Dear Friends,

The Annual Research Digest for the term Jan- Jun 2014 a compilation of the Indexed publications of the institution is provided herewith. Though this is mean to include all publications that were generated by our scientists students and faculty during this time period-there are certainly likely to be lacunae.

Do browse through the document and let us know if there are more of your publications which need to be added. We would like to thank Dodd Memorial Library, the staff at the research office and Dr. Mohan for assistant in compiling the current issue.

Dr. Nihal Thomas MD MNAMS DNB (Endo) FRACP (Endo) FRCP (Edin) FRCP (Glas) Addl. Vice-Principal (Research)
Special request to CMC Faculty

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Dr. Nihal Thomas  MD MNAMS DNB (Endo) FRACP (Endo) FRCP (Edin) FRCP (Glas)
Addl. Vice-Principal (Research)

Al Sheikh YA(1), Marie MA(2), John J(3), Krishnappa LG(4), Dabwab KH(4). Prevalence of 16S rRNA methylase genes among β-Lactamase-producing Enterobacteriaceae clinical isolates in Saudi Arabia. Libyan J Med. 2014 Jul 7;9:24432. doi: 10.3402/ljm.v9.24432. eCollection 2014. Author information: (1)Clinical Laboratory Sciences Department, College of Applied Medical Sciences, King Saud University, Riyadh, Kingdom of Saudi Arabia; Chair of Medical and Molecular Genetics Research, Clinical Laboratory Sciences Department, College of Applied Medical Sciences, King Saud University, Riyadh, Kingdom of Saudi Arabia. (2)Clinical Laboratory Sciences Department, College of Applied Medical Sciences, King Saud University, Riyadh, Kingdom of Saudi Arabia; dr.mmarie2000@gmail.com. (3)Department of Clinical Microbiology, Christian Medical College and Hospital, Vellore, Tamil Nadu, India; Department of Biotechnology, School of Life Sciences, Pondicherry University, Pondicherry, India. (4)Clinical Laboratory Sciences Department, College of Applied Medical Sciences, King Saud University, Riyadh, Kingdom of Saudi Arabia. Background: Co production of 16S rRNA methylases gene and β-Lactamase gene among Enterobacteriaceae isolates conferring resistance to both therapeutic options has serious implications for clinicians worldwide. Methods: To study co existence of 16S rRNA methylases (armA, rmtA, rmtB, rmtC, rmtD, and npmA) and β-Lactamase (blaTEM-1,blaSHV-12,blaCTX-M-14) genes, we screened all phenotypic positive β-Lactamase producing enterobacteriaceae by polymerase chain reaction (PCR) targeting above gene. A total of 330 enterobacteriaceae strains were collected during study period out of that 218 isolates were identified phenotypically as β-Lactamase producers, which include 50 (22.9%) Escherichia coli; 92 (42.2%) Klebsiella pneumoniae, 44 (20.2%), Citrobactor freundii and 32 (14.7%) Enterobacter spp. Results: Among this 218, only 188 isolates harbored the resistant gene for β-Lactamase production. Major β-Lactamase producing isolates were bla Conclusion: β-Lactamase producing isolates appears to coexist with 16S rRNA methylase predominantly armA and rmtB genes in the same isolate. We conclude the major β-Lactamase and 16S rRNA methylases co-producer was K. pneumoniae followed by E. coli. We suggest further work on evaluating other β-lactamases types and novel antibiotic resistance mechanisms among Enterobacteriaceae.

Anand R(1), Gill KD, Mahdi AA. Therapeutics of Alzheimer’s disease: Past, present and future. Neuropharmacology. 2014 Jan;76 Pt A:27-50. doi: 10.1016/j.neuropharm.2013.07.004. Epub 2013 Jul 25. Author information: (1)Department of Biochemistry, Christian Medical College, Vellore 632002, Tamilnadu, India. Electronic address: griffindoc@gmail.com. Alzheimer’s disease (AD) is the most common cause of dementia worldwide. The etiology is multifactorial, and pathophysiology of the disease is complex. Data indicate an exponential rise in the number of cases of AD, emphasizing the need for developing an effective treatment. AD also imposes tremendous emotional and financial burden to the patient’s family and community. The disease has been studied over a century, but acetylcholinesterase inhibitors and memantine are the only drugs currently approved for its management. These drugs provide symptomatic improvement alone but do less to modify the disease process. The extensive insight into the molecular and cellular pathomechanism in AD over the past few decades has provided us significant progress in the understanding of the disease. A number of novel strategies that seek to modify the disease process have been developed. The major
developments in this direction are the amyloid and tau based therapeutics, which could hold the key to treatment of AD in the near future. Several putative drugs have been thoroughly investigated in preclinical studies, but many of them have failed to produce results in the clinical scenario; therefore it is only prudent that lessons be learnt from the past mistakes. The current rationales and targets evaluated for therapeutic benefit in AD are reviewed in this article. This article is part of the Special Issue entitled ‘The Synaptic Basis of Neurodegenerative Disorders’.

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BACKGROUND: Apolipoprotein E (ApoE), a protein primarily involved in lipoprotein metabolism, occurs in three isoforms (E2, E3 and E4). Studies evaluating the association between APOE genotype and incidence of malignancies have given inconclusive results.

OBJECTIVE: The objective of the present study was to analyze the association between APOE genotype and incidence of cancer by a meta-analysis.

METHODS: We conducted a literature search in the electronic databases for studies with information on APOE genotype in malignancies. Sixteen studies (14 case-control and 2 cohort; 77,970 controls and 12,010 cases) were included for the present meta-analysis. Pooled odds ratios (OR) with 95 % confidence intervals (CI) were calculated assuming a random-effect model for all the genotypes and alleles. Subgroup analyses based on study design, ethnicity of populations, site of cancer and source of controls were performed as a post hoc measure. Appropriate tests to detect heterogeneity, publication bias and sensitivity were done at all stages. The review protocol is registered with the PROSPERO database vide registration number CRD42013006496.

RESULTS: The pooled effect measure for the comparisons did not reveal an association in primary analyses. In the subgroup analyses, we observed a negative association between APOE4+ genotypes and overall risk of cancer in the cohort study subgroup (pooled OR 0.86; 95 % CI 0.82-0.91; p < 0.00001; I (2) = 0 %). Sensitivity analyses did not alter the overall pooled effect measure, and there were no evidences to suggest a publication bias.

CONCLUSION: Overall, the present meta-analysis did not show any association between APOE alleles and genotypes with incidence of cancer in general.


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Adeno-associated virus (AAV) based vectors have emerged as important tools for gene therapy in humans. The recent successes seen in Phase I/II clinical trials have also highlighted the issues related to the host and vector-related immune response that preclude the universal application of this promising vector system. A fundamental insight into the biological mechanisms by which AAV infects the host cell and a thorough understanding of the immediate and long-lived cellular responses to AAV infection is
likely to offer clues and help design better intervention strategies to improve the therapeutic efficiency of AAV vectors. This article reviews the biology of AAV-host cellular interactions and outlines their application in the development of novel and improved AAV vector systems.

**INTL** PMID: 24588706  [PubMed - in process]  BS


Detection of cancer DNA in plasma of patients with early-stage breast cancer.


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PURPOSE: Detecting circulating plasma tumor DNA (ptDNA) in patients with early-stage cancer has the potential to change how oncologists recommend systemic therapies for solid tumors after surgery. Droplet digital polymerase chain reaction (ddPCR) is a novel sensitive and specific platform for mutation detection.

**EXPERIMENTAL DESIGN:** In this prospective study, primary breast tumors and matched pre- and postsurgery blood samples were collected from patients with early-stage breast cancer (n = 29). Tumors (n = 30) were analyzed by Sanger sequencing for common PIK3CA mutations, and DNA from these tumors and matched plasma were then analyzed for PIK3CA mutations using ddPCR.

