.pub2. Review. PubMed PMID: 26871982.

BACKGROUND: Rocuronium bromide is a routinely used muscle relaxant in anaesthetic practice. Its use, however, is associated with intense pain on injection. While it is well established that rocuronium bromide injection causes pain in awake patients, anaesthetized patients also tend to show withdrawal movements of the limbs when this muscle relaxant is administered. Various strategies, both pharmacological and non-pharmacological, have been studied to reduce the incidence and severity of pain on rocuronium bromide injection. We wanted to find out which of the existing modalities was best to reduce pain on rocuronium injection.
OBJECTIVES: The objectives of this review were to assess the ability of both pharmacological and non-pharmacological interventions to reduce or eliminate the pain that accompanies rocuronium bromide administration.
SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL 2013, Issue 7), MEDLINE via Ovid SP (1966 to July 2013) and EMBASE via Ovid SP (1980 to July 2013). We also searched specific websites. We reran the searches in February 2015 and will deal with the 11 studies of interest found through this search when we update the review.
SELECTION CRITERIA: We included all randomized controlled trials (RCTs) that compared the use of any drug or a non-pharmacological method with control patients, or those receiving no treatment to reduce the severity of pain with rocuronium injection. Our primary outcome was pain on rocuronium bromide injection measured by a pain score assessment. Our secondary outcomes were rise in heart rate and blood pressure following administration of rocuronium and adverse events related to the interventions.
DATA COLLECTION AND ANALYSIS: We used the standardized methods for conducting a systematic review as described in the Cochrane Handbook for Systematic Reviews of Interventions. Two authors independently extracted details of trial methodology and outcome data from reports of all trials considered eligible for inclusion. We made all analyses on an intention-to-treat basis. We used a fixed-effect model where there was no evidence of significant heterogeneity between studies and a

random-effects model if heterogeneity was likely.
MAIN RESULTS: We included 66 studies with 7840 participants in the review, though most analyses were based on data from fewer participants. In total there are 17 studies awaiting classification. No studies were at a low risk of bias. We noted substantial statistical and clinical heterogeneity between trials. Most of the studies reported the primary outcome pain as assessed by verbal response from participants in an awake state but some trials reported withdrawal of the injected limb as a proxy for pain after induction of anaesthesia in response to rocuronium administration. Few studies reported adverse events and no study reported heart rate and blood pressure changes after administration of rocuronium. Lidocaine was the most commonly studied intervention drug, used in 29 trials with 2256 participants. The risk ratio (RR) of pain on injection if given lidocaine compared to placebo was 0.23 (95% confidence interval (CI) 0.17 to 0.31; I^2 = 65%, low quality of evidence). The RR of pain on injection if fentanyl and remifentanil were given compared to placebo was 0.42 (95% CI 0.26 to 0.70; I^2 = 79%, low quality of evidence) and (RR 0.10, 95% CI 0.04 to 0.26; I^2 = 74%, low quality of evidence), respectively. Pain on injection of intervention drugs was reported with the use of lidocaine and acetaminophen in one study. Cough was reported with the use of fentanyl (one study), remifentanil (five studies, low quality evidence) and alfentanil (one study). Breath holding and chest tightness were reported with the use of remifentanil in two studies (very low quality evidence) and one study (very low quality evidence), respectively. The overall rate of complications was low.
AUTHORS' CONCLUSIONS: The evidence to suggest that the most commonly investigated pharmacological interventions reduce pain on injection of rocuronium is of low quality due to risk of bias and inconsistency. There is low or very low quality evidence for adverse events, due to risk of bias, inconsistency and imprecision of effect. We did not compare the various interventions with one another and so cannot comment on the superiority of one intervention over another. Complications were reported more often with use of opioids.

DOI: 10.1002/14651858.CD009346.pub2
PMID: 26871982 [PubMed - indexed for MEDLINE]

85: Prakash S, Sagar R. Psychiatric classification: Current debate and future directions. Asian J Psychiatr. 2016 Apr;20:15-21. doi: 10.1016/j.ajp.2016.01.013. Epub 2016 Feb 13. Review. PubMed PMID: 27025466.

Classification of health related conditions can be a complex task. This is particularly so in case of psychiatric disorders. The present paper reviews the fundamentals of psychiatric classification, including its basis, history, methods of evaluation, the journey so far and future directions. The various criticisms of current classificatory systems and possible solutions are discussed. Special reference to the research domain criteria (RDoC) approach has been made and implications discussed.

DOI: 10.1016/j.ajp.2016.01.013
PMID: 27025466 [PubMed - in process]

86: Praveen EP, Chouhan S, Sahoo J, Goel SK, Dwivedi SN, Khurana ML, Kulshreshtha B, Ammini AC. Effect of Different Insulin Response Patterns During Oral Glucose Tolerance Test on Glycemia in Individuals with Normal Glucose Tolerance. Diabetes Technol Ther. 2016 May;18(5):316-26. doi: 10.1089/dia.2015.0379. Epub 2016 Feb 17. PubMed PMID: 26886065.

BACKGROUND: Research is still going on for detecting the earliest glucose homeostasis derangements in individuals, which is crucial for the prevention of glucose intolerance. This cross-sectional study analyzes different insulin response patterns during the oral glucose tolerance test (OGTT) and their implications on glycemia in normoglycemic individuals.
SUBJECTS AND METHODS: The sample frame was the "Offspring of Individuals with

Diabetes Study" database. All participants underwent OGTT. Blood samples were collected at 0, 30, 60, and 120 min for measurement of insulin, C-peptide, and proinsulin levels. Normal glucose tolerant individuals were selected for analysis.
RESULTS: Four hundred fifty subjects (mean age, 25 years) were included and divided into two groups according to timing of plasma insulin peaking during OGTT: Group 1, peaking at 30 min; and Group 2, peaking at 60 or 120 min. Body mass index (BMI) and insulin resistance were comparable between the groups; however, Group 2 showed a significantly higher 60- and 120-min glucose level and lower disposition index. Based on the magnitude of the insulin levels, Group 1 was subdivided into Group N (normal pattern) and Group E (exaggerated pattern) with a 30-min insulin cutoff of 74 μU/mL (Group E, ≥74 μU/mL). Group 2 was subdivided into Group DL (delayed and limited pattern; 60-min insulin <73.0 μU/mL and 120-min insulin <80.0 μU/mL) and Group DE (delayed and exaggerated pattern; 60-min insulin ≥73.0 μU/mL or 120-min insulin ≥80.0 μU/mL). Group DE showed a significantly higher area under the curve (AUC) of glucose compared with the other groups and had a lower disposition index and high-density lipoprotein levels. Group DL had significantly lower insulin resistance and BMI compared with Group E but showed a similar AUC of glucose.
CONCLUSIONS: A delayed insulin pattern was associated with higher postprandial glucose levels. Individuals with delayed and exaggerated insulin secretion may have a higher risk for glucose intolerance.

DOI: 10.1089/dia.2015.0379
PMID: 26886065 [PubMed - in process]

87: Purkait S, Mallick S, Sharma V, Kumar A, Pathak P, Jha P, Biswas A, Julka PK, Gupta D, Suri A, Upadhyay AD, Suri V, Sharma MC, Sarkar C. A simplified approach for molecular classification of glioblastomas (GBMs): experience from a tertiary care center in India. Brain Tumor Pathol. 2016 Jul;33(3):183-90. doi: 10.1007/s10014-016-0251-y. Epub 2016 Feb 10. PubMed PMID: 26865311.

This study aims to establish a simplified molecular classification of glioblastomas (GBMs) based on molecular genetic alterations. GBM cases (n-114) were evaluated for IDH-1 and TP53 mutation by Sanger sequencing, PDGFRA and EGFR amplification by FISH, NF1 and YKL40 expression by qRT-PCR. Subsequently they were classified into four subgroups: classical like (CL), proneural like (PN), mesenchymal like (MES) and neural like (NEU). CL subtype was most frequent (39 %), followed by PN (32 %) and MES (20 %) subtypes. PN subtype had significantly younger age at presentation and longest survival (median PFS-82.5 weeks; 1 and 2 years OS-90.6 and 71.3 %). Other three subgroups had equally poor prognosis and hence, clubbed together as non-proneural (Non-PN) (median PFS-39 weeks; 1 and 2 years OS-66 and 0 %). Hence, we recommended this relatively easy method of subclassifying GBMs into PN and Non-PN which are statistically different in prognosis (both OS and PFS on uni and multivariate analysis). Although evaluation of six molecular alterations for identifying these two subgroups is still cumbersome, we propose segregation of PN subtype alone based on assessment of IDH1, TP53 and PDGFRA status, which is relatively easy and may be amenable to routine practice.

DOI: 10.1007/s10014-016-0251-y
PMID: 26865311 [PubMed - in process]

88: 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. 2016 Feb 2. doi: 10.1111/bpa.12364. [Epub ahead of print] 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. 176 cases of glioma were assessed for ATRX immunohistochemistry and

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 co-deletion. Mosaic/heterogeneous staining was detected almost 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.

DOI: 10.1111/bpa.12364
PMID: 26833422 [PubMed - as supplied by publisher]

89: Purkait S, Sharma V, Kumar A, Pathak P, Mallick S, Jha P, Sharma MC, Suri V, Julka PK, Suri A, Sharma BS, Sarkar C. Expression of DNA methyltransferases 1 and 3B correlates with EZH2 and this 3-marker epigenetic signature predicts outcome in glioblastomas. Exp Mol Pathol. 2016 Apr;100(2):312-20. doi: 10.1016/j.yexmp.2016.02.002. Epub 2016 Feb 15. PubMed PMID: 26892683.

This study aims to analyze expression of EZH2 and DNA-methyltransferases (DNMT1, 3A and 3B) in astrocytic tumors and investigate their link as well as their correlation with survival, especially in GBMs. Expression of EZH2 and DNMTs (DNMT1, DNMT3A and DNMT3B) in different grades of astrocytomas (n=93) was assessed by qRT-PCR and immunohistochemistry. GBM-U87MG cell line was used for functional studies. Strong immunopositivity (LI≥25%) for EZH2, DNMT1 and DNMT3B was detected in 52%, 56% and 64% cases of GBMs respectively, which was significantly higher as compared to Grade II/III cases. Similarly, their median fold change of mRNA expression was also significantly higher in GBMs. There was also a significant positive correlation between DNMT1/DNMT3B and EZH2 mRNA and protein expression, which was in concordance with TCGA data set. Inhibition of DNMTs in cell line by Azacytidine resulted in down-regulation of EZH2, while knock-down of EZH2 by siRNA was not associated with any significant alteration of DNMTs, indicating that EZH2 expression in GBMs is possibly regulated by DNMTs, but not the reverse. Strong immunopositivity for EZH2, DNMT1 and DNMT3B were individually associated with significantly shorter survival and showed no correlation with IDH1 mutation status. In addition, the combination of these 3 markers represented an independent prognostic signature with cases having weak/negative expression of all 3 markers being associated with best prognosis. For the first time, the present study describes an epigenetic prognostic signature in GBMs based on immunohistochemical expression of EZH2, DNMT1 and 3B which can be used easily in routine neuropathology practice.

DOI: 10.1016/j.yexmp.2016.02.002
PMID: 26892683 [PubMed - in process]

90: Rajeshwari M, Kakkar A, Nalwa A, Suri V, Sarkar C, Satyarthee GD, Garg A, Sharma MC. WNT-activated medulloblastoma with melanotic and myogenic differentiation: Report of a rare case. Neuropathology. 2016 Aug;36(4):372-5. doi: 10.1111/neup.12281. Epub 2016 Feb 12. PubMed PMID: 26869281.

Medulloblastoma (MB) with melanotic and myogenic differentiation, previously known as melanotic medullomyoblastoma, is an extremely rare histological variant of MB showing melanocytic as well as skeletal muscle differentiation. Only 10

cases of this rare tumor have been reported in the literature to date. We report this case of a 2-year-old male child who presented with a midline cerebellar mass, which on histopathological examination showed classic MB intermixed with cells containing melanin pigment, along with rhabdomyoblasts, spindle cells and occasional strap cells, which corresponded to WNT subgroup on molecular classification. The cell of origin of this MB variant is likely to be neural crest-derived stem cells which are capable of multilineage differentiation. Significant findings from previous reports and important differential diagnoses are discussed. Documentation of these tumors is important to characterize the clinical behaviour and to identify distinct genetic features, if any.