**RESULTS:** Sequencing of tumors identified seven PIK3CA exon 20 mutations (H1047R) and three exon 9 mutations (E545K). Analysis of tumors by ddPCR confirmed these mutations and identified five additional mutations. Presurgery plasma samples (n = 29) were then analyzed for PIK3CA mutations using ddPCR. Of the 15 PIK3CA mutations detected in tumors by ddPCR, 14 of the corresponding mutations were detected in presurgical ptDNA, whereas no mutations were found in plasma from patients with PIK3CA wild-type tumors (sensitivity 93.3%, specificity 100%). Ten patients with mutation-positive ptDNA presurgery had ddPCR analysis of postsurgery plasma, with five patients having detectable ptDNA postsurgery.

**CONCLUSIONS:** This prospective study demonstrates accurate mutation detection in tumor tissues using ddPCR, and that ptDNA can be detected in blood before and after surgery in patients with early-stage breast cancer. Future studies can now address whether ptDNA detected after surgery identifies patients at risk for recurrence, which could guide chemotherapy decisions for individual patients.


Chauhan A(1), Mehla R(2), Vijayakumar TS(3), Handy I(2).

Endocytosis-mediated HIV-1 entry and its significance in the elusive behavior of the virus in astrocytes.


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Astrocytes protect neurons but also evoke a proinflammatory response to injury and viral infections including HIV. We investigated the mechanism of HIV-1 infection in primary astrocytes, which showed minimal but productive viral infection independent of CXCR4. As with ectopic-CD4-expressing astrocytes, lysosomotropic agents led to increased HIV-1 infection in wild-type but not Rab 5, 7, and 11-ablated astrocytes. Instead, HIV-1 infection was decreased in Rab-depleted astrocytes, corroborating viral entry by endocytosis. HIV-1 produced persistent infection in astrocytes (160 days); no evidence of latent infection was seen. Notably, one caveat is that endosomal modifiers enhanced wild-type HIV-1 infection (M- and T-tropic) in astrocytes, suggesting endocytic entry of the virus. Impeding endocytosis by inhibition of Rab 5, 7 or 11 will inhibit HIV infection in astrocytes. Although the contribution of such low-level infection in astrocytes to neurological complications is unclear, it may serve as an elusive viral reservoir in the central nervous system.

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Dutta AK.
Narrow band imaging endoscopy for real-time assessment of duodenal villi.
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Janardhanan J(1), Prakash JA(2), Abraham OC(1), Varghese GM(3).
Comparison of a conventional and nested PCR for diagnostic confirmation and genotyping of Orientia tsutsugamushi.
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A nested polymerase chain reaction (PCR) targeting the 56-kDa antigen gene is currently the most commonly used molecular technique for confirmation of scrub typhus and genotyping of Orientia tsutsugamushi. In this study, we have compared the commonly used nested PCR (N-PCR) with a single-step conventional PCR (C-PCR) for amplification and genotyping. Eschar samples collected from 24 patients with scrub typhus confirmed by IgM enzyme-linked immunosorbent assay were used for DNA extraction following which amplifications were carried out using nested and C-PCR methods. The amplicons were sequenced and compared to other sequences in the database using BLAST. Conventional PCR showed a high positivity rate of 95.8% compared to the 75% observed using N-PCR. On sequence analysis, the N-PCR amplified region showed more variation among strains than the C-PCR amplified region. The C-PCR, which is more economical, provided faster and better results compared to N-PCR.

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Jelovac D(1), Beaver JA(1), Balukrishna S(2), Wong HY(1), Toro PV(1), Cimino-Mathews A(1), Argani P(1), Stearns V(1), Jacobs L(1), VanDenBerg D(1), Kessler J(1), Jeter S(1), Park BH(3), Wolff AC(1).
A PIK3CA mutation detected in plasma from a patient with synchronous primary breast and lung cancers.
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Digital polymerase chain reaction is a new technology that enables detection and quantification of cancer DNA molecules from peripheral blood. Using this technique, we identified mutant PIK3CA DNA in circulating ptDNA (plasma tumor DNA) from a patient
with concurrent early stage breast cancer and non-small cell lung cancer. The patient underwent successful resection of both her breast and lung cancers, and using standard Sanger sequencing the breast cancer was shown to harbor the identical PIK3CA mutation identified in peripheral blood. This case report highlights potential applications and concerns that can arise with the use of ptDNA in clinical oncology practice.

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Khera PS, Keshava SN.
An indigenous model for learning ultrasound-guided interventions.
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Ultrasound-guided interventions require good hand-eye coordination with respect to probe control and needle orientation. We describe a method of making an ultrasound phantom for practice purpose using an edible jelly mixture. The phantom is easy to make, reproducible, cheap, and simulates in vivo target.

**NAT** PMID: 25024521 [PubMed] BS

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Identification of rare and novel deletions that cause (δβ)0-thalassaemia and hereditary persistence of foetal haemoglobin in Indian population.
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**OBJECTIVES:** Hereditary persistence of foetal haemoglobin (HPFH) and (δβ)(0) -thalassaemia are conditions caused by large deletions that involve δ- and β-globin genes in the β-globin cluster, and they are characterized by increased haemoglobin (HbF) levels in adults. Significant phenotypic diversity is observed between the different mutations that cause these conditions. Molecular characterization of these deletions is important for accurate molecular diagnosis, and they will also provide the information on the cis-acting genetic regulatory elements present in the α-globin cluster.

**METHODS:** We performed gap-PCR, multiplex ligation-dependent probe amplification (MLPA), quantitative fluorescent multiplex PCR (QF-MPCR) and DNA sequencing to detect and characterize the deletions in the β-globin cluster. RESULTS: We characterized six different deletions resulting in (δβ)(0) -thalassaemia or HPFH in 51 unrelated families.

**CONCLUSION:** With the help of multiple genetic tools, we performed comprehensive genetic analysis of HPFH and (δβ)(0) -thalassaemia in Indian population and could define the molecular basis of these conditions in this population. We also identified two novel HPFH mutations, 49.98 kb (HPFH-9) and 86.7 kb (HPFH-10) deletions, in this population.

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Oommen V(1), Kanthakumar P(2).
A simple model of the accommodating lens of the human eye.
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Ostrovidov S(1), Shi X(1), Zhang L(1), Liang X(1), Kim SB(2), Fujie T(3), Ramalingam M(4), Chen M(1), Nakajima K(1), Al-Hazmi F(5), Bae H(6), Memic A(7), Khademhosseini A(8).

Myotube formation on gelatin nanofibers - multi-walled carbon nanotubes hybrid scaffolds.

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Engineering functional muscle tissue requires the formation of densely packed, aligned, and mature myotubes. To enhance the formation of aligned myotubes with improved contractibility, we fabricated aligned electrospun gelatin multi-walled carbon nanotubes (MWNTs) hybrid fibers that were used as scaffolds for the growth of myoblasts (C2C12). The MWNTs significantly enhanced myotube formation by improving the mechanical properties of the resulting fibers and upregulated the activation of mechanotransduction related genes. In addition, the fibers enhanced the maturation of the myotubes and the amplitude of the myotube contractions under electrical stimulation (ES). Such hybrid material scaffolds may be useful to direct skeletal muscle cellular organization, improve cellular functionality and tissue formation.

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Mutations Seen Among Patients With Pheochromocytoma and Paraganglioma at a Referral Center From India.
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Determining the mutational status of susceptibility genes including RET, VHL, SDHx (SDHB, SDHC, SDHD) among patients with pheochromocytoma/paraganglioma (PCC/PGL) is gaining importance. These genes have not been systematically characterized among patients with PCC/PGL from India. The aim of the work was to screen the most frequently mutated genes among patients with PCC/PGL to determine the frequency and spectrum of mutations...
seen in this region. Fifty patients with PCC/PGL treated at our tertiary care hospital between January 2010 and June 2012 were screened for mutations in susceptibility genes using an algorithmic approach. Thirty-two percent (16/50) of patients were found to be positive for mutations including mutations among RET (n=4), VHL (n=6), SDHB (n=3), and SDHD (n=3) genes. None of these patients were positive for SDHC mutations. A significant association was found between young patients with bilateral tumors and VHL mutations (p=0.002). Two of the 3 patients with extra-adrenal SDHB associated tumors, had unique mutations, viz., c.436delT (exon 5) and c.788_857del (exon 8), one of which was malignant. High frequency of mutations seen among patients in this study emphasizes the need to consider mutational analysis among Indian patients with PCC/PGL.

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Pai R(1), Manipadam MT, Singh P, Ebenazer A, Samuel P, Rajaratnam S.
Usefulness of Succinate dehydrogenase B (SDHB) immunohistochemistry in guiding mutational screening among patients with pheochromocytoma-paraganglioma syndromes.
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Genetic testing of pheochromocytomas (PCC) and paragangliomas (PGL), although expensive, is gradually becoming a part of the routine laboratory investigation for patients with PCC-PGL syndrome. Recently, Succinate dehydrogenase B (SDHB) immunohistochemistry has been shown to be an excellent indicator of germline mutations in the SDH genes and could help significantly reduce cost. This study assesses the utility of SDHB immunohistochemical analysis when used to guide genetic analysis, with emphasis on cost benefits it could provide in a resource-limited setting. Forty-four cases of PCC/PGL characterized by genetic analysis were included to determine their SDHB expression pattern by immunohistochemistry. SDHB antibody expression was negative among three cases each, with SDHB and SDHD mutations. Immunohistochemistry results were positive for all three cases of RET, a single case of neurofibromatosis and for two cases with Von Hippel-Lindau (VHL) mutations while the remaining two cases with VHL mutations showed a diffuse ‘cytoplasmic blush’. Thirty of the remaining 31 samples demonstrated positive staining and were negative for mutations, while a lone sample that was negative for staining and mutation was not included in the final analysis as the internal control for the sample was not adequately stained. Cost analysis in our settings showed that triaging with SDHB immunohistochemistry could potentially reduce costs by USD 320-500 per patient. SDHB immunohistochemistry, when used as a guide to genetic testing, can significantly reduce the effort, time and costs of testing among patients with PCC-PGL, a huge benefit in resource limited settings.

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INTL PMID: 24735130

Parangama C(1), Anu E(2), Sukria N(3).
Endoanal ultrasound assessment of sphincter defects and thinning—correlation with anal manometry.
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BACKGROUND AND STUDY AIMS: This study aims to determine if anal sphincter defects/thinning observed at endoanal ultrasound correlates with anal pressures recorded at anal manometry.

PATIENTS AND METHODS: A total of 30 consecutive patients with history suggestive of anal sphincter pathology underwent anal endosonography with documentation of internal and external sphincter defects/thinning. The same patients underwent anal manometry with documentation of maximum resting and maximum squeeze pressures. Patients with a
sphincter defect (SD) were compared to patients without a sphincter defect (NSD) and both groups were compared with respect to findings in manometry. The Mann-Whitney U test was used for statistical analysis. This study was approved by the Institutional Ethics Committee.

RESULTS: A statistically significant correlation was found between decreased maximal resting pressure and decreased internal anal sphincter (IAS) thickness or an IAS defect. The correlation between MSP and external sphincter pathology was significantly less consistent in our study.

CONCLUSION: Our study showed a statistically significant correlation between maximum resting pressure and observation of internal sphincter defects at endoanal ultrasound. The patients with documented internal sphincter defects have significantly reduced maximum resting pressures. There was however, no correlation between external sphincter defects and decrease in maximum squeeze pressure as has been observed in other studies. Until a manometry cut-off can be set to discriminate between the absence and presence of defects, both manometry and ultrasound should be offered to patients with history suggesting anal sphincter pathology.

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INTL PMID: 23888959 [PubMed - in process] BS

Peedicayil J.
Epigenetics and the war on mental illness.
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INTL PMID: 24589890 [PubMed - as supplied by publisher] BS

Peedicayil J.
Epigenetic approaches for bipolar disorder drug discovery.
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Introduction: Bipolar disorder (BD) is a common psychiatric disorder which can be devastating to affected patients, if not adequately treated. Although effective drugs are presently available for treating BD, many patients do not respond adequately. There are also problems with the current management of patients with this disorder: drug-resistant BD, rapid-cycling BD and cognitive decline in BD patients despite drug therapy. In this context, new and more effective drugs will be valuable in the clinical management of BD patients. Areas covered: This article discusses the potential of the use of epigenetic drugs in the management of BD. Although several classes of epigenetic drugs are under investigation, at present, most attention is focused on two classes of epigenetic drugs: DNA methyltransferase inhibitors and histone deacetylase inhibitors (HDACis). Several preclinical drug trials of HDACis for the treatment of BD have been conducted.
Expert opinion: HDACis have shown promising results in preclinical studies of BD. However, the currently available HDACis suffer from acting non-specifically on HDAC isozymes. More isozyme-specific HDACis are likely to have greater efficacy and less toxicity than the current HDACis. It is suggested that efforts should be made to develop such HDACis. Once such HDACis with adequate ability to cross the blood-brain barrier become available, investigators could consider proceeding to clinical trials of HDACis for the treatment of BD.

Prithishkumar IJ(1), Felicia C(2).
Histology of the cricothyroid membrane: a clinical perspective.

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Puncture of the cricothyroid membrane is a component of several clinical procedures. Among the several complications are the immediate risk of bleeding, long-term risk of subglottic stenosis and hoarseness of voice. Presence of blood vessels in the cricothyroid membrane has also been implicated in the extralaryngeal spread of laryngeal cancers. Though various authors have described the attachments of the cricothyroid membrane, very few have studied its histology. We studied the histology of the cricothyroid membrane using hematoxylin and eosin, Mallory’s trichrome and Verhoeff’s special stain. The cricothyroid membrane was found to be continuous on its deeper aspect with the mucosa of the subglottic larynx and lined by pseudostratified ciliated columnar epithelium. The membrane was observed to be fibroelastic, containing equal proportions of collagen and elastic fibers and numerous fibroblast nuclei. Numerous blood vessels are seen traversing through the membrane, which probably connect intralaryngeal with other extralaryngeal vessels. These histological findings help to further understand the complications of cricothyrotomy and spread of laryngeal cancer.

Rabi S(1), Jacob TM, Indrasingh I.
Demonstration of CD1a-positive and zinc iodide-osmium-positive Langerhans cells in the human eyelid.

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Raghupathy V(1), Oommen A(2), Ramachandran A(3).
Dimethylformamide interferes with Coomassie dye staining of proteins on blue native gel electrophoresis.

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Blue native gel electrophoresis (BN-PAGE) is used extensively for characterization of mitochondrial respiratory complexes and uses the binding of Coomassie brilliant blue G-250 to visualize proteins. Oxidative modification of sulfhydryl groups of such proteins can be evaluated by labeling with iodoacetamide conjugated to biotin (BIAM) and detected with streptavidin peroxidase on Western blots following BN-PAGE. However, dissolving BIAM in dimethylformamide, a recommended solvent, reduces Coomassie blue G staining to proteins during BN-PAGE. This interference is prevented by dissolving BIAM in dimethyl sulfoxide. Precautions in the use of the dye
for protein staining subsequent to BIAM labeling are discussed.