DOI: 10.1111/neup.12281
PMID: 26869281 [PubMed - in process]

91: Rao R, Mandal P, Gupta R, Ramshankar P, Mishra A, Ambekar A, Jhanjee S, Dhawan A. Factors Affecting Drug Use During Incarceration: A Cross-Sectional Study of Opioid-Dependent Persons from India. J Subst Abuse Treat. 2016 Feb;61:13-7. doi: 10.1016/j.jsat.2015.08.009. Epub 2015 Sep 21. PubMed PMID: 26470597.

INTRODUCTION: Substance abuse and criminality share a complex relationship. The rates of substance use among the prisoners, and that of criminal acts among substance users in community setting are high. Data from South Asian countries, including from India are inadequate. This study aimed to assess the pattern of criminal acts among opioid-dependent subjects and their substance use pattern in the month before, during and after imprisonment.
METHODS: Using a cross-sectional study design and purposive sampling, opioid-dependent subjects (n=101) attending two community drug treatment clinics who have had any contact with the law were assessed using a specifically-designed tool to record criminal acts and substance use before, during and after last imprisonment.
RESULTS: Most subjects (93%) had committed illegal acts in their lifetime. Physical assault was the most common illegal act, while 23% reported selling drugs and 9% reported committing serious crimes. About 95% were arrested and 92% had spent time in police lockups. About 29% were arrested for drugs possession or drug use, and 3% of injecting drug users arrested for carrying injection equipment. About 85% had been imprisoned at least once, of whom 88% used psychoactive substances in the 1-month period before their last imprisonment. Opioids were the most common substances used daily (68%), followed by cannabis (34%) and alcohol (22%). Ninety-seven percent reported the availability of substances in prisons, and 65% also used substances during their last imprisonment. Cannabis (35%) was the most common substances used in prison followed by opioids (19%). Seventy-six percent used substances soon after prison release, and 13% of opioid users experienced opioid overdose soon after prison release. Use of cannabis, injecting drugs, and opioid use before imprisonment were predictors of substance use in prison.
CONCLUSION: Opioid-dependent people have various contacts with the law, including imprisonment. Many users are dependent on substances during prison-entry, which is an important reason for their continued substance use in prisons. There is a need to provide substance abuse treatment across all stages of criminal justice system.

DOI: 10.1016/j.jsat.2015.08.009
PMID: 26470597 [PubMed - in process]

92: Rastogi N, Singh A, Singh PK, Tyagi TK, Pandey S, Shin K, Kaur P, Sharma S, Singh TP. Structure of iron saturated C-lobe of bovine lactoferrin at pH 6.8 indicates a weakening of iron coordination. Proteins. 2016 May;84(5):591-9. doi: 10.1002/prot.25004. Epub 2016 Feb 24. PubMed PMID: 26850578.

The bilobal lactoferrin is an approximately 76 kDa glycoprotein. It sequesters two Fe(3+) ions together with two CO(3)(2-) ions. The C-terminal half (residues, Tyr342-Arg689, C-lobe) of bovine lactoferrin (BLF) (residues Ala1-Arg689) was prepared by limited proteolysis using trypsin. Both C-lobe and intact BLF were saturated to 100%. Both of them retained up to nearly 85% of iron at pH 6.5. At pH 5.0, C-lobe retained 75% of iron whereas intact protein could retain only slightly more than 60%. At pH 4.0 both contained 25% iron and at pH 2.0 they were left with iron concentration of only 10%. The structure of iron saturated C-lobe was determined at 2.79 Å resolution and refined to R(cryst) and R(free) factors of 0.205 and 0.273, respectively. The structure contains two crystallographically independent molecules, A and B. They were found to have identical structures with an r.m.s. shift of 0.5 Å for their C(α) atoms. A high solvent content of 66% was observed in the crystals. The average value of an overall B-factor was 68.0 Å(2). The distance of 2.9 Å observed for the coordination bond between Fe(3+) ion and N(e2) of His595 appeared to be considerably longer than the normally observed values of 1.9-2.2 Å. This indicated that the coordination bond involving His595 may be absent. Other coordination distances were observed in the range of 2.1-2.3 Å. Based on the present structure of iron saturated C-lobe, it may be stated that His595 is the first residue to dissociate from ferric ion when the pH is lowered.

DOI: 10.1002/prot.25004
PMID: 26850578 [PubMed - in process]

93: Ray B, Agarwal S, Lohani N, Rajeswari MR, Mehrotra R. Structural, conformational and thermodynamic aspects of groove-directed-intercalation of flavopiridol into DNA. J Biomol Struct Dyn. 2016 Feb 17:1-18. [Epub ahead of print] PubMed PMID: 26599132.

Certain plant-derived alkaloids and flavonoids have shown propitious cytotoxic acitvity against different types of cancer, having deoxyribose nucleic acid (DNA) as their main cellular target. Flavopiridol, a semi-synthetic derivative of rohitukine (a natural compound isolated from Dysoxylum binectariferum plant), has attained much attention owing to its anticancer potential against various haematological malignancies and solid tumours. This work focuses on investigating interaction between flavopiridol and DNA at molecular level in order to decipher its underlying mechanism of action, which is not well understood. To define direct influence of flavopiridol on the structural, conformational and thermodynamic aspects of DNA, various spectroscopic and calorimetric techniques have been used. ATR-FTIR and SERS spectral outcomes indicate a novel insight into groove-directed-intercalation of flavopiridol into DNA via direct binding with nitrogenous bases guanine (C6=O6) and thymine (C2=O2) in DNA groove together with slight external binding to its sugar-phosphate backbone. Circular dichroism spectral analysis of flavopiridol-DNA complexes suggests perturbation in native B-conformation of DNA and its transition into C-form, which may be localized up to a few base pairs of DNA. UV-visible spectroscopic results illustrate dual binding mode of flavopiridol when interacts with DNA having association constant, Ka = 1.18 × 10(4) M(-1). This suggests moderate type of interaction between flavopiridol and DNA. Further, UV melting analysis also supports spectroscopic outcomes. Thermodynamically, flavopiridol-DNA complexation is an enthalpy-driven exothermic process. These conclusions drawn from this study could be helpful in unveiling mechanism of cytoxicity induced by flavopiridol that can be further applied in the development of flavonoid-based new chemotherapeutics with more specificity and better efficacy.

DOI: 10.1080/07391102.2015.1118708
PMID: 26599132 [PubMed - as supplied by publisher]

94: Rodriguez-Luna D, Stewart T, Dowlatshahi D, Kosior JC, Aviv RI, Molina CA, Silva Y, Dzialowski I, Lum C, Czlonkowska A, Boulanger JM, Kase CS, Gubitz G, Bhatia R, Padma V, Roy J, Subramaniam S, Hill MD, Demchuk AM; PREDICT/Sunnybrook ICH CTA Study Group. Perihematomal Edema Is Greater in the Presence of a Spot Sign but Does Not Predict Intracerebral Hematoma Expansion. Stroke. 2016 Feb;47(2):350-5. doi: 10.1161/STROKEAHA.115.011295. Epub 2015 Dec 22. PubMed PMID: 26696644.

BACKGROUND AND PURPOSE: Perihematomal edema volume may be related to intracerebral hemorrhage (ICH) volume at baseline and, consequently, with hematoma expansion. However, the relationship between perihematomal edema and hematoma expansion has not been well established. We aimed to investigate the relationship among baseline perihematomal edema, the computed tomographic angiography spot sign, hematoma expansion, and clinical outcome in patients with acute ICH.
METHODS: Predicting Hematoma Growth and Outcome in Intracerebral Hemorrhage Using Contrast Bolus CT (PREDICT) was a prospective observational cohort study of ICH patients presenting within 6 hours from onset. Patients underwent computed tomography and computed tomographic angiography scans at baseline and 24-hour computed tomography scan. A post hoc analysis of absolute perihematomal edema and relative perihematomal edema (absolute perihematomal edema divided by ICH) volumes was performed on baseline computed tomography scans (n=353). Primary outcome was significant hematoma expansion (>6 mL or >33%). Secondary outcomes were early neurological deterioration, 90-day mortality, and poor outcome.
RESULTS: Absolute perihematomal edema volume was higher in spot sign patients (24.5 [11.5-41.8] versus 12.6 [6.9-22] mL; P<0.001), but it was strongly correlated with ICH volume (ρ=0.905; P<0.001). Patients who experienced significant hematoma expansion had higher absolute perihematomal edema volume (18.4 [10-34.6] versus 11.8 [6.5-22] mL; P<0.001) but similar relative perihematomal edema volume (1.09 [0.89-1.37] versus 1.12 [0.88-1.54]; P=0.400). Absolute perihematomal edema volume and poorer outcomes were higher by tertiles of ICH volume, and perihematomal edema volume did not independently predict significant hematoma expansion.
CONCLUSIONS: Perihematomal edema volume is greater at baseline in the presence of a spot sign. However, it is strongly correlated with ICH volume and does not independently predict hematoma expansion.

95: Roy S, Pathy S, Kumar R, Mohanti BK, Raina V, Jaiswal A, Taywade S, Garg K, Thulkar S, Mohan A, Mathur S, Behera D. Efficacy of 18F-fluorodeoxyglucose positron emission tomography/computed tomography as a predictor of response in locally advanced non-small-cell carcinoma of the lung. Nucl Med Commun. 2016 Feb;37(2):129-38. doi: 10.1097/MNM.0000000000000422. PubMed PMID: 26544097.

OBJECTIVE: The study assessed the role of (18)F-fluorodeoxyglucose ((18)F-FDG) Positron emission tomography (PET)/computed tomography (CT) in evaluating the prognostic value of metabolic response for progression-free survival (PFS) and overall survival (OS) in patients with locally advanced non-small-cell lung cancer (NSCLC).
PATIENTS AND METHODS: Thirty patients with locally advanced NSCLC were enrolled in this prospective study and randomly allocated to one of two treatment arms. Arm A (n=15) received two cycles of neoadjuvant chemotherapy [paclitaxel (200 mg/m(2)) and carboplatin (AUC5)] and external beam radiotherapy (60 Gy/30 fractions/6 weeks). Arm B (n=15) received the same neoadjuvant chemotherapy followed by external beam radiotherapy (48 Gy/20 fractions/4 weeks) with concomitant cisplatin 30 mg/m(2) weekly. Patients underwent (18)F-FDG PET/CT at baseline and after 6 weeks of completion of intended treatment. Pretreatment and post-treatment maximum standardized uptake values (SUVmax) were noted. Patients with a reduction of SUVmax more than 50% were considered to be metabolic responders and those with a reduction 50% or less as nonresponders. Median follow-up was 18.98 months.
RESULTS: Twenty-one patients completed the intended treatment. The median

pretreatment and post-treatment SUVmax values were 14 and 6.4 for arm A and 15.3 and 3.5 for arm B, respectively. Significant decrease in SUVmax was observed in both arms. Metabolic response in arm A and arm B was 50 and 64%, respectively. The median PFS and OS of the responders were 22.31 and 24.73 months and those for nonresponders were 7.83 and 8.26 months, respectively. No significant difference in OS and PFS was observed between responders and nonresponders in the two arms. CONCLUSION: PET/CT distinguishes responders from nonresponders early after completion of chemoradiation in patients with locally advanced NSCLC, but did not provide any prognostic significance.

96: Sankar MJ, Sankar J, Mehta M, Bhat V, Srinivasan R. Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity. Cochrane Database Syst Rev. 2016;2:CD009734. doi: 10.1002/14651858.CD009734.pub2. Epub 2016 Feb 27. Review. PubMed PMID: 26932750.