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INTL PMID: 24662748 [PubMed - in process] BS

Rajagopal K(1), Chilbule SK, Madhuri V.
Viability, proliferation and phenotype maintenance in cryopreserved human iliac apophyseal chondrocytes.
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Cryopreservation preserves cells at low temperature and creates a reserve for future use while executing the clinical translation. Unlike articular chondrocyte, cryopreservation protocol and its outcome are not described in iliac apophyseal chondrocytes, a potential source of chondrocytes in cartilage engineering. This study for the first time describes the cryopreservation of human iliac apophyseal chondrocytes. Four cartilage samples were procured from iliac crests of children undergoing hip surgery after consent. The total chondrocyte yield was divided into two groups. First group was grown as monolayer while second group was cryopreserved following the slow cooling method in the medium containing 10 % Dimethyl sulfoxide for 3 months. Group two cells were also grown as a monolayer following thawing. Viability, time to confluence, population doubling time and phenotype maintenance were compared for both the groups. Viability was 65.75 % after 3 months of cryopreservation at -196 °C, as compared to 94.19 % for fresh chondrocytes (p = 0.001). Fresh and cryopreserved cells reached confluence on 10th and 15th day of culture respectively. Population doubling time was significantly more in fresh than cryopreserved chondrocytes on 10th and 15th day (p = 0.0006) in culture. Both fresh and cryopreserved cells maintain their chondrocyte phenotype as assessed by immunocytochemistry. Relative gene expression by real time polymerase chain reaction showed similar upregulation of mRNA of Collagen 2, SOX 9, Aggrecan and Collagen 1 in cryopreserved chondrocyte as compared to fresh chondrocyte. Iliac apophyseal chondrocytes cryopreserved for 3 months maintained the phenotype successfully 2 weeks after thawing in culture. The viability and proliferation rates after thawing were adequate for a clinical translation of these cells.

INTL PMID: 23934174 [PubMed - in process] BS

Involvement of oxidative stress, Nuclear Factor kappa B and the Ubiquitin proteasomal pathway in dysferlinopathy.
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AIMS: Dysferlinopathies are autosomal recessive neuromuscular disorders arising from mutations of the protein dysferlin that preferentially affect the limbs which waste and weaken. The pathomechanisms of the diseases are not known and effective treatment is not available. Although free radicals and upstream signaling by the redox sensitive transcription factor, NF-κB, in activation of the ubiquitin pathway are shown to occur in several muscle wasting disorders, their involvement in dysferlinopathy is not known. This study analyzed the role of oxidative stress, NF-κB and the ubiquitin pathway in dysferlinopathic muscle and in dysferlin knockdown human myoblasts and myotubes.

MAIN METHODS: Fourteen dysferlinopathic muscle biopsies and 8 healthy control muscle biopsies were analyzed for oxidative stress, NF-κB activation and protein ubiquitinylation and human primary myoblasts and myotubes knocked down for dysferlin were studied for their state of oxidative stress.

KEY FINDINGS: Dysferlinopathic muscle biopsies showed NF-κB p65 signaling induced protein
ubiquitinylation in response to oxidative stress. Dysferlin knock down primary muscle cell cultures confirmed that oxidative stress is induced in the absence of dysferlin in muscle.

SIGNIFICANCE: Anti-oxidants that also inhibit nitrosative stress and NF-κB activation, might prove to be of therapeutic benefit in slowing the progression of muscle wasting that occurs with dysferlinopathy.

Ramachandran J(1), Sajith KG.
All that glitters is not gold: Elevated liver enzymes do not mean liver disease always.
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Ramamoorthy H(1), Abraham P, Isaac B.
Mitochondrial dysfunction and electron transport chain complex defect in a rat model of tenofovir disoproxil fumarate nephrotoxicity.
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The long-term use of tenofovir, a commonly used anti-HIV drug, can result in renal damage. The mechanism of tenofovir disoproxil fumarate (TDF) nephrotoxicity is not clear, although it has been shown to target proximal tubular mitochondria. In the present study, the effects of chronic TDF treatment on the proximal tubular function, renal mitochondrial function, and the activities of the electron transport chain (ETC) complexes were studied in rats. Damage to proximal tubular mitochondria and proximal tubular dysfunction was observed. The impaired mitochondrial function such as the respiratory control ratio, 2-(4,5-dimethyl-2-thiazolyl)-3,5-diphenyl-2H-tetrazolium bromide (MTT) reduction, and mitochondrial swelling was observed. The activities of the electron chain complexes I, II, IV, and V were decreased by 46%, 20%, 26%, and 21%, respectively, in the TDF-treated rat kidneys. It is suggested that TDF induced proximal tubular mitochondrial dysfunction and ETC defects may impair ATP production, resulting in proximal tubular damage and dysfunction.
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Sabapathy V(1), Sundaram B(1), V M S(2), Mankuzhy P(1), Kumar S(1).
Human Wharton’s Jelly Mesenchymal Stem Cells plasticity augments scar-free skin wound healing with hair growth.
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Human mesenchymal stem cells (MSCs) are a promising candidate for cell-based transplantation and regenerative medicine therapies. Thus in the present study Wharton’s Jelly Mesenchymal Stem Cells (WJ-MSCs) have been derived from extra embryonic umbilical cord matrix following removal of both arteries and vein. Also, to overcome the clinical limitations posed by fetal bovine serum (FBS) supplementation because of xenogeneic origin of FBS, usual FBS cell culture supplement has been replaced with human platelet lysate (HPL). Apart from general characteristic features of bone marrow-derived MSCs, wharton jelly-derived MSCs have the ability to maintain phenotypic attributes, cell growth kinetics, cell cycle pattern, in vitro multilineage differentiation plasticity, apoptotic pattern, normal karyotype-like intrinsic mesenchymal stem cell properties in long-term in vitro cultures. Moreover, the WJ-MSCs exhibited the in vitro multilineage differentiation capacity by giving rise to differentiated cells of not only mesodermal lineage but also to the cells of ectodermal and endodermal lineage. Also, WJ-MSC did not present any aberrant cell state upon in vivo transplantation in SCID mice and in vitro soft agar assays. The immunomodulatory potential assessed by gene expression levels of immunomodulatory factors
upon exposure to inflammatory cytokines in the fetal WJ-MSCs was relatively higher compared to adult bone marrow-derived MSCs. WJ-MSCs seeded on decellularized amniotic membrane scaffold transplantation on the skin injury of SCID mice model demonstrates that combination of WJ-MSCs and decellularized amniotic membrane scaffold exhibited significantly better wound-healing capabilities, having reduced scar formation with hair growth and improved biomechanical properties of regenerated skin compared to WJ-MSCs alone. Further, our experimental data indicate that indocyanin green (ICG) at optimal concentration can be resourcefully used for labeling of stem cells and in vivo tracking by near infrared fluorescence non-invasive live cell imaging of labelled transplanted cells, thus proving its utility for therapeutic applications.

**Results:** The two major viral infections observed were EBV and CMV. The univariate analysis of CMV load showed significant association with cryptococcal meningitis, oral hairy leukoplakia (OHL), CMV retinitis, CD4 counts and WHO staging (P < 0.05) while the multivariate analysis showed an association with OHL (P = 0.02) and WHO staging (P = 0.05). Univariate analysis showed an association of EBV load with CD4 counts and WHO staging (P < 0.05) and multivariate analysis had association only with CD4 counts. The CMV load was significantly associated with elevated SGPT and SGOT level (P < 0.05) while the EBV had only with SGOT.

**Conclusion:** This study showed an association of EBV and CMV load with CD4+ T cell counts, WHO staging and elevated liver enzymes. These viral infections can accelerate HIV disease and multiplex real-time PCR can be used for the early detection. Genotype 1 and 2 of EBV and genotype gB1 and gB2 of CMV were the prevalent in the HIV-1 subtype C-infected south Indians.
pathways, namely PKR-like ER kinase, activating transcription factor 6, and inositol-requiring protein-1. Once activated, UPR triggers the production of ER molecular chaperones and stress response proteins to help reduce the protein load within the ER. This occurs by degradation of the misfolded proteins and ensues in the arrest of protein translation machinery. If the burden of protein load in ER is beyond its processing capacity, UPR can activate pro-apoptotic pathways or autophagy leading to cell death. Viruses are naturally evolved in hijacking the host cellular translation machinery to generate a large amount of proteins. This phenomenon disrupts ER homeostasis and leads to ER stress. Alternatively, in the case of gutted vectors used in gene therapy, the excess load of recombinant vectors administered and encountered by the cell can trigger UPR. Thus, in the context of gene therapy, UPR becomes a major roadblock that can potentially trigger inflammatory responses against the vectors and reduce the efficiency of gene transfer.

INTL

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OBJECTIVE: The objective of the following study is to determine 1p, 19q status in a cohort of glial neoplasms.

Materials and methods: Fluorescence in situ hybridization for determination of 1p, 19q deletions in 100 glial neoplasms diagnosed between January 2007 and March 2011, was performed using Vysis dual color probes localizing to 1p36/1q25; 19q13/19p13.

RESULTS: Out of the 100 tumors, 78 tumors were either pure oligodendrogial (OD) neoplasms or had an OD component. 1p and 19q codeletions were seen in 72.7% of oligodendrogliomas (World Health Organization [WHO] Grade II), 90.9% of anaplastic oligodendrogliomas (WHO Grade III), 22.2% of mixed oligoastrocytomas (WHO Grade II) and 42.9% of the anaplastic oligoastrocytomas (WHO Grade III). Of the 29 tumors that were diagnosed as glioblastoma multiforme (GBM), 11 had an OD component of which four showed codeletions of 1p and 19q (36.4%) and two tumors showed epidermal growth factor receptor (EGFR) amplification (20%) without 1p19q codeletions. Amongst the remaining 18 GBMs without an OD component, three cases showed EGFR amplification (16.7%), one case showed isolated deletion of 1p and none showed 1p19q codeletions. Polysomies involving 1p and/or 19q with or without deletions were seen in 76.9% of mixed oligoastrocytic tumors, 7.7% of pure OD tumors and one glioblastoma.

CONCLUSIONS: 1p19q codeletion is an early molecular change in the genesis of OD tumors, which is retained at the time of progression. Mixed tumors more frequently show polysomies of 1p and 19q. The presence of codeletion in a third of the GBMs with an OD component with its absence in GBMs without an OD component, justifies categorization of these tumors as a separate entity.

NAT

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Klebsiella pneumoniae strains producing extended-spectrum β-lactamases (ESBL) exhibit resistance to antibiotic classes. The production of ESBLs (TEM-1, TEM-2, SHV-1, OXA-1) results in resistance to ampicillin, ticarcillin, piperacillin and cephalosporins. High levels of β-lactamases leads to development of resistance to β-lactamase inhibitors. The present study deals with characterizing antimicrobial resistance pattern among septicemia causing K. pneumoniae and the prevalence of inhibitor resistant OXA-1 β-lactamase genes among them. Of 151 study isolates, 59 were resistant to piperacillin/tazobactam and these isolates were further selected for blaOXA-1 screening. Amplification of β-lactamases genes by conventional PCR showed the presence of blaOXA-1 genes among 12 K. pneumoniae (20.3%) isolates. OXA-1 β-lactamase producing strains were found to be resistant to piperacillin/tazobactam (100%), levofloxacin (91.6%), amikacin (75%), cefoxitin (50%), ertapenem (25%), imipenem (16.6%) and meropenem (16.6%); all were susceptible to tigecycline. 3D models of OXA-1 β-lactamase were generated and docking was performed with various β-lactam antibiotics. Molecular docking (MD) revealed the molecular basis of drug sensitivity. MD simulation results clearly confirmed the notable loss in stability for tigecycline-blaOXA-1 complex. Findings of the present study will provide useful insights for understanding the mechanism of resistance and help with strategies for the development of new antibiotics. The conventional PCR assay designed in this study can be routinely used in clinical microbiology laboratories to determine the blaOXA-1 genes.

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Expression of iron-related proteins in the duodenum is up-regulated in patients with chronic inflammatory disorders.


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Mechanisms responsible for derangements in Fe homeostasis in chronic inflammatory conditions are not entirely clear. The aim of the present study was to test the hypothesis that inflammation affects the expression of Fe-related proteins in the duodenum and monocytes of patients with chronic inflammatory disorders, thus contributing to dysregulated Fe homeostasis. Duodenal mucosal samples and peripheral blood monocytes obtained from patients with chronic inflammatory disorders, namely ulcerative colitis (UC), Crohn’s disease (CD) and rheumatoid arthritis, were used for gene and protein expression studies. Hb levels were significantly lower and serum C-reactive protein levels were significantly higher in patients in the disease groups. The gene expression of several Fe-related proteins in the duodenum was significantly up-regulated in patients with UC and CD. In patients with UC, the protein expression of divalent metal transporter 1 and ferroportin, which are involved in the absorption of dietary non-haem Fe, was also found to be significantly higher in the duodenal mucosa. The gene expression of the duodenal proteins of interest correlated positively with one another and negatively with Hb. In patients with UC, the gene expression of Fe-related proteins in monocytes was found to be unaffected. In a separate group of patients with UC, serum hepcidin levels were found to be significantly lower than those in the control group. In conclusion, the expression of Fe-related proteins was up-regulated in the duodenum of patients with chronic
inflammatory conditions in the present study. The effects appeared to be secondary to anaemia and the consequent erythropoietic drive.

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Thakur A(1), Muniswami D(2), Tharion G(2), Kanakasabapathy I(3).
Immunohistological and electrophysiological characterization of Globose basal stem cells.

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OBJECTIVES: In the past few decades, variety of foetal, embryonic and adult stem and progenitor cells have been tried with conflicting outcome for cell therapy of central nervous system injury and diseases. Cellular characteristics and functional plasticity of Globose basal stem cells (GBCs) residing in the olfactory epithelium of rat olfactory mucosa have not been studied in the past by the neuroscientists due to unavailability of specific markers for GBCs. In the present research, we standardized some techniques to isolate GBCs from rat olfactory epithelium in pure form using a highly selective GBC-III antibody passaged through fluorescence activated cell sorter (FACS). We also characterized these cells immunohistologically using various pluripotent stem cell markers. This work also throws some light on ionic channels present on these stem cells which are responsible for their neuron induction potential.

MATERIALS AND METHODS: Globose basal stem cells were isolated from rat olfactory epithelium using GBC-III antibody and were characterized as multipotent stem cells using various neural progenitor markers. Ionic channels on GBCs were studied with voltage clamping.

RESULTS: GBCs could be isolated in pure (99% purity) form and were found to be stained positive for all neural progenitor cell markers. Voltage gated Na(+) channels were completely absent, which proves the unexcitable nature of GBCs. Leaky K(+) channels were found to be present on the GBC which was of no significance.

CONCLUSION: This research work can be helpful in understanding the nature of these stem cells and utilising them in future as potent candidates for neuro-regenerative therapies.

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[PubMed] BS

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OBJECTIVE: To investigate the magnitude of association of FTO variants with obesity, type 2 diabetes (T2DM), and related traits among Asian Indians.

METHODS: Random-effect meta-analysis was performed on pooled data from eight studies (n = 28,394) for obesity and related traits and six studies (n = 24,987) for assessment of T2DM risk in Indians where FTO variants were reported.

RESULTS: The minor A-allele of the FTO variant rs9939609 was associated with increased risk of obesity (OR 1.15, 95% CI 1.08-1.21, p = 2.14 × 10(-5) ), BMI (β = 0.30 kg/m2, 95% CI 0.21-0.38, p = 4.78×10(-11) ) and other regional adiposity measurements [waist (β = 0.74 cm, 95% CI 0.49-0.99), HC (β = 0.52, 95% CI 0.26-0.78), and waist-hip ratio (WHR) (β = 0.002, 95% CI 0.001-0.004)] in Indians (p ≤ 0.001). An increased risk for T2DM (OR 1.11; 95% CI 1.04-1.19, p = 0.002) was observed, which attenuated when adjusted for age, gender, and BMI (OR 1.09; 95%CI 1.02-1.16, p = 0.01).