BACKGROUND: Vascular endothelial growth factor (VEGF) plays a key role in angiogenesis in fetal life. Recently, researchers have attempted to use anti-VEGF agents for the treatment of retinopathy of prematurity (ROP), a vasoproliferative disorder. There is currently uncertainty regarding the safety and efficacy of these agents in preterm infants with ROP.
OBJECTIVES: To evaluate the efficacy and safety of anti-VEGF drugs when used either as monotherapy, i.e. without concomitant cryotherapy or laser therapy or in combination with planned cryo/laser therapy in preterm infants with type 1 ROP (defined as zone I any stage with plus disease, zone I stage 3 with or without plus disease or zone II stage 2 or 3 with plus disease).
SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL 2016, Issue 1), MEDLINE (1966 to January 1, 2016), EMBASE (1980 to January 1, 2016), CINAHL (1982 to January 1, 2016), conference proceedings, and previous reviews.
SELECTION CRITERIA: Randomised or quasi-randomised controlled trials that evaluated the efficacy and safety of administration, or both, of anti-VEGF agents compared with conventional therapy in premature infants with ROP.
DATA COLLECTION AND ANALYSIS: We used standard Cochrane and Cochrane Neonatal methods for data collection and analysis.
MAIN RESULTS: Three trials, in which 239 infants participated, fulfilled the inclusion criteria. Two trials compared intravitreal bevacizumab with conventional laser therapy (monotherapy) while the third compared intravitreal pegaptanib plus laser treatment with laser and cryotherapy (combination therapy) in infants with type 1 ROP.Of the two studies that evaluated intravitreal bevacizumab, one randomized infants while the other randomized eyes of the infants to the intervention and control groups. The former did not report any difference in the incidence of complete or partial retinal detachment between the groups (143 infants; RR 1.04, 95% CI 0.21 to 5.13; RD 0.00, 95% CI -0.06 to 0.07; very low quality evidence) but reported a significant reduction in the risk of refractive errors - very high myopia - at 30 months of age (211 eyes; RR 0.06, 95% CI 0.02 to 0.20; RD -0.40, 95% CI -0.50 to -0.30; low quality evidence) and recurrence of ROP by 54 weeks' postmenstrual age (143 infants; RR 0.22, 95% CI 0.08 to 0.62; RD -0.20, 95% CI -0.31 to -0.09; moderate quality evidence) in the bevacizumab group. The study found no difference in the risk of mortality before discharge from the hospital (150 infants; RR 1.50; 95% CI 0.26 to 8.75; RD 0.01; 95% CI -0.04 to 0.07; low quality evidence), mortality at 30 months of age (150 infants; RR 0.86, 95% CI 0.30 to 2.45; RD -0.01; 95% CI -0.10 to 0.08; low quality evidence), corneal opacity requiring corneal transplant (286 eyes; RR 0.34, 95% CI 0.01 to 8.26; RD -0.01; 95% CI -0.03 to 0.02; very low quality evidence), or lens opacity requiring cataract removal (286 eyes; RR 0.15, 95% CI 0.01 to 2.79; RD -0.02; 95% CI -0.05 to 0.01; very low quality evidence). The second trial that randomized eyes of the infants did not find any difference in the risk of complete retinal detachment between the eyes randomized to bevacizumab and those that were randomized to laser therapy (13 eyes; RR 0.33, 95% CI 0.01 to 7.50; RD -0.08, 95% CI -0.27 to 0.11).When used in combination with laser therapy, intravitreal pegaptanib was found to reduce the risk of retinal detachment when compared to laser/cryotherapy alone (152 eyes; RR 0.26, 95% CI 0.12 to 0.55; RD -0.29, 95% CI -0.42 to -0.16; low quality evidence). The

incidence of recurrence of ROP by 55 weeks' postmenstrual age was also lower in the pegaptanib + laser therapy group (76 infants; RR 0.29, 95% CI 0.12 to 0.7; RD -0.35, 95% CI -0.55 to -0.16; low quality evidence). There was no difference in the risk of perioperative retinal haemorrhages between the two groups (152 eyes; RR 0.62, 95% CI 0.24 to 1.56; RD -0.05, 95% CI -0.16 to 0.05; very low quality evidence). The risk of delayed systemic adverse effects with either of the drugs is, however, not known.
AUTHORS' CONCLUSIONS:
IMPLICATIONS FOR PRACTICE: Intravitreal bevacizumab reduces the risk of refractive errors during childhood when used as monotherapy while intravitreal pegaptanib reduces the risk of retinal detachment when used in conjunction with laser therapy in infants with type 1 ROP. Quality of evidence was, however, low for both the outcomes because of the risk of detection and other biases. Effect on other critical outcomes and, more importantly, the long-term systemic adverse effects of the drugs are not known. The insufficient data precludes strong conclusions favouring routine use of intravitreal anti-VEGF agents in preterm infants with type 1 ROP.
IMPLICATIONS FOR RESEARCH: Further studies are needed to evaluate the effect of anti-VEGF agents on structural and functional outcomes in childhood and delayed systemic adverse effects such as myocardial dysfunction and adverse neurodevelopmental outcomes.

DOI: 10.1002/14651858.CD009734.pub2
PMID: 26932750 [PubMed - indexed for MEDLINE]

97: Sankhyan A, Sharma C, Dutta D, Sharma T, Chosdol K, Wakita T, Watashi K, Awasthi A, Acharya SK, Khanna N, Tiwari A, Sinha S. Inhibition of preS1-hepatocyte interaction by an array of recombinant human antibodies from naturally recovered individuals. Sci Rep. 2016 Feb 18;6:21240. doi: 10.1038/srep21240. PubMed PMID: 26888694; PubMed Central PMCID: PMC4758072.

Neutralizing monoclonal antibodies are being found to be increasingly useful in viral infections. In hepatitis B infection, antibodies are proven to be useful for passive prophylaxis. The preS1 region (21-47a.a.) of HBV contains the viral hepatocyte-binding domain crucial for its attachment and infection of hepatocytes. Antibodies against this region are neutralizing and are best suited for immune-based neutralization of HBV, especially in view of their not recognizing decoy particles. Anti-preS1 (21-47a.a.) antibodies are present in serum of spontaneously recovered individuals. We generated a phage-displayed scFv library using circulating lymphocytes from these individuals and selected four preS1-peptide specific scFvs with markedly distinct sequences from this library. All the antibodies recognized the blood-derived and recombinant preS1 containing antigens. Each scFv showed a discrete binding signature, interacting with different amino acids within the preS1-peptide region. Ability to prevent binding of the preS1 protein (N-terminus 60a.a.) to HepG2 cells stably expressing hNTCP (HepG2-hNTCP-C4 cells), the HBV receptor on human hepatocytes was taken as a surrogate marker for neutralizing capacity. These antibodies inhibited preS1-hepatocyte interaction individually and even better in combination. Such a combination of potentially neutralizing recombinant antibodies with defined specificities could be used for preventing/managing HBV infections, including those by possible escape mutants.

DOI: 10.1038/srep21240
PMCID: PMC4758072
PMID: 26888694 [PubMed - in process]

98: Saraswat M, JoenvÃ¤Ã¤rÃ¤ S, Tomar AK, Singh S, Yadav S, Renkonen R. N-Glycoproteomics of Human Seminal Plasma Glycoproteins. J Proteome Res. 2016 Mar 4;15(3):991-1001. doi: 10.1021/acs.jproteome.5b01069. Epub 2016 Feb 4. PubMed PMID: 26791533.

Seminal plasma aids sperm by inhibiting premature capacitation, helping in the intracervical transport and formation of an oviductal sperm reservoir, all of

which appear to be important in the fertilization process. Epitopes such as Lewis x and y are known to be present on seminal plasma glycoproteins, which can modulate the maternal immune response. It is suggested by multiple studies that seminal plasma glycoproteins play, largely undiscovered, important roles in the process of fertilization. We have devised a strategy to analyze glycopeptides from a complex, unknown mixture of protease-digested proteins. This analysis provides identification of the glycoproteins, glycosylation sites, glycan compositions, and proposed structures from the original sample. This strategy has been applied to human seminal plasma total glycoproteins. We have elucidated glycan compositions and proposed structures for 243 glycopeptides belonging to 73 N-glycosylation sites on 50 glycoproteins. The majority of the proposed glycan structures were complex type (83%) followed by high-mannose (10%) and then hybrid (7%). Most of the glycoproteins were either sialylated, fucosylated, or both. Many Lewis x/a and y/b epitopes bearing glycans were found, suggesting immune-modulating epitopes on multiple seminal plasma glycoproteins. The study also shows that large scale N-glycosylation mapping is achievable with current techniques and the depth of the analysis is roughly proportional to the prefractionation and complexity of the sample.

DOI: 10.1021/acs.jproteome.5b01069
PMID: 26791533 [PubMed - in process]

99: Sardar A, Khanna P, Singh A, Sharma A. Long-standing meningomyelocele can be a predictor of difficult airway and postoperative hypoventilation: challenge to the anaesthesiologist. BMJ Case Rep. 2016 Feb 16;2016. pii: bcr2016214456. doi: 10.1136/bcr-2016-214456. PubMed PMID: 26884079.

A 15-year-old female patient presented with severe pain in the abdomen and obstructive uropathy. She underwent Yang-Monti ileovesicostomy under general anaesthesia. She is a known case of long-standing meningomyelocele (MMC) and presented with its potential complications such as difficult airway and restrictive lung disease. We describe the successful anaesthetic management of a case of anticipated difficult airway and postoperative hypoventilation as a sequel of kyphosis due to MMC. Her airway was secured with fibre optic-guided intubation in a semirecumbent position. Postoperative hypoventilation, hypercarbia and respiratory acidosis were managed conservatively, followed by staged weaning in the intensive care unit. Obstruction of the catheterisable continent channel of the neurogenic bladder itself may present with uropathy and urosepsis, which were also taken care of preoperatively.

DOI: 10.1136/bcr-2016-214456
PMID: 26884079 [PubMed - in process]

100: Sharma C, Biswas NR, Ojha S, Velpandian T. Comprehensive evaluation of formulation factors for ocular penetration of fluoroquinolones in rabbits using cassette dosing technique. Drug Des Devel Ther. 2016 Feb 22;10:811-23. doi: 10.2147/DDDT.S95870. eCollection 2016. PubMed PMID: 26955263; PubMed Central PMCID: PMC4769009.

OBJECTIVE: Corneal permeability of drugs is an important factor used to assess the efficacy of topical preparations. Transcorneal penetration of drugs from aqueous formulation is governed by various physiological, physiochemical, and formulation factors. In the present study, we investigated the effect of formulation factors like concentration, pH, and volume of instillation across the cornea using cassette dosing technique for ophthalmic fluoroquinolones (FQs). MATERIALS AND METHODS: Sterile cocktail formulations were prepared using four congeneric ophthalmic FQs (ofloxacin, sparfloxacin, pefloxacin mesylate, and gatifloxacin) at concentrations of 0.025%, 0.5%, and 0.1%. Each formulation was adjusted to different pH ranges (4.5, 7.0, and 8.0) and assessed for transcorneal penetration in vivo in rabbit's cornea (n=4 eyes) at three different volumes (12.5, 25, and 50 µL). Aqueous humor was aspirated through paracentesis after

applying local anesthesia at 0, 5, 15, 30, 60, 120, and 240 minutes postdosing. The biosamples collected from a total of 27 groups were analyzed using liquid chromatography-tandem mass spectroscopy to determine transcorneal permeability of all four FQs individually.
RESULTS: Increase in concentration showed an increase in penetration up to 0.05%; thereafter, the effect of concentration was found to be dependent on volume of instillation as we observed a decrease in transcorneal penetration. The highest transcorneal penetration of all FQs was observed at pH 7.0 at concentration 0.05% followed by 0.025% at pH 4.5. Lastly, increasing the volume of instillation from 12.5 to 50 µL showed a significant fall in transcorneal penetration.
CONCLUSION: The study concludes that formulation factors showed discernible effect on transcorneal permeation; therefore, due emphasis should be given on drug development and design of ophthalmic formulation.

DOI: 10.2147/DDDT.S95870
PMCID: PMC4769009
PMID: 26955263 [PubMed - in process]

101: Sharma DN, Gandhi AK, Bhatla N, Kumar S, Rath GK. High-dose-rate interstitial brachytherapy for female peri-urethral cancer. J Contemp Brachytherapy. 2016 Feb;8(1):41-7. doi: 10.5114/jcb.2016.57461. Epub 2016 Jan 27. PubMed PMID: 26985196; PubMed Central PMCID: PMC4793063.