CONCLUSIONS: Our study provides evidence of association between common FTO variant and obesity risk among Indians with comparable effect sizes as in Caucasians. The attenuation of FTO-T2DM risk on BMI adjustment reinforces that BMI does not fully account
for the adiposity effects among Asian Indians who are more centrally obese.

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Zwerling A(1), Pai M(2), Michael JS(3), Christopher DJ(4).
Serial testing using interferon-ã release assays in nursing students in India.

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Triphasic ceramic scaffold in paediatric and adolescent bone defects.

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We evaluated novel triphasic hydroxyapatite tricalcium phosphate calcium silicate scaffold (HASi) in the management of paediatric bone defects. Their main advantage is considered to be adequate strength and stimulation of bone formation without resorting to autograft. A total of 42 children younger than 16 years of age were recruited over a period of 1 year and were treated with this synthetic bone substitute as a stand-alone graft for pelvic, femur, calcaneal and ulnar osteotomies, cystic bone lesions, subtalar arthrodesis and segmental bone defects. Forty children, 22 boys and 18 girls, mean age 8.3 years and a mean follow-up of 18.51 months, were available for evaluation. Analysis showed that younger age, cancellous defects and no internal fixation were associated with significantly faster healing. Partial incorporation was observed in 22.5% and complete incorporation in 77.5% of cases at 18 months of follow-up. Sex, type of defect, BMI and the shape of the ceramic graft did not significantly affect the rate of healing. Complications attributable to HASi included four nonunions, three of which were diaphyseal. HASi was found to be safe in children with cancellous or benign cavitory defects. It is not suitable for diaphyseal and segmental bone defects as a stand-alone graft.

Bhandari N(1), Rongsen-Chandola T(1), Bavdekar A(2), John J(3), Antony K(4), Taneja S(1), Goyal N(1), Kawade A(2), Kang G(3), Rathore SS(1), Juvekar S(2), Muliyl J(3), Arya A(1), Shaikh H(2), Abraham V(3), Vrati S(5), Proschan M(6), Kohberger R(7), Thiry G(8), Glass R(6), Greenberg HB(9), Curlin G(6), Mohan K(10), Harshavardhan GV(10), Prasad S(10), Rao TS(11), Boslego J(12), Bhan MK(13); India Rotavirus Vaccine Group.
Efficacy of a monovalent human-bovine (116E) rotavirus vaccine in Indian infants:a randomised, double-blind, placebo-controlled trial.

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BACKGROUND: Rotavirus is the most common cause of severe dehydrating gastroenteritis in developing countries. Safe, effective, and affordable rotavirus vaccines are needed in these countries. We aimed to assess the efficacy and tolerability of a monovalent human-bovine rotavirus vaccine for severe rotavirus gastroenteritis in low-resource urban and rural settings in India.

METHODS: We did a randomised double-blind, placebo-controlled, multicentre trial at three sites in Delhi (urban), Pune (rural), and Vellore (urban and rural) between March 11, 2011, and Nov 5, 2012. Infants aged 6-7 weeks were randomly assigned (2:1), via a central interactive voice or web response system with a block size of 12, to receive either three doses of oral human-bovine natural reassortant vaccine (116E) or placebo at ages 6-7 weeks, 10 weeks, and 14 weeks. Infants’ families, study investigators, paediatricians in referral hospitals, laboratory staff, and committee members were all masked to treatment allocation. The primary outcome was incidence of severe rotavirus gastroenteritis (e”11 on the Vesikari scale). Efficacy outcomes and adverse events were ascertained through active surveillance. Analysis was by intention to treat and per protocol. The trial is registered with Clinical Trial Registry-India (CTRI/2010/091/000102) and ClinicalTrials.gov (NCT01305109).

FINDINGS: 4532 infants were assigned to receive the 116E vaccine and 2267 to receive placebo, of whom 4354 (96%) and 2187 (96%) infants, respectively, were included in the primary per-protocol efficacy analysis. 71 events of severe rotavirus gastroenteritis were reported in 4752 person-years in infants in the vaccine group compared with 76 events in 2360 person-years in those in the placebo group; vaccine efficacy against severe rotavirus gastroenteritis was 53·6% (95% CI 35·0-66·9; p=0·0013) and 56·4% (36·6-70·1; p<0·0001) in the first year of life. The number of infants needed to be immunised to prevent one severe rotavirus gastroenteritis episode was 55 (95% CI 37-97). The incidence of severe rotavirus gastroenteritis per 100 person-years was 1·5 in the vaccine group and 3·2 in the placebo group, with an incidence rate ratio of 0·46 (95% CI 0·33-0·65). Prevalence of immediate, solicited, and serious adverse events was similar in both groups. One case of urticaria in the vaccine group and one each of acute gastroenteritis and suspected sepsis in the placebo group were regarded as related to the study product. We recorded six cases of intussusception in the vaccine group and two in the placebo group, all of which happened after the third dose. 25 (<1%) infants in the vaccine group and 17 (<1%) in the placebo group died; no death was regarded as related to the study product.

INTERPRETATION: Monovalent human-bovine (116E) rotavirus vaccine is effective and well tolerated in Indian infants.

FUNDING: Department of Biotechnology and the Biotechnology Industry Research Assistance Council, Government of India; Bill & Melinda Gates Foundation to PATH, USA; Research Council of Norway; UK Department for International Development; National Institutes of Health, Bethesda, USA; and Bharat Biotech International, Hyderabad, India.

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BACKGROUND: Childhood tuberculosis (TB) is a neglected global public health problem. Short treatment courses with rifampicin-containing anti-TB drugs given daily for six-months cure over 90% of
infected children, but poor adherence reduces treatment success. Intermittent, short-course anti-TB regimens, given two or three times a week under direct observation, are associated with higher adherence in observational studies; but how they compare with daily treatment in relation to cure is unclear. Current international and national recommendations differ on use of intermittent regimens to treat TB in children.

**OBJECTIVES:** To compare the efficacy and safety of intermittent, short-course anti-TB regimens (twice- or thrice-weekly) with daily short-course anti-TB regimens in treating childhood TB.

**SEARCH METHODS:** We searched the Cochrane Infectious Disease Group Specialized Register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, LILACS, clinical trials registries, regional databases, conference proceedings, and references without language restrictions up to 30 May 2013; and contacted experts for relevant published, unpublished, and on-going trials.

**SELECTION CRITERIA:** Randomized controlled trials (RCTs) and quasi-RCTs of children aged 15 years or younger, diagnosed with TB (according to the World Health Organization diagnostic categories 1, 2, or 3), who were treated with intermittent twice-weekly or thrice-weekly, short-course anti-TB regimens compared to daily short-course anti-TB treatment regimens. All regimens had to contain rifampicin for at least the first two months.

**DATA COLLECTION AND ANALYSIS:** The review authors independently screened and selected trials, assessed risk of bias, and extracted data. We sought clarifications from trial authors. We pooled relative risks with their 95% confidence intervals and used a random-effects model where there was significant heterogeneity. We assessed overall evidence-quality using the GRADE approach.

**MAIN RESULTS:** We included four trials published between 1996 to 2000 that randomized 563 children (465 evaluable) aged five months to 15 years to intermittent twice-weekly versus daily anti-TB treatment. Two trials were from India, one from South Africa, and one from Turkey. All trials used rifampicin and isoniazid, three trials used pyrazinamide, and one trial used streptomycin. The drug combination, and the duration of intermittent and daily treatments differed between trials, and no trials used drug combinations and schedules currently recommended for childhood TB. No trial reported if any child was HIV-positive. In comparisons of twice-weekly versus daily anti-TB treatment regimens, the trials did not detect differences in the number of patients cured, but trials were small, and the comparator regimens were not standard (four trials, 465 children; very low quality evidence). Trials were underpowered to provide estimates for death (two trials, 213 participants, very low quality evidence), relapse (one trial, 214 participants, very low quality evidence), and treatment limiting adverse events (four trials, 441 participants, very low quality evidence). Reported adherence to treatment was similar (87% versus 84%; four trials, 458 children, very low quality evidence) We did not find trials comparing the commonly used thrice-weekly anti-TB short-course regimen with the daily treatment regimen. AUTHORS’

**CONCLUSIONS:** Trials conducted to date are insufficient to support or refute the use of intermittent twice- or thrice-weekly, short-course treatment regimens over daily short-course treatment in children with TB. Further randomized trials conducted in high TB-transmission settings will help inform policy and practice.

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**Slit2-Robo signaling in inflammation and kidney injury.**

**Pediatr Nephrol.** 2014 Apr 29. [Epub ahead of print]

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Acute kidney injury is an increasingly common global health problem and is associated with severe morbidity and mortality. In addition to facing high mortality rates, the survivors of acute kidney injury are at increased risk of developing chronic kidney disease and end-stage renal disease. Renal ischemia-reperfusion injury (IRI) is the most common cause of acute kidney injury, and results from impaired delivery of oxygen and nutrients to the kidney. Massive leukocyte influx into the post-ischemic kidney is one of the hallmarks of IRI. The recruited leukocytes exacerbate tissue damage and, if uncontrolled, initiate
the progressive changes that lead to renal fibrosis and chronic kidney disease. Early on, recruitment and activation of platelets promotes microthrombosis in the injured kidney, further exacerbating kidney damage. The diversity, complexity, and multiplicity of pathways involved in leukocyte recruitment and platelet activation make it extremely challenging to control these processes, and past efforts have met with limited success in human trials. A generalized strategy to inhibit infiltration of inflammatory leukocytes and platelets, thereby reducing inflammation and injury, may prove to be more beneficial. In this review, we summarize recent findings demonstrating that the neuronal guidance cues, Slit and Roundabout (Robo), prevent the migration of multiple leukocyte subsets towards diverse inflammatory chemoattractants, and have potent anti-platelet functions in vitro and in vivo. These properties uniquely position Slit2 as a novel therapeutic that could be used to prevent acute kidney injury associated with IRI.

RESULTS: Children in the IG showed an increase of 11.2 % in BMC versus the CG, who showed an 8.9 % fall (p < 0.0001). Net intervention-attributable difference in BMC was 20.1 %. BMD increased in both groups (IG 2.8 % vs CG 0.74 %), but the difference was not statistically significant (p = 0.27).

CONCLUSIONS: Short-term, high-dose glucocorticoid therapy decreases the BMC of the lumbar spine in steroid-naïve children with NS. Vitamin D and calcium co-administration not only prevents this decline, but also enhances BMC of the lumbar spine.

BACKGROUND AND AIM: Narrow band imaging with magnification enables detailed assessment of duodenal villi and may be useful in predicting the presence of villous atrophy or normal villi. We aimed to assess the morphology of duodenal villi using magnification narrow band imaging and correlate it with histology findings in patients with clinically suspected malabsorption syndrome.

METHODS: Patients with clinical suspicion of malabsorption presenting at a tertiary care center were prospectively recruited in this diagnostic intervention study. Patients underwent upper gastrointestinal endoscopy using magnification narrow band imaging. The villous morphology in the second part of the duodenum was assessed independently by two endoscopists and the presence of normal or atrophic
villi was recorded. Biopsy specimen was obtained from the same area and was examined by two pathologists together. The sensitivity and specificity of magnification narrow band imaging in detecting the presence of duodenal villous atrophy was calculated and compared to the histology.

RESULTS: One hundred patients with clinically suspected malabsorption were included in this study. Sixteen patients had histologically confirmed villous atrophy. The sensitivity and specificity of narrow band imaging in predicting villous atrophy was 87.5% and 95.2%, respectively, for one endoscopist. The corresponding figures for the second endoscopist were 81.3% and 92.9%, respectively. The interobserver agreement was very good with a kappa value of 0.87.

CONCLUSION: Magnification narrow band imaging performed very well in predicting duodenal villous morphology. This may help in carrying out targeted biopsies and avoiding unnecessary biopsies in patients with suspected malabsorption.


**MESSAGE:** Skimmed milk preparation may be used for enteral nutrition of babies with congenital chylothorax where other feeding alternatives or commercial formulas are either not successful or are not available.

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Oral bisoprolol improves surgical field during functional endoscopic sinus surgery.


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**BACKGROUND:** The success of functional endoscopic sinus surgery (FESS) depends on visual clarity of the surgical field, through the endoscope. The objective of this double-blind, randomized, controlled study was to determine if a pre-operative dose of bisoprolol (2.5 mg) would reduce the bleeding during FESS and improve the visualization of the operative field.

**MATERIALS AND METHODS:** Thirty American Society of Anesthesiologists I or II patients, scheduled for FESS were randomized to receive either a placebo (Group A) or 2.5 mg of bisoprolol (Group B) 90 min prior to the surgery. All the patients received standard anesthesia and monitoring. The aim was to maintain the mean arterial pressure (MAP) of 60-70 mmHg, by titrating dose of isoflurane and fentanyl. The concentration of isoflurane used was recorded every 15 min. At the end of the surgery, the volume of blood loss was measured and the surgeon was asked to grade the operative field as per the Fromme-Boezaart Scale.

**RESULT:** The blood loss was significantly (P < 0.0001) more in the control group (398.67 ± 228.79 ml) as compared with that in the bisoprolol group (110.67 ± 45.35 ml). The surgical field was graded better in those who received bisoprolol as compared with those in the control group (P < 0.0001). The volume percent of isoflurane and the dose of fentanyl used was significantly lower in those who received bisoprolol. During the operative period, the MAPs were 70.0 ±
2.7 (Group A) and 62.6 ± 3.6 mmHg (Group B) and the heart rate was 99.8 ± 5.0/min (Group A) and 69.2 ± 4.4/min (Group B). These differences were statistically significant (P < 0.001).

CONCLUSION: This clinical trial has demonstrated that administration of a single pre-operative dose of bisoprolol (2.5 mg) can significantly reduce the blood loss during FESS and improve the visualization of the operating field.

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Joel S(1), Joselyn A(2), Cherian VT(3), Nandhakumar A(4), Raju N(2), Kaliaperumal I(5).
Low-dose ketamine infusion for labor analgesia: A double-blind, randomized, placebo controlled clinical trial.
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BACKGROUND: Most primary and secondary level hospitals in developing countries provide inadequate labor analgesia due to various medical, technical and economic reasons. This clinical trial was an effort to study the efficacy, safety and feasibility of intravenous (IV) ketamine to provide labor analgesia.

MATERIALS AND METHODS: A total of 70 parturients were consented and randomly assigned to receive either IV ketamine or 0.9% saline. A loading dose of ketamine (0.2 mg/kg) was followed-by an infusion (0.2 mg/kg/h) until the delivery of the neonate. Similar volume of saline was infused in the placebo-group. Intramuscular meperidine was the rescue analgesic in both groups. The pain score, hemodynamic parameters of mother and fetus and the anticipated side-effects of ketamine were observed for. The newborn was assessed by the Neonatologist.

RESULTS: The pain score showed a decreasing trend in the ketamine group and after the 1(st) h more than 60% of women in the ketamine group had pain relief, which was statistically significant. There was no significant clinical change in the maternal hemodynamics and fetal heart rate. However, 17 (48.5%) of them had transient light headedness in the ketamine group. All the neonates were breast fed and the umbilical cord blood pH was between 7.1 and 7.2. The overall satisfaction was significantly high in the intervention group (P = 0.028).

CONCLUSION: A low-dose ketamine infusion (loading dose of 0.2 mg/kg delivered over 30 min, followed-by an infusion at 0.2 mg/kg/h) could provide acceptable analgesia during labor and delivery.