PURPOSE: Peri-urethral cancer (PUC) in females is a rare malignancy. Surgery is not usually contemplated due to associated morbidity. Radiation therapy (RT) can be employed in the form of interstitial brachytherapy (IBT) alone for early lesions, and external beam radiation therapy (EBRT) with or without IBT for advanced lesions. We report our first experience in the literature to evaluate the role of high-dose-rate (HDR) IBT in female PUC.
MATERIAL AND METHODS: Between 2008 and 2013, 10 female patients with PUC (5 primary and 5 recurrent) were treated with HDR-IBT with or without EBRT at our center. Size of the lesion ranged from 1.5 cm to 5.0 cm. A 2-3 plane free-hand implant was performed using plastic catheters. The prescribed dose of HDR-IBT was 42 Gy in 14 fractions for brachytherapy alone (5 patients), and 18-21 Gy for the boost along with EBRT (5 patients). Patients were followed up regularly for assessment of disease control and toxicity.
RESULTS: At a median follow up of 25 months, six patients were disease free at their last follow up. Four patients developed recurrence: 2 at inguinal nodes, 1 at local site, and 1 at both local as well as inguinal nodes. Moist desquamation was the commonest acute toxicity observed in all 5 patients treated with IBT alone, which healed within 4 weeks' time. Overall, grade II delayed complication rate was 30%.
CONCLUSIONS: Though small sample size, the results of our study have shown that HDR-IBT provides good loco-regional control with acceptable toxicity for female PUC.

DOI: 10.5114/jcb.2016.57461
PMCID: PMC4793063
PMID: 26985196 [PubMed]

102: Sharma JB, Sneha J, Singh UB, Kumar S, Roy KK, Singh N, Dharmendra S, Vanamail P. Comparative Study of Laparoscopic Abdominopelvic and Fallopian Tube Findings Before and After Antitubercular Therapy in Female Genital Tuberculosis With Infertility. J Minim Invasive Gynecol. 2016 Feb 1;23(2):215-22. doi: 10.1016/j.jmig.2015.09.023. Epub 2015 Oct 8. PubMed PMID: 26455527.

STUDY OBJECTIVE: To study the effect of antitubercular treatment (ATT) on the laparoscopic abdominopelvic and fallopian tube findings in female genital tuberculosis (FGBT).
DESIGN: Prospective cohort (Canadian Task Force classification II2).
SETTING: Tertiary referral center in northern India.
PATIENTS: Fifty women with infertility and diagnosed with FGTB on laparoscopy, histopathology findings, or endometrial sampling (acid-fast bacilli culture,

granuloma on histopathology, positive polymerase chain reaction).
INTERVENTIONS: Diagnostic laparoscopy in all women diagnosed with FGTB before and after a 6-month course of ATT (2 months of rifampicin, isoniazid, pyrazinamide, and ethambutol, followed by 4 months of rifampicin and isoniazid). All procedures were performed by the same surgeon between June 2012 and May 2014.
MEASUREMENTS AND MAIN RESULTS: The mean patient age was 28.7 years, mean parity was 0.9, and mean body mass index was 23.6 kg/m(2). Infertility was seen in all 50 women (66% primary infertility, 34% secondary infertility), with a mean duration of 6.06 years. Abnormal laparoscopic findings of FGTB included tubercles in the pelvic peritoneum, fallopian tube, and ovary in 27 women (54%) before ATT and in only 1 (2.04%) woman after ATT ($p < .001$). Caseous nodules and encysted ascites were seen in 4 women (8%) before ATT, and in no women after ATT ($p < .001$); however, there was no change from before ATT to after ATT in the rate of pelvic adhesions (42% vs 42.5%) and perihepatic adhesions (56% vs 58%). Laparoscopic findings in fallopian tubes included hydrosalpinx (32%), pyosalpinx (4%), beaded tubes (12%), nonvisualization of tube (20%), and tubal blockage on the right side (56%), left side (50%), and both sides (38%) before ATT. Hydrosalpinx, beaded tubes, and nonvisualized tube were seen in 33.4%, 4.1%, and 20.8% cases, respectively, after ATT; however, free spill increased to 52% on the right side and 50% on left side after ATT.
CONCLUSION: ATT improves laparoscopic findings in FGTB with infertility. However, advanced fibrotic lesions (eg, pelvic and perihepatic adhesions, bilateral blocked tubes) do not improve with ATT.

DOI: 10.1016/j.jmig.2015.09.023
PMID: 26455527 [PubMed - indexed for MEDLINE]

103: Sharma N, Arora T, Kaur M, Titiyal JS, Agarwal T. Surrogate scleral rim with fibrin glue: a novel technique to expand the pool of donor tissues for Descemet stripping automated endothelial keratoplasty. Br J Ophthalmol. 2016 Feb;100(2):156-8. doi: 10.1136/bjophthalmol-2015-306903. Epub 2015 Jun 30. PubMed PMID: 26130671.

Descemet stripping automated endothelial keratoplasty is being performed in increasing number of cases each year. An adequate scleral rim on all sides is mandatory for the donor cornea to be mounted on the artificial anterior chamber for microkeratome-assisted dissection. Occasionally, the scleral rim may however be inadequate. The primary cause of inadequate scleral rim is poorly trained technicians in in-situ excision technique. Hence, we devised a novel technique for performing successful microkeratome-assisted dissection in donor corneas with inadequate scleral rim. A surrogate scleral rim was obtained from the donor tissue not fit for optical keratoplasty. It was then glued to the optical grade donor cornea that had an inadequate scleral rim either focally or circumferentially. The combination was then used for a successful microkeratome-assisted dissection followed by endothelial keratoplasty.

DOI: 10.1136/bjophthalmol-2015-306903
PMID: 26130671 [PubMed - indexed for MEDLINE]

104: Sharma N, Aron N, Kakkar P, Titiyal JS. Continuous intraoperative OCT guided management of post-deep anterior lamellar keratoplasty descemet's membrane detachment. Saudi J Ophthalmol. 2016 Apr-Jun;30(2):133-6. doi: 10.1016/j.sjopt.2016.01.001. Epub 2016 Feb 13. PubMed PMID: 27330393; PubMed Central PMCID: PMC4908052.

Continuous intraoperative optical coherence tomography (iOCT) integrated into the operating microscope is a new modification in the current operating microscope to

aid in the surgical procedures involving both the anterior and the posterior segment. This helps in intraoperative planning, modification of the surgical steps if required and confirmation of the surgical endpoint in the operating room itself. iOCT was used for the successful management of descemet's membrane detachment (DMD) following deep anterior lamellar keratoplasty (DALK) with intracameral injection of 20% Sulphur hexafluoride. The gas was injected under direct visualization through the microscope with continuous real time monitoring of the change in height of the detached Descemet's membrane (DM). Additionally stab incisions were given through the anterior cornea due to the presence of residual fluid above the DM which was visible on continuous iOCT images. This led to the successful apposition of the DM which otherwise would have remained detached due to the residual fluid. This highlights the importance of continuous iOCT monitoring of the ophthalmic surgical procedures in order to produce a successful anatomical outcome of the surgery without disruption of the surgical procedure.

DOI: 10.1016/j.sjopt.2016.01.001
PMCID: PMC4908052
PMID: 27330393 [PubMed]

105: Sihota R, Rishi K, Srinivasan G, Gupta V, Dada T, Singh K. Functional evaluation of an iridotomy in primary angle closure eyes. Graefes Arch Clin Exp Ophthalmol. 2016 Jun;254(6):1141-9. doi: 10.1007/s00417-016-3298-x. Epub 2016 Feb 19. PubMed PMID: 26895159.

OBJECTIVE: To evaluate the functional efficacy of an iridotomy in primary angle closure (PAC) eyes by measuring IOP responses to provocative tests before and after iridotomy.
DESIGN: Prospective cohort study.
SUBJECTS: 50 consecutive adult patients, 40-60 years of age, having primary angle closure.
METHODS: Clinical examination, perimetry, biometry and ultrasound biomicroscopy of the angle were done. A darkroom prone provocative test (DRPPT), a mydriatic test and a Valsalva maneuver were performed before and after the iridotomy.
MAIN OUTCOME MEASURES: IOP change in response to the provocative tests before and after iridotomy, and correlation with baseline parameters.
RESULTS: IOP at baseline and after iridotomy was 14.4±2.7 mmHg and 14.3±2.6 mmHg, respectively (p=0.)83. There was no significant change on diurnal phasing before and after an iridotomy (p=0.)11. The mean IOP rise was 5.9±3.7 mmHg on the DRPPT, 4.3±3.5 mmHg on the Mydriatic test and 9.1±4.9 mmHg on the Valsalva maneuver, and was reduced significantly to 3.2±2.1 mmHg, 2.3±1.8 and 6.4±3.5, respectively(p<0.001 for all tests). The decrease in pupillary block component for all 50 eyes was 46.5 % for the mydriatic test, 45.8 % for the DRPPT and 29.7 % for the Valsalva maneuver. PAC eyes positive on the DRPPT and mydriatic test prior to an iridotomy became negative after laser iridotomy in 75.9 and 84.6 % eyes, respectively, but on the Valsalva maneuver, only 23.8 % became negative. After iridotomy, eyes that continued to be positive on the mydriatic test had a significantly thicker lens (p=0.02), decreased TCPD (p=0.014) and narrower trabecular-iris angle (p=0.048). On the DRPPT, they had a thicker lens (p=0.03), shorter iris thickness (p=0.025) and TCPD (p=0.032), and on the Valsalva maneuver, they had a narrower scleral-ciliary process angle (SCPA; p=0.019) and shorter TCPD (p=0.015).
CONCLUSIONS: This comprehensive functional evaluation of laser iridotomy in early PAC eyes showed a significant reduction in the pupillary block component of IOP response to provocative testing, possibly decreasing IOP fluctuations over time. An iridotomy does not, however, significantly change mean IOP or diurnal phasing of IOP in PAC eyes. Eyes with a very narrow angle or a thick lens may continue to have angle closure due to other pathomechanisms for angle closure.

DOI: 10.1007/s00417-016-3298-x
PMID: 26895159 [PubMed - in process]

106: Singh I, Agnihotri A, Sharma A, Verma AK, Das P, Thakur B, Sreenivas V, Gupta SD, Ahuja V, Makharia GK. Patients with celiac disease may have normal weight or may even be overweight. Indian J Gastroenterol. 2016 Jan;35(1):20-4. doi: 10.1007/s12664-016-0620-9. Epub 2016 Feb 18. PubMed PMID: 26892766.

BACKGROUND: It is believed that patients with celiac disease (CeD) are likely to be underweight. Data from west suggest that 8% to 40% of them can be overweight or obese. We reviewed data on body mass index (BMI) of our patients with CeD and derived the correlations between BMI and other disease characteristics.
METHODS: We retrospectively studied case records of 210 adolescent and adult patients with CeD at the Celiac Disease Clinic. We classified BMI as underweight, normal weight, overweight, and obese based on the Consensus Statement for Diagnosis of Obesity, Abdominal Obesity and the Metabolic Syndrome for Asian Indians for those with age >18 years and revised Indian Association of Pediatrics BMI-for-age charts for those between 12 and 18 years.
RESULTS: Of 210 patients, 76 (36.2%) were underweight, 115 (54.8%) were normal weight, 13 (6.2%) were overweight, and 6 (2.9%) were obese. There was no difference in the proportion of underweight between male and female patients with CeD. The mean age of underweight patients was similar to those having normal or overweight. There was no difference in the mean duration of symptoms; frequencies of diarrhea, anorexia, and weakness; anemia; titer of anti-tissue transglutaminase antibody; and severity of villous atrophy in those with underweight or normal weight or overweight.
CONCLUSIONS: In our practice, only one third of patients with CeD had low BMI. A diagnosis of CeD should not be excluded if patient has normal or high BMI.

DOI: 10.1007/s12664-016-0620-9
PMID: 26892766 [PubMed - in process]

107: Singh L, Saini N, Pushker N, Sen S, Sharma A, Kashyap S. Prognostic significance of NADPH oxidase-4 as an indicator of reactive oxygen species stress in human retinoblastoma. Int J Clin Oncol. 2016 Aug;21(4):651-7. doi: 10.1007/s10147-016-0951-7. Epub 2016 Feb 8. PubMed PMID: 26857459.

BACKGROUND: Reactive oxygen species (ROS) have been shown to enhance the proliferation of cancer cells. NADPH oxidases (NOX4) are a major intracellular source of ROS and are found to be associated with cancer and tumor cell invasion. Therefore, the purpose of this study is to evaluate the expression of NOX4 protein in human retinoblastoma.
METHODS: Immunohistochemical expression of NOX4 protein was analyzed in 109 specimens from prospective cases of retinoblastoma and then correlated with clinicopathological parameters and patient survival. Western blotting confirmed and validated the immunoreactivity of NOX4 protein.
RESULTS: In our study we found a male preponderance (55.9 %), and 25/109 (22.9 %) were bilateral. Massive choroidal invasion was the histopathological high-risk factor (HRF) most frequently observed, in 42.2 % of the cases. NOX4 protein was expressed in 67.88 % (74/109) of primary retinoblastoma cases and was confirmed by Western blotting. NOX4 was statistically significant with massive choroidal invasion and pathological TNM staging. There was a statistically significant difference in overall survival in patients with NOX4 expression ($p = 0.0461$).
CONCLUSION: This is the first study to show the expression of NOX4 protein in retinoblastoma tumors. Hence, a retinoblastoma tumor may exhibit greater ROS stress. This protein may prove to be useful as a future therapeutic target for improving the management of retinoblastoma.

DOI: 10.1007/s10147-016-0951-7
PMID: 26857459 [PubMed - in process]

108: Singh N, Pati HP, Tyagi S, Deka R, Sharma R, Saxena R. Proposed minimal panel of antibodies for cost-effectiveness and accuracy in acute leukemias immunophenotyping: Prospective study at a tertiary care center. Hematology. 2016 Jul;21(6):338-42. doi: 10.1080/10245332.2016.1139792. Epub 2016 Feb 24. PubMed

PMID: 26907095.

INTRODUCTION: Flowcytometry has an essential role in the diagnosis and classification of acute leukemias. However, there exists a great degree of inter-laboratory variability on issues like panel selection, antibody combinations, gating strategies, fluorochromes, and clonal selection.
AIM: The primary aim of this study was to derive a minimal panel of antibodies and evaluate its diagnostic usefulness in acute leukemias by flowcytometry by using the detailed immune-phenotype of different lineage-specific or non-specific markers.
MATERIALS AND METHODS: This prospective observational study involved 400 newly diagnosed cases of acute leukemias. Bone marrow aspirate samples were subjected to morphological evaluation, cytogenetics and flow cytometric immunophenotyping.
RESULTS: A minimal panel of eight antibodies comprising of CD45/CD34/CD19/MPO/cytoCD3/CD64/CD117/CD79a was derived by applying different permutations and combinations with a diagnostic yield of 97.5%. The minimal panel was further validated by testing in an independent cohort of patients with similar demographic characteristics, where it showed a high diagnostic yield of 98% in comparison with the screening panels proposed by other recently published studies.
CONCLUSION: It may be concluded that the diagnostic performance of the eight antibody panel is better than most other panels used across the different laboratories in terms of yield, number of antibodies used and the scientific approach used to derive and validate the results and so henceforth may be applied in any setting with limited resources for better diagnostic accuracy.

DOI: 10.1080/10245332.2016.1139792
PMID: 26907095 [PubMed - in process]

109: Singh N, Sahu DK, Mishra A, Agarwal P, Goel MM, Chandra A, Singh SK, Srivastava C, Ojha BK, Gupta DK, Kant R. Multiomics approach showing genome-wide copy number alterations and differential gene expression in different types of North-Indian pediatric brain tumors. Gene. 2016 Feb 1;576(2 Pt 2):734-42. doi: 10.1016/j.gene.2015.09.078. Epub 2015 Oct 8. PubMed PMID: 26456192.

PURPOSE: Based on copy number alterations and transcriptional profiles, the posterior fossa tumors (medulloblastoma (MB), ependymoma and pilocytic astrocytoma) have been classified into various subgroups. The study design was aimed to identify and catalog genome-wide copy number alterations and differential gene expression in different types of North-Indian pediatric posterior fossa tumors and matched control tissue through Molecular Inversion Probe (MIP) Based and Human Transcriptome Array.
EXPERIMENTAL DESIGN: MIP based OncoScan Array and Human Transcriptome Array 2.0 were used to molecularly-categorize histopathologically and immunohistochemically proven tumor samples on the basis of copy number variations and altered gene expression patterns and/or alternative splicing events.
RESULTS: Based on molecular, histopathological/immunohistochemical and age-dependent factors MB was subgrouped into group-3 MB, Wnt and SHH; ependymoma into balanced, numerical and structural/anaplastic; and pilocytic astrocytoma was stratified age-dependently. Compared with the vermis tissue of MB, the vermis tissue of ependymoma showed higher levels of gain and losses compared with their counter tumor parts implicating metastasis within the confined region. Group-3 MB and anaplastic ependymoma represented highest differentially expressed genes both at gene and exon levels in the CN altered regions compared with other subgroups of MB and ependymoma respectively.
CONCLUSION: This multiomics approach based molecular characterization of posterior fossa tumors together with clinical and histopathological factors may help us in the area of personalized medicine.

DOI: 10.1016/j.gene.2015.09.078
PMID: 26456192 [PubMed - indexed for MEDLINE]

110: Singh N, Sahu DK, Chowdhry R, Mishra A, Goel MM, Faheem M, Srivastava C, Ojha BK, Gupta DK, Kant R. IsoSeq analysis and functional annotation of the infratentorial ependymoma tumor tissue on PacBio RSII platform. Meta Gene. 2015 Nov 23;7:70-5. doi: 10.1016/j.mgene.2015.11.004. eCollection 2016 Feb. PubMed PMID: 26862483; PubMed Central PMCID: PMC4707247.

Here, we sequenced and functionally annotated the long reads (1-2 kb) cDNAs library of an infratentorial ependymoma tumor tissue on PacBio RSII by Iso-Seq protocol using SMRT technology. 577 MB, data was generated from the brain tissues of ependymoma tumor patient, producing 1,19,313 high-quality reads assembled into 19,878 contigs using Celera assembler followed by Quiver pipelines, which produced 2952 unique protein accessions in the nr protein database and 307 KEGG pathways. Additionally, when we compared GO terms of second and third level with alternative splicing data obtained through HTA Array2.0. We identified four and twelve transcript cluster IDs in Level-2 and Level-3 scores respectively with alternative splicing index predicting mainly the major pathways of hallmarks of cancer. Out of these transcript cluster IDs only transcript cluster IDs of gene PNMT, SNN and LAMB1 showed Reads Per Kilobase of exon model per Million mapped reads (RPKM) values at gene-level expression (GE) and transcript-level (TE) track. Most importantly, brain-specific genes--PNMT, SNN and LAMB1 show their involvement in Ependymoma.

DOI: 10.1016/j.mgene.2015.11.004
PMCID: PMC4707247
PMID: 26862483 [PubMed]

111: Singh PK, Chandra PS, Vaghani G, Savarkar DP, Garg K, Kumar R, Kale SS, Sharma BS. Management of pediatric single-level vertebral hemangiomas presenting with myelopathy by three-pronged approach (ethanol embolization, laminectomy, and instrumentation): a single-institute experience. Childs Nerv Syst. 2016 Feb;32(2):307-14. doi: 10.1007/s00381-015-2941-x. Epub 2015 Dec 21. PubMed PMID: 26686533.

PURPOSE: Pediatric vertebral hemangiomas (VH) are exceedingly rare benign and highly vascular tumours of the spine. There are no guidelines available for management of these patients in literature. Purpose of this study is to evaluate the role of intraoperative ethanol embolization, surgical decompression, and instrumented fusion in pediatric symptomatic VH with single-level involvement. METHODS: Surgery consisted of intraoperative bilateral pedicular absolute alcohol injection and laminectomy at the level of pathology followed by a short-/long-segment instrumented fusion using pedicle screws and rod. Seven patients (mean age 14 ± 2.4 years, range 10-17 years, five females and two males) (age < 18 years) who were treated using this technique at our institute since March 2008 to December 2013 were enrolled in this retrospective study. Demographical, clinical, radiological, operative details, and postoperative events were retrieved from hospital records. During follow-up visits, clinical status and imaging were recorded. Outcome assessed with clinical and neurological outcome score of American Spinal Injury Association (ASIA) Impairment Scale. RESULTS: Duration of symptoms ranged from 3 to 60 months (mean, 14.7 ± 20.4 months). Clinical features include myelopathy with motor and sensory involvement in all (five were paraplegic), back pain in two patients, and bladder involvement in two patients. The preoperative American Spinal Injury Association (ASIA) Impairment Scale (AIS) were B in five patients and C and D in one patient each. All had pan vertebral body VH with severe cord compression in the thoracic region on imaging study. Mean duration of surgery was 248.6 ± 60 minutes (range 195-310 min) and blood loss was 535 ml (range 200-1500 ml). Immediate embolization was achieved in all patients, which allowed laminectomy and soft tissue hemangioma removal relatively easy. Post surgery, at mean follow-up of 45.3 (±23.2) months (range 1-78 months), all patients showed improvement in power (sphincter improvement in two patients). ASIA were E in six patients and D in one patient at

the last follow-up.
CONCLUSION: The present study is the largest series of pediatric symptomatic VH. This procedure is a safe, efficient method to treat symptomatic pediatric VH with severe cord compression. It seems to serve the purpose of providing embolization, cord decompression, rigid fusion at the same sitting without adding new morbidity, and preventing excessive blood loss.

DOI: 10.1007/s00381-015-2941-x
PMID: 26686533 [PubMed - in process]

112: Singh PM, Borle A, Rewari V, Makkar JK, Trikha A, Sinha AC, Goudra B. Aprepitant for postoperative nausea and vomiting: a systematic review and meta-analysis. Postgrad Med J. 2016 Feb;92(1084):87-98. doi: 10.1136/postgradmedj-2015-133515. Epub 2015 Dec 1. Review. PubMed PMID: 26627976.

Postoperative nausea and vomiting (PONV) is an important clinical problem. Aprepitant is a relatively new agent for this condition which may be superior to other treatment. A systematic review was performed after searching a number of medical databases for controlled trials comparing aprepitant with conventional antiemetics published up to 25 April 2015 using the following keywords: 'Aprepitant for PONV', 'Aprepitant versus 5-HT3 antagonists' and 'NK-1 versus 5-HT3 for PONV'. The primary outcome for the pooled analysis was efficacy of aprepitant in preventing vomiting on postoperative day (POD) 1 and 2. 172 potentially relevant papers were identified of which 23 had suitable data. For the primary outcome, 14 papers had relevant data. On POD1, 227/2341 patients (9.7%) patients randomised to aprepitant had a vomiting episode compared with 496/2267 (21.9%) controls. On POD2, the rate of vomiting among patients receiving aprepitant was 6.8% compared with 12.8% for controls. The OR for vomiting compared with controls was 0.48 (95% CI 0.34 to 0.67) on POD1 and 0.54 (95% CI 0.40 to 0.72) on POD2. Aprepitant also demonstrated a better profile with a lower need for rescue antiemetic and a higher complete response. Efficacy for vomiting prevention was demonstrated for 40 mg, 80 mg and 125 mg without major adverse effects. For vomiting comparison there was significant unexplainable heterogeneity (67.9% and 71.5% for POD1 and POD2, respectively). We conclude that (1) aprepitant reduces the incidence of vomiting on both POD1 and POD2, but there is an unexplained heterogeneity which lowers the strength of the evidence; (2) complete freedom from PONV on POD1 is highest for aprepitant with minimum need for rescue; and (3) oral aprepitant (80 mg) provides an effective and safe sustained antivomiting effect.

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PMID: 26627976 [PubMed - in process]

113: Singh PM, Borle A, Shah D, Sinha A, Makkar JK, Trikha A, Goudra BG. Optimizing Prophylactic CPAP in Patients Without Obstructive Sleep Apnoea for High-Risk Abdominal Surgeries: A Meta-regression Analysis. Lung. 2016 Apr;194(2):201-17. doi: 10.1007/s00408-016-9855-6. Epub 2016 Feb 19. PubMed PMID: 26896040.