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John J(1), Giri S(1), Karthikeyan AS(1), Iturriza-Gomara M(2), Muliyl J(1), Abraham A(1), Grassly NC(3), Kang G(1).
Effect of a single inactivated poliovirus vaccine dose on intestinal immunity against poliovirus in children previously given oral vaccine: an open-label, randomised controlled trial.
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BACKGROUND: Intestinal immunity induced by oral poliovirus vaccine (OPV) is imperfect and wanes with time, permitting transmission of infection by immunised children. Inactivated poliovirus vaccine (IPV) does not induce an intestinal mucosal immune
response, but could boost protection in children who are mucosally primed through previous exposure to OPV. We aimed to assess the effect of IPV on intestinal immunity in children previously vaccinated with OPV.

**METHODS:** We did an open-label, randomised controlled trial in children aged 1-4 years from Chinnallapuram, Vellore, India, who were healthy, had not received IPV before, and had had their last dose of OPV at least 6 months before enrolment. Children were randomly assigned (1:1) to receive 0.5 mL IPV intramuscularly (containing 40, 8, and 32 D antigen units for serotypes 1, 2, and 3) or no vaccine. The randomisation sequence was computer generated with a blocked randomisation procedure with block sizes of ten by an independent statistician. The laboratory staff did blinded assessments. The primary outcome was the proportion of children shedding poliovirus 7 days after a challenge dose of serotype 1 and 3 bivalent OPV (bOPV). A second dose of bOPV was given to children in the no vaccine group to assess intestinal immunity resulting from the first dose. A per-protocol analysis was planned for all children who provided a stool sample at 7 days after bOPV challenge. This trial is registered with Clinical Trials Registry of India, number CTRI/2012/09/003005.

**FINDINGS:** Between Aug 19, 2013, and Sept 13, 2013, 450 children were enrolled and randomly assigned into study groups. 225 children received IPV and 225 no vaccine. 222 children in the no vaccine group and 224 children in the IPV group had stool samples available for primary analysis 7 days after bOPV challenge. In the IPV group, 27 (12%) children shed serotype 1 poliovirus and 17 (8%) shed serotype 3 poliovirus compared with 43 (19%) and 57 (26%) in the no vaccine group (risk ratio 0.62, 95% CI 0.40-0.97, p=0.0375; 0.30, 0.18-0.49, p<0.0001). No adverse events were related to the study interventions.

**INTERPRETATION:** The substantial boost in intestinal immunity conferred by a supplementary dose of IPV given to children younger than 5 years who had previously received OPV shows a potential role for this vaccine in immunization activities to accelerate eradication and prevent outbreaks of poliomyelitis.

**FUNDING:** Bill & Melinda Gates Foundation.

**BACKGROUND & OBJECTIVES:** Soil-transmitted helminths (STH) are a major public health problem in tropical and sub-tropical countries, affecting the physical growth and cognitive development in school-age children. This study was aimed to assess the prevalence and risk factors of STH infection among school children aged 6-14 yr in Vellore and Thiruvanamalai districts in south India.

**METHODS:** Children aged 6-14 yr, going to government and government aided schools (n=33, randomly selected) in Vellore and Thiruvanamalai districts were screened to estimate the prevalence of STH, and a case control study was done on a subset to assess the risk factors for the infection.

**RESULTS:** The prevalence of STH was 7.8 per cent, varying widely in schools from 0 to 20.4 per cent, in 3706 screened children. Hookworm (8.4%) rates were high in rural areas, while Ascaris (3.3%) and Trichuris (2.2%) were more prevalent among urban children. Consumption of deworming tablets (OR=0.25, P < 0.01) offered protection, while residing in a field hut (OR=6.73, P=0.02) and unhygienic practices like open air defaecation (OR=5.37, P < 0.01), keeping untrimmed nails (OR=2.53, P=0.01) or eating food fallen on the ground (OR=2.52, P=0.01) were important risk factors for STH infection.

**INTERPRETATION & CONCLUSIONS:** Our study indicated that school children with specific risk factors in the studied area were vulnerable subpopulation with elevated risk of STH infection. Identifying risk factors and dynamics of transmission in vulnerable groups can help to plan for effective prevention strategies.

Cervicovaginal atresia with hematometra: restoring menstrual and sexual function by utero-coloneovaginoplasty.


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BACKGROUND: Cervicovaginal atresia is a rare Mullerian anomaly. The management of cervicovaginal atresia has evolved from historical recommendations of hysterectomy to various reconstructive procedures more recently. The latter carries a risk of significant morbidity and unknown fertility. We present our experience in the management of this complex anomaly.

METHODS: Twenty patients with cervicovaginal atresia were operated in our hospital from January 2004 through December 2013. The details of their anatomical variations and functional outcomes were analyzed.

RESULTS: Eighteen out of twenty patients had cervical agenesis. Two patients had cervical hypoplasia. All patients underwent utero-coloneovaginoplasty. Postoperatively, all patients have regular menstrual cycles. One patient is married, sexually active and has satisfactory coital function. One patient had a bowel anastomotic leak that required a diversion ileostomy. Two patients developed mild stenosis. One patient has mild neovaginal mucosal prolapse. No patient has developed pyometra.

CONCLUSION: Patients with cervicovaginal atresia need to be counselled about the various reconstructive options available and the potential risks. Social and economic factor play a significant role in determining the plan of management. For patients from conservative societies, utero-coloneovaginoplasty provides a safe conduit for the passage of menstrual flow and coitus, at the cost of permanent infertility.

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CV serotype, ≥88.6% and ≥96.3% of the catch-up immunogenicity according-to-protocol cohort had antibody concentrations ≥0.2 µg/mL; ≥71.4% and ≥90.6% had OPA titers ≥8. At least 1 serious adverse event was reported by 2 children in the early booster (skin infection, gastroenteritis) and 1 child in the catch-up group (febrile convulsion, urinary tract infection); all were resolved, none were considered vaccine-related by investigators. PHiD-CV induced robust immune responses regardless of age at booster. Booster vaccination following 2 catch-up doses induced robust immune responses indicative of effective priming and immunological memory.

RESULTS: Demographic data, duration of surgery, total dose of fentanyl and propofol requirement, blood loss, and the recovery time were comparable between the 2 groups. Both drugs reduced the isoflurane requirement during surgery. However, the reduction was more and statistically significant with dexmedetomidine compared with clonidine group at 1 and 2 hours after proning (P=0.001, 0.039 at 1 and 2 h). Both drugs are equally effective in controlling the hemodynamics, and the number of episodes of hypotension, hypertension, and bradycardia were comparable between the 2 groups.

CONCLUSIONS: Both clonidine and dexmedetomidine have anesthetic-sparing effect; however, it was more with dexmedetomidine than with clonidine. Recovery from isoflurane anesthesia was similar between both groups. Both are equally effective in controlling the hemodynamic response and reducing the blood loss during spine surgery.
Nithyananth M(1), Priscilla AJ(2), Boopalan PV(1), Titus VT(1), Lee VN(1).

Time required for effective action of phenol against giant cell tumour cells.


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Comment in

PURPOSE: To evaluate the time required for effective action of phenol against the giant cell tumour (GCT) cells.

METHODS: Fresh GCT cells were harvested from 9 patients with primary GCT of the distal femur (n=4), proximal tibia (n=4), and proximal humerus (n=1), with the Campanacci tumour grades 3 (n=6), 2 (n=2), and 1 (n=1). Specimens were immersed in 80% phenol for one, 3, 6, and 10 minutes, and were assessed by a single pathologist for irreversible cell death and the depth of phenol penetration.

RESULTS: Phenol caused consistent GCT cell death in 6 of the 9 specimens after 3 minutes and in all 9 specimens after 6 minutes, compared to none in controls (p<0.0001). The mean depths of phenol penetration were 15 (range, 11-20) and 19 (range, 15-25) cell thickness after 6 and 10 minutes, respectively (p<0.0001).

CONCLUSION: GCT cells immersed in 80% phenol for 6 minutes resulted in consistent cell death.

Ojha R, George