INTRODUCTION: Prophylactic continuous positive airway pressure (CPAP) can prevent pulmonary adverse events following upper abdominal surgeries. The present meta-regression evaluates and quantifies the effect of degree/duration of (CPAP) on the incidence of postoperative pulmonary events.
METHODS: Medical databases were searched for randomized controlled trials involving adult patients, comparing the outcome in those receiving prophylactic postoperative CPAP versus no CPAP, undergoing high-risk abdominal surgeries. Our meta-analysis evaluated the relationship between the postoperative pulmonary complications and the use of CPAP. Furthermore, meta-regression was used to

quantify the effect of cumulative duration and degree of CPAP on the measured outcomes.
RESULTS: Seventy-three potentially relevant studies were identified, of which 11 had appropriate data, allowing us to compare a total of 362 and 363 patients in CPAP and control groups, respectively. Qualitatively, Odds ratio for CPAP showed protective effect for pneumonia [0.39 (0.19-0.78)], atelectasis [0.51 (0.32-0.80)] and pulmonary complications [0.37 (0.24-0.56)] with zero heterogeneity. For prevention of pulmonary complications, odds ratio was better for continuous than intermittent CPAP. Meta-regression demonstrated a positive correlation between the degree of CPAP and the incidence of pneumonia with a regression coefficient of +0.61 (95 % CI 0.02-1.21, P = 0.048, τ (2) = 0.078, r (2) = 7.87 %). Overall, adverse effects were similar with or without the use of CPAP.
CONCLUSIONS: Prophylactic postoperative use of continuous CPAP significantly reduces the incidence of postoperative pneumonia, atelectasis and pulmonary complications in patients undergoing high-risk abdominal surgeries. Quantitatively, increasing the CPAP levels does not necessarily enhance the protective effect against pneumonia. Instead, protective effect diminishes with increasing degree of CPAP.

DOI: 10.1007/s00408-016-9855-6
PMID: 26896040 [PubMed - in process]

114: Singh R, Baby B, Damodaran N, Srivastav V, Suri A, Banerjee S, Kumar S, Kalra P, Prasad S, Paul K, Anand S, Kumar S, Dhiman V, Ben-Israel D, Kapoor KS. Design and Validation of an Open-Source, Partial Task Trainer for Endonasal Neuro-Endoscopic Skills Development: Indian Experience. World Neurosurg. 2016 Feb;86:259-69. doi: 10.1016/j.wneu.2015.09.045. Epub 2015 Sep 26. PubMed PMID: 26410199.

BACKGROUND: Box trainers are ideal simulators, given they are inexpensive, accessible, and use appropriate fidelity.
OBJECTIVE: The development and validation of an open-source, partial task simulator that teaches the fundamental skills necessary for endonasal skull-base neuro-endoscopic surgery.
METHODS: We defined the Neuro-Endo-Trainer (NET) SkullBase-Task-GraspPickPlace with an activity area by analyzing the computed tomography scans of 15 adult patients with sellar suprasellar parasellar tumors. Four groups of participants (Group E, n = 4: expert neuroendoscopists; Group N, n =19: novice neurosurgeons; Group R, n = 11: neurosurgery residents with multiple iterations; and Group T, n = 27: neurosurgery residents with single iteration) performed grasp, pick, and place tasks using NET and were graded on task completion time and skills assessment scale score.
RESULTS: Group E had lower task completion times and greater skills assessment scale scores than both Group N and R ($P \leq 0.03$, 0.001). The performance of Groups N and R was found to be equivalent; in self-assessing neuro-endoscopic skill, the participants in these groups were found to have equally low pretraining scores (4/10) with significant improvement shown after NET simulation (6, 7 respectively). Angled scopes resulted in decreased scores with tilted plates compared with straight plates (30° $P \leq 0.04$, 45° $P \leq 0.001$). With tilted plates, decreased scores were observed when we compared the 0° with 45° endoscope (right, $P \leq 0.008$; left, $P \leq 0.002$).
CONCLUSIONS: The NET, a face and construct valid open-source partial task neuroendoscopic trainer, was designed. Presimulation novice neurosurgeons and neurosurgical residents were described as having insufficient skills and preparation to practice neuro-endoscopy. Plate tilt and endoscope angle were shown to be important factors in participant performance. The NET was found to be a useful partial-task trainer for skill building in neuro-endoscopy.

DOI: 10.1016/j.wneu.2015.09.045
PMID: 26410199 [PubMed - indexed for MEDLINE]

115: Singh UB, Pandey P, Mehta G, Bhatnagar AK, Mohan A, Goyal V, Ahuja V, Ramachandran R, Sachdeva KS, Samantaray JC. Genotypic, Phenotypic and Clinical Validation of GeneXpert in Extra-Pulmonary and Pulmonary Tuberculosis in India. PLoS One. 2016 Feb 19;11(2):e0149258. doi: 10.1371/journal.pone.0149258. eCollection 2016. PubMed PMID: 26894283; PubMed Central PMCID: PMC4760939.

BACKGROUND: Newer molecular diagnostics have brought paradigm shift in early diagnosis of tuberculosis [TB]. WHO recommended use of GeneXpert MTB/RIF [Xpert] for Extra-pulmonary [EP] TB; critics have since questioned its efficiency.
METHODS: The present study was designed to assess the performance of GeneXpert in 761 extra-pulmonary and 384 pulmonary specimens from patients clinically suspected of TB and compare with Phenotypic, Genotypic and Composite reference standards [CRS].
RESULTS: Comparison of GeneXpert results to CRS, demonstrated sensitivity of 100% and 90.68%, specificity of 100% and 99.62% for pulmonary and extra-pulmonary samples. On comparison with culture, sensitivity for Rifampicin [Rif] resistance detection was 87.5% and 81.82% respectively, while specificity was 100% for both pulmonary and extra-pulmonary TB. On comparison to sequencing of rpoB gene [Rif resistance determining region, RRDR], sensitivity was respectively 93.33% and 90% while specificity was 100% in both pulmonary and extra-pulmonary TB. GeneXpert assay missed 533CCG mutation in one sputum and dual mutation [517 & 519] in one pus sample, detected by sequencing. Sequencing picked dual mutation [529, 530] in a sputum sample sensitive to Rif, demonstrating, not all RRDR mutations lead to resistance.
CONCLUSIONS: Current study reports observations in a patient care setting in a high burden region, from a large collection of pulmonary and extra-pulmonary samples and puts to rest questions regarding sensitivity, specificity, detection of infrequent mutations and mutations responsible for low-level Rif resistance by GeneXpert. Improvements in the assay could offer further improvement in sensitivity of detection in different patient samples; nevertheless it may be difficult to improve sensitivity of Rif resistance detection if only one gene is targeted. Assay specificity was high both for TB detection and Rif resistance detection. Despite a few misses, the assay offers major boost to early diagnosis of TB and MDR-TB, in difficult to diagnose pauci-bacillary TB.

DOI: 10.1371/journal.pone.0149258
PMCID: PMC4760939
PMID: 26894283 [PubMed - indexed for MEDLINE]

116: Subramanian K, Kattimani S, Sarkar S, Rajkumar RP. Current adherence attitudes can reflect the course and outcome of bipolar disorder-type I. Asian J Psychiatr. 2016 Apr;20:11. doi: 10.1016/j.ajp.2016.01.007. Epub 2016 Feb 2. PubMed PMID: 27025464.

117: Suchal K, Malik S, Gamad N, Malhotra RK, Goyal SN, Ojha S, Kumari S, Bhatia J, Arya DS. Mangiferin protect myocardial insults through modulation of MAPK/TGF-Î² pathways. Eur J Pharmacol. 2016 Apr 5;776:34-43. doi: 10.1016/j.ejphar.2016.02.055. Epub 2016 Feb 24. PubMed PMID: 26921754.

Mangiferin, a xanthone glycoside isolated from leaves of Mangifera indica (Anacardiaceae) is known to modulate many biological targets in inflammation and oxidative stress. The present study was designed to investigate whether mangiferin exerts protection against myocardial ischemia-reperfusion (IR) injury and possible role of Mitogen Activated Protein Kinase (MAPKs) and Transforming Growth Factor-β (TGF-β) pathways in its cardioprotection. Male albino Wistar rats were treated with mangiferin (40 mg/kg, i.p.) for 15 days. At the end of the treatment protocol, rats were subjected to IR injury consisting of 45 min ischemia followed by 1h reperfusion. IR-control rats caused significant cardiac dysfunction, increased serum cardiac injury markers, lipid peroxidation and a significant decrease in tissue antioxidants as compared to sham group. Histopathological examination of IR rats revealed myocardial necrosis, edema and

infiltration of inflammatory cells. However, pretreatment with mangiferin significantly restored myocardial oxidant-antioxidant status, maintained membrane integrity, and attenuated the levels of proinflammatory cytokines, pro-apoptotic proteins and TGF-β. Furthermore, mangiferin significantly reduced the phosphorylation of p38, and JNK and enhanced phosphorylation of ERK1/2. These results suggest that mangiferin protects against myocardial IR injury by modulating MAPK mediated inflammation and apoptosis.

DOI: 10.1016/j.ejphar.2016.02.055
PMID: 26921754 [PubMed - in process]

118: Sudhaman S, Prasad K, Behari M, Muthane UB, Juyal RC, Thelma BK. Discovery of a frameshift mutation in podocalyxin-like (PODXL) gene, coding for a neural adhesion molecule, as causal for autosomal-recessive juvenile Parkinsonism. J Med Genet. 2016 Jul;53(7):450-6. doi: 10.1136/jmedgenet-2015-103459. Epub 2016 Feb 10. PubMed PMID: 26864383.

BACKGROUND: Mutations in known genes for inherited forms of Parkinson's disease (PD) account for <30% of familial PD (FPD) implying that more causal gene(s) remain to be identified. We attempted to discover the putative causal variant in an Indian family with autosomal-recessive juvenile Parkinsonism (ARJP), tested negative for mutations in PARK2, PINK1 and DJ1.
METHODS: Whole exomes of two affected siblings were sequenced. Variants prioritised were screened for segregation with disease in the family by targeted sequencing. Gene thus identified was screened for index/additional exonic mutations, if any, in an independent PD cohort by PCR sequencing. Variants observed were functionally validated in differentiated PC12 cells.
RESULTS: A novel homozygous frameshift mutation, c.89_90insGTCGCCCC in exon 1 of podocalyxin-like gene (PODXL, 7q32-33), resulting in loss of protein, segregated with disease in the family. Mutant allele was absent in 186 healthy controls screened by PCR sequencing and in control exomes available in the laboratory and public databases. Screening of additional 212 sporadic and 68 FPD cases identified three novel heterozygous missense variants namely c.1285C>A, c.1118G>A and c.881G>A in three unrelated cases. Significant differences in neurite branching and length ($p<0.0001$) were observed in PC12 cells with wild-type and mutant constructs.
CONCLUSIONS: Based on the genetic and functional evidence in this study and literature support on the role of PODXL in neural development, a novel frameshift mutation in PODXL seems to be the likely cause of ARJP in this family. This is the first report suggesting the possible role of a neurodevelopmental pathway in PD aetiology.

DOI: 10.1136/jmedgenet-2015-103459
PMID: 26864383 [PubMed - in process]

119: Talwar S, Ramakrishnan P, Anderson RH, Choudhary SK, Makhija N, Kumar S, Airan B. Left Isomerism of the Atrial Appendages With Sinus Venosus Defect and Anomalous Systemic Venous Drainage. World J Pediatr Congenit Heart Surg. 2016 Sep;7(5):661-4. doi: 10.1177/2150135115610283. Epub 2016 Feb 16. PubMed PMID: 26884453.

We present a case with left isomerism, interruption of the inferior caval vein, anomalous systemic venous drainage with partially anomalous pulmonary venous drainage, and a sinus venosus type of atrial septal defect in the absence of a right superior caval vein. This report is of interest because of a rare combination of these anomalies, which was accurately diagnosed and successfully repaired.

DOI: 10.1177/2150135115610283
PMID: 26884453 [PubMed - in process]

120: Talwar S, Bansal A, Choudhary SK, Kothari SS, Juneja R, Saxena A, Airan B. Results of Fontan operation in patients with congenitally corrected transposition of great arteriesâ€ . Interact Cardiovasc Thorac Surg. 2016 Feb;22(2):188-93. doi:
10.1093/icvts/ivv316. Epub 2015 Nov 20. PubMed PMID: 26590305.

OBJECTIVES: The purpose of this study was to examine the outcome after the Fontan operation in patients with congenitally corrected transposition of great arteries with ventricular septal defect and pulmonary stenosis (ccTGA-VSD-PS).
METHODS: Patient- and procedure-related variables were analysed in 23 patients with ccTGA-VSD-PS operated between April 2003 and April 2015.
RESULTS: The mean age was 14.07 ± 6.38 years (range 4-23, median 11 years), with 82% patients being male (19/23). Dextrocardia was present in 52% (12/23) of patients and left superior vena cava was present in 26% (6/23) of patients. Most patients underwent extracardiac Fontan (n = 18), whereas in 5 patients lateral tunnel Fontan was performed. All patients received polytetrafluoroethylene grafts of size 18-22 mm for extracardiac Fontan. In 8 patients, conduits were fenestrated to reduce the intraconduit pressure. The mean hospital stay was 15.7 ± 11.24 days (5-60, median 14 days). The most common cause for prolonged hospital stay was pleural effusion in 5 patients (21.7%). One 7-year old patient developed conduit thrombosis, intracranial bleed, seizures and died. The mean follow-up was 46.4.4 ± 32.2 months (range 8-142, median 42 months) and was available for 21 patients (91.3%). There was 1 mid-term non-cardiac death after 3 years of operation. Of the total, 85.7% (18/21) patients in follow-up are in NYHA class I, whereas 3 patients are in class II. The actuarial event-free survival rate was 81.8 ± 13.2% at 10 years.
CONCLUSIONS: In ccTGA-VSD-PS patients with non-routable VSD and in those with difficult options for biventricular repair, the Fontan approach provides satisfactory mid-term palliation.

DOI: 10.1093/icvts/ivv316
PMID: 26590305 [PubMed - in process]

121: Tang SJ, Vilmann AS, Saftoiu A, Wang W, Streba CT, Fink PP, Griswold M, Wu R, Dietrich CF, Jenssen C, Hocke M, Kantowski M, Pohl J, Fockens P, Annema JT, van der Heijden EH, Havre RF, Pham KD, Kunda R, Deprez PH, Mariana J, Vazquez-Sequeiros E, Larghi A, Buscarini E, Fusaroli P, Lahav M, Puri R, Garg PK, Sharma M, Maluf-Filho F, Sahai A, Brugge WR, Lee LS, Aslanian HR, Wang AY, Shami VM, Markowitz A, Siddiqui AA, Mishra G, Scheiman JM, Isenberg G, Siddiqui UD, Shah RJ, Buxbaum J, Watson RR, Willingham FF, Bhutani MS, Levy MJ, Harris C, Wallace MB, NolsÃ¸e CP, Lorentzen T, Bang N, SÃ¸rensen SM, Gilja OH, D'Onofrio M, Piscaglia F, Gritzmann N, Radzina M, Sparchez ZA, Sidhu PS, Freeman S, McCowan TC, de Araujo CR Jr, Patel A, Ali MA, Campbell G, Chen E, Vilmann P. EUS Needle Identification Comparison and Evaluation study (withÂ videos). Gastrointest Endosc. 2016 Sep;84(3):424-433.e2. doi: 10.1016/j.gie.2016.01.068. Epub 2016 Feb 10. PubMed PMID: 26873530.

BACKGROUND AND AIMS: EUS-guided FNA or biopsy sampling is widely practiced. Optimal sonographic visualization of the needle is critical for image-guided interventions. Of the several commercially available needles, bench-top testing and direct comparison of these needles have not been done to reveal their inherent echogenicity. The aims are to provide bench-top data that can be used to guide clinical applications and to promote future device research and development.

METHODS: Descriptive bench-top testing and comparison of 8 commonly used EUS-FNA needles (all size 22 gauge): SonoTip Pro Control (Medi-Globe); Expect Slimline (Boston Scientific); EchoTip, EchoTip Ultra, EchoTip ProCore High Definition (Cook Medical); ClearView (Conmed); EZ Shot 2 (Olympus); and BNX (Beacon Endoscopic), and 2 new prototype needles, SonoCoat (Medi-Globe), coated by echogenic polymers made by Encapson. Blinded evaluation of standardized and unedited videos by 43 EUS endoscopists and 17 radiologists specialized in GI US examination who were unfamiliar with EUS needle devices.
RESULTS: There was no significant difference in the ratings and rankings of these needles between endosonographers and radiologists. Overall, 1 prototype needle was rated as the best, ranking 10% to 40% higher than all other needles ($P < .01$). Among the commercially available needles, the EchoTip Ultra needle and the ClearView needle were top choices. The EZ Shot 2 needle was ranked statistically lower than other needles (30%-75% worse, $P < .001$).
CONCLUSIONS: All FNA needles have their inherent and different echogenicities, and these differences are similarly recognized by EUS endoscopists and radiologists. Needles with polymeric coating from the entire shaft to the needle tip may offer better echogenicity.

DOI: 10.1016/j.gie.2016.01.068
PMID: 26873530 [PubMed - in process]

122: Tripathi H, Mehdi MU, Gupta D, Sen S, Kashyap S, Nag TC, Purwar M, Jassal M, Agrawal AK, Mohanty S, Tandon R. Long-term preservation of donor corneas in glycerol for keratoplasty: exploring new protocols. Br J Ophthalmol. 2016 Feb;100(2):284-90. doi: 10.1136/bjophthalmol-2015-306944. Epub 2015 Oct 27. PubMed PMID: 26508778.

AIM: To evaluate the role of temperature and adjunctive dehydration in better long-term preservation of human corneas when preserved and stored in glycerol.
METHODS: Different preservation temperatures and effects of adding silica gel in glycerol-preserved corneal tissues were evaluated. Human corneal tissues not suitable for optical keratoplasty initially preserved in McCarey-Kaufman medium were transferred to glycerol and stored at four different temperatures for 3 months as follows: tissues in anhydrous glycerol with and without silica gel at -80°C, -20°C, 4°C and at room temperature (RT). Parameters evaluated included microbial sterility, thickness (Digimatic micrometer), transparency (slit lamp examination, UV-Vis spectrophotometer), mechanical strength (Instron 5848 Microtester), tissue integrity (H&E staining), antigenicity (immunohistochemistry) and ultrastructure of collagen (transmission electron microscopy, TEM).
RESULTS: Microbial test after 3 months of glycerol preservation confirmed sterility of the tissues. The thickness increased in corneas preserved at RT with and without silica gel ($p<0.001$). RT corneas had the lowest transparency and tensile strength. Tissues in anhydrous glycerol stored with and without silica gel at -80°C were the most transparent ($p<0.001$) and had the highest tensile strength ($p<0.001$). Tissue integrity was maintained and expression of Human Leukocyte Antigen D related (HLA-DR) was less in glycerol-preserved corneas at -80°C. TEM studies indicated that parallel alignment of stromal collagen was disrupted at RT-preserved corneas.
CONCLUSIONS: Corneal tissue preserved at -80°C was the best method for preservation as it maintained the sterility, thickness, optical transparency, mechanical strength and ultrastructural features.

DOI: 10.1136/bjophthalmol-2015-306944
PMID: 26508778 [PubMed - indexed for MEDLINE]

123: Tripathy K, Chawla R, Meena S, Agarwal P. Unilateral giant peripapillary drusen and retinal drusenoid deposits in a case of X-linked retinoschisis. BMJ Case Rep. 2016 Feb 23;2016. pii: bcr2016214558. doi: 10.1136/bcr-2016-214558. PubMed PMID: 26907824.

A 25-year-old man with X-linked retinoschisis presented with multiple giant optic nerve head drusen and multiple retinal drusenoid deposits in one eye. There was an area of coarse pigmentation in the lower half of the retina, with convex upper borders extending on either side of the optic disc, suggestive of a spontaneously resolved retinal detachment. The possible aetiopathogenesis of such occurrence is discussed.

DOI: 10.1136/bcr-2016-214558
PMID: 26907824 [PubMed - in process]

124: Tripathy K, Sharma YR. Inverted hypopyon in the eye. BMJ Case Rep. 2016 Feb 17;2016. pii: bcr2016214638. doi: 10.1136/bcr-2016-214638. PubMed PMID: 26887888.

125: Tripathy K, Chawla R, Sharma YR, Vohra R. Rickettsia retinitis cases in India: a few comments. J Ophthalmic Inflamm Infect. 2016 Dec;6(1):7. doi: 10.1186/s12348-016-0076-1. Epub 2016 Feb 27. PubMed PMID: 26920002; PubMed Central PMCID: PMC4769237.

An important cause of infectious retinitis, not well-described in Indian literature, has been analyzed in detail systematically by Kawali A. and colleagues. However, Rickettsia retinitis (RR) was diagnosed at titres of 1:160 by the Weil-Felix test (WFT). The sensitivity and specificity of WFT at this level are poor compared to the gold standard immunofluorescent antibody assay. However, we understand that financial constraints of the Indian patients limit the availability of more definite tests. In our opinion, the optical coherence tomography features of RR described by the authors may be mimicked by other causes of retinitis, such as toxoplasma retinitis or even cotton wool spots. Infectious retinitis including RR should be treated by an antimicrobial agent with or without oral steroids until larger series or randomized controlled trials prove otherwise.

DOI: 10.1186/s12348-016-0076-1
PMCID: PMC4769237
PMID: 26920002 [PubMed]

126: Varghese A, Khakha DC, Chadda RK. Pattern and Type of Aggressive Behavior in Patients with Severe Mental Illness as Perceived by the Caregivers and the Coping Strategies Used by Them in a Tertiary Care Hospital. Arch Psychiatr Nurs. 2016 Feb;30(1):62-9. doi: 10.1016/j.apnu.2015.10.002. Epub 2015 Oct 17. PubMed PMID: 26804503.

Aggressive behavior by patients with severe mental illness is a major problem needing intervention. This descriptive cross sectional study examined the perception and coping strategies of caregivers with a sample of 100 toward aggressive behavior by patients with severe mental illness in the outpatient and inpatient unit of the department of psychiatry in a tertiary care hospital. The data were collected by a semistructured interview using Revised Overt Aggression Scale-modified, Aggressive Behavior and Intervention Checklist, Ways of Coping Checklist-Hindi Adaptation and Impact of Patient Aggression on Carers Scale-Adapted. The caregivers perceived aggression in varying extent from the patients. Majority used problem-focused coping to deal with aggressive behavior. Most of the caregivers perceived insisting to take medicines and talking about patient's illness as the triggers for aggressive behavior which was managed by talking to the patient calmly, lovingly and by leaving the patient alone. The

findings strongly suggest aggressive behavior as a frequent problem faced by family members of patient with severe mental illness. Nursing interventions should focus on counseling and psycho education for empowering caregivers to utilize strategies to reduce occurrence of aggressive behavior from patient and ways to effectively cope with the situation.

DOI: 10.1016/j.apnu.2015.10.002
PMID: 26804503 [PubMed - in process]

127: Vashist A, Prithvi Raj D, Gupta UD, Bhat R, Tyagi JS. The Î±10 helix of DevR,
the Mycobacterium tuberculosis dormancy response regulator, regulates its DNA binding and activity. FEBS J. 2016 Apr;283(7):1286-99. doi: 10.1111/febs.13664. Epub 2016 Feb 20. PubMed PMID: 26799615.

The crystal structures of several bacterial response regulators provide insight into the various interdomain molecular interactions potentially involved in maintaining their 'active' or 'inactive' states. However, the requirement of high concentrations of protein, an optimal pH and ionic strength buffers during crystallization may result in a structure somewhat different from that observed in solution. Therefore, functional assessment of the physiological relevance of the crystal structure data is imperative. DevR/DosR dormancy regulator of Mycobacterium tuberculosis (Mtb) belongs to the NarL subfamily of response regulators. The crystal structure of unphosphorylated DevR revealed that it forms a dimer through the α5/α6 interface. It was proposed that phosphorylation may trigger extensive structural rearrangements in DevR that culminate in the formation of a DNA-binding competent dimeric species via α10-α10 helix interactions. The α10 helix-deleted DevR protein (DevRΔα10) was hyperphosphorylated but defective with respect to in vitro DNA binding. Biophysical characterization reveals that DevRΔα10 has an open but less stable conformation. The combined cross-linking and DNA-binding data demonstrate that the α10 helix is essential for the formation and stabilization of the DNA-binding proficient DevR structure in both the phosphorylated and unphosphorylated states. Genetic studies establish that Mtb strains expressing DevRΔα10 are defective with respect to dormancy regulon expression under hypoxia. The present study highlights the indispensable role of the α10 helix in DevR activation and function under hypoxia and establishes the α10-α10 helix interface as a novel target for developing inhibitors against DevR, a key regulator of hypoxia-triggered dormancy.

DOI: 10.1111/febs.13664
PMID: 26799615 [PubMed - indexed for MEDLINE]

128: Vashist P, Gupta N, Tandon R, Gupta SK, Dwivedi S, Mani K. Population-based assessment of vision-related quality of life in corneal disease: results from the CORE study. Br J Ophthalmol. 2016 May;100(5):588-93. doi: 10.1136/bjophthalmol-2015-307619. Epub 2016 Feb 25. PubMed PMID: 26917676.

OBJECTIVE: To assess the impact of corneal disease on vision-related quality of life (VR-QoL) in a rural North Indian population.
DESIGN: Cross-sectional, population-based study.
METHODS: The Corneal Opacity Rural Epidemiological (CORE) study included 12 899 participants from 25 randomly selected clusters of rural Gurgaon, Haryana, India, with the primary objective of determining the prevalence of corneal disease in the general population during July 2011 to January 2013. VR-QoL was assessed through Indian Vision Function questionnaire (IND-VFQ-33) in adult participants (aged ≥18 years) detected with corneal opacity and equal number of healthy controls (no ocular pathology with visual acuity of 6/6 binocularly) selected from the same clusters. Scores of the three subscales of IND-VFO-33

(vision-specific mobility, psychosocial impact and visual symptoms) were computed, analysed and compared separately across various groups.
RESULTS: Overall, 12 113 participants of all ages underwent detailed ophthalmic examination and VR-QoL was assessed in 435 cases with corneal disease and 435 controls without any ophthalmic disease. The diseased population had significantly higher scores and hence poorer VR-QoL across all three domains of vision function (scores of 28 vs 22; 6 vs 5 and 14 vs 9, respectively; p<0.0001) and the scores were inversely related with the level of visual impairment in patients with corneal disease. Patients with unilateral corneal disease also had poorer VR-QoL scores as compared with healthy controls (p<0.0001).
CONCLUSIONS: VR-QoL is impaired in patients with corneal disease, more so in patients with corneal blindness. This is the first population-based study to document VR-QoL through IND-VFQ-33 in the Indian population with corneal disease.

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129: Vinay K, Yadav S. Uncommon presentation of a less common tumour. Indian J Med Res. 2016 Feb;143(2):249-50. doi: 10.4103/0971-5916.180233. PubMed PMID: 27121528; PubMed Central PMCID: PMC4859139.

130: Vitola JV, Mut F, AlexÃ¡nderson E, Pascual TN, Mercuri M, Karthikeyan G, Better N, Rehani MM, Kashyap R, Dondi M, Paez D, Einstein AJ; INCAPS Investigators Group. Opportunities for improvement on current nuclear cardiology practices and radiation exposure in Latin America: Findings from the 65-country IAEA Nuclear Cardiology Protocols cross-sectional Study (INCAPS). J Nucl Cardiol. 2016 Feb 22. [Epub ahead of print] PubMed PMID: 26902484.

BACKGROUND: Comparison of Latin American (LA) nuclear cardiology (NC) practice with that in the rest of the world (RoW) will identify areas for improvement and lead to educational activities to reduce radiation exposure from NC.
METHODS AND RESULTS: INCAPS collected data on all SPECT and PET procedures performed during a single week in March-April 2013 in 36 laboratories in 10 LA countries (n = 1139), and 272 laboratories in 55 countries in RoW (n = 6772). Eight "best practices" were identified a priori and a radiation-related Quality Index (QI) was devised indicating the number used. Mean radiation effective dose (ED) in LA was higher than in RoW (11.8 vs 9.1 mSv, p < 0.001). Within a populous country like Brazil, a wide variation in laboratory mean ED was found, ranging from 8.4 to 17.8 mSv. Only 11% of LA laboratories achieved median ED <9 mSv, compared to 32% in RoW (p < 0.001). QIs ranged from 2 in a laboratory in Mexico to 7 in a laboratory in Cuba. Three major opportunities to reduce ED for LA patients were identified: (1) more laboratories could implement stress-only imaging, (2) camera-based methods of ED reduction, including prone imaging, could be more frequently used, and (3) injected activity of (99m)Tc could be adjusted reflecting patient weight/habitus.
CONCLUSIONS: On average, radiation dose from NC is higher in LA compared to RoW, with median laboratory ED <9 mSv achieved only one third as frequently as in RoW. Opportunities to reduce radiation exposure in LA have been identified and guideline-based recommendations made to optimize protocols and adhere to the "as low as reasonably achievable" (ALARA) principle.

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131: Whitcomb DC, Frulloni L, Garg P, Greer JB, Schneider A, Yadav D, Shimosegawa T. Chronic pancreatitis: An international draft consensus proposal for a new mechanistic definition. Pancreatology. 2016 Mar-Apr;16(2):218-24. doi: 10.1016/j.pan.2016.02.001. Epub 2016 Feb 16. PubMed PMID: 26924663.

BACKGROUND: A definition of chronic pancreatitis (CP) is needed for diagnosis and distinguishing CP from other disorders. Previous definitions focused on morphology. Advances in epidemiology, genetics, molecular biology, modeling and other disciplines provide new insights into pathogenesis of CP, and allow CP to be better defined.
METHODS: Expert physician-scientists from the United States, India, Europe and Japan reviewed medical and scientific literature and clinical experiences. Competing views and approaches were debated until a new consensus definition was reached.
RESULTS: CP has been defined as 'a continuing inflammatory disease of the pancreas, characterized by irreversible morphological change, and typically causing pain and/or permanent loss of function'. Focusing on abnormal morphology makes early diagnosis challenging and excludes inflammation without fibrosis, atrophy, endocrine and exocrine dysfunction, pain syndromes and metaplasia. A new mechanistic definition is proposed--'Chronic pancreatitis is a pathologic fibro-inflammatory syndrome of the pancreas in individuals with genetic, environmental and/or other risk factors who develop persistent pathologic responses to parenchymal injury or stress.' In addition, "Common features of established and advanced CP include pancreatic atrophy, fibrosis, pain syndromes, duct distortion and strictures, calcifications, pancreatic exocrine dysfunction, pancreatic endocrine dysfunction and dysplasia." This definition recognizes the complex nature of CP, separates risk factors from disease activity markers and disease endpoints, and allows for a rational approach to early diagnosis, classification and prognosis.
CONCLUSIONS: Initial agreement on a mechanistic definition of CP has been reached. This definition should be debated in rebuttals and endorsements, among experts and pancreatic societies until international consensus is reached.

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132: Wierzbicka M, Bartochowska A, Strnad V, Strojan P, Mendenhall WM, Harrison LB, Rinaldo A, Sahai P, Wiegand S, Ferlito A. The role of brachytherapy in the treatment of squamous cell carcinoma of the head and neck. Eur Arch Otorhinolaryngol. 2016 Feb;273(2):269-76. doi: 10.1007/s00405-014-3332-8. Epub 2014 Oct 22. PubMed PMID: 25338181.

Brachytherapy is a form of intensive local irradiation, allowing effective protection of surrounding structures with preservation of organ function and results in a favorable therapeutic ratio. It can be used alone, adjuvantly after surgery, and as a local boost in combination with external-beam radiation therapy. This paper is a literature review on the role of brachytherapy in the management of head and neck cancers with a special emphasis on papers published in the last 5 years. Technical details, effectiveness and potential toxicities of brachytherapy when used in different combinations with other therapeutic modalities and tumor sites are presented. Brachytherapy is an attractive treatment option in the management of primary malignancies and recurrent tumors in previously irradiated areas of the head and neck. It is effective and safe, and results in good functional and oncological outcomes.

DOI: 10.1007/s00405-014-3332-8
PMID: 25338181 [PubMed - in process]

133: Yadav K, Akanksha, Jaryal AK, Coshic P, Chatterjee K, Deepak KK. Effect of hypovolemia on efficacy of reflex maintenance of blood pressure on orthostatic challenge. High Blood Press Cardiovasc Prev. 2016 Mar;23(1):25-30. doi: 10.1007/s40292-016-0130-y. Epub 2016 Feb 16. PubMed PMID: 26883243.

INTRODUCTION: Blood volume is an important determinant of the efficacy of the

negative feedback mechanisms that maintain blood pressure. However, its effect on time profile and magnitude of the responses remain unstudied.
AIM: To study the effect of mild hypovolemia on time profiles and magnitude of changes in blood pressure and heart rate in healthy subjects before and after blood donation.
METHODS: Fifty six healthy volunteer donors who signed up for blood donation were recruited (age 35 ± 7 years; weight 75 ± 9 Kg). Baseline beat to beat blood pressure and Lead II ECG was recorded for 5 min followed by orthostatic challenge for 3 min before and after blood donation.
RESULTS: The donation of 450 ml of blood did not lead to any changes in the resting systolic, diastolic or mean blood pressure. However, there was a significant decrease in pulse pressure after blood donation along with an increase in the heart rate. During orthostatic challenge, after blood donation there was a greater fall in systolic, diastolic, mean and pulse pressure along with a greater increase in heart rate as compared to before the blood donation. The latency to response and the total time to recovery of blood pressure and heart rate increased significantly after blood donation.
CONCLUSION: Maintenance of blood pressure after orthostatic challenge is not compromised after mild hypovolemia produced by donation of 450 ml of blood. However, mild hypovolemia results in increase in latency of response and is accompanied with larger magnitude of fall in blood pressure during orthostatic challenge.

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PMID: 26883243 [PubMed - in process]

134: Yadav K, Aggarwal S, Guleria S, Kumar R. Comparative study of laparoscopic and mini-incision open donor nephrectomy: have we heard the last word in the debate? Clin Transplant. 2016 Mar;30(3):328-34. doi: 10.1111/ctr.12700. Epub 2016 Feb 8. PubMed PMID: 26780835.

OBJECTIVE: Laparoscopic donor nephrectomy (LDN) is generally considered a better option than open donor nephrectomy (ODN) as it is associated with better cosmesis, less post-operative pain and faster recovery. Mini-incision donor nephrectomy (MDN) has proven to be an effective and less invasive modification of classic ODN. Our aim was to compare the peri-operative outcomes and quality of life of donors following laparoscopic and mini-incision ODN.
METHODS: One hundred patients, underwent donor nephrectomy using laparoscopic approach (n = 50) or open mini-incision approach (n = 50) over a period of 18 months. Data were entered into a prospective database and analyzed retrospectively.
RESULTS: The mean operative (skin to skin) time for MDN, 53.9 min (range, 40-75 min), was significantly shorter than the 93.7 min (range, 75-140 min) for LDN. The laparoscopic donors had a longer hospital stay, warm ischemia time and higher operative and post-operative cost. There was no significant difference in the pain scores, graft function, or quality of life between the two groups.
CONCLUSIONS: MDN compares well with the laparoscopic approach in terms of post-operative pain, graft function and quality of life of donors. Significantly less operative time along with the reduced cost makes it a better option in our predominantly lower BMI patient population.

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135: Yaseen R, Pushpalatha H, Reddy GB, Ismael A, Ahmed A, Dheyaa A, Ovais S, Rathore P, Samim M, Akthar M, Sharma K, Shafi S, Singh S, Javed K. Design and synthesis of pyridazinone-substituted benzenesulphonylurea derivatives as anti-hyperglycaemic agents and inhibitors of aldose reductase - an enzyme embroiled in diabetic complications. J Enzyme Inhib Med Chem. 2016 Feb 16:1-13. [Epub ahead of print] PubMed PMID: 26879420.

Thirty new aryl-pyridazinone-substituted benzenesulphonylurea derivatives (I-XXX) were synthesized and evaluated for their anti-hyperglycaemic activity in glucose-fed hyperglycaemic normal rats. Twenty-three compounds (III-XI, XIV-XVII, XIX-XXIV, XXVI and XXVIII-XXX) showed more or comparable area under the curve (AUC) reduction percentage (ranging from 21.9% to 35.5%) as compared to the standard drug gliclazide (22.0%). On the basis of docking results, 18 compounds were screened for their in vitro ability to inhibit rat lens aldose reductase. Ten compounds (III-VI, XII, XVI-XVIII, XXI and XXVII) showed ARI activity with IC50 ranging from 34 to 242 µM. Out of these, two compounds IV and V showed best ARI activity which is comparable with that of quercetin. As a result, two compounds (IV and V) possessing significant dual action (anti-hyperglycaemic and aldose reductase inhibition) were identified and may be used as lead compounds for developing new drugs.

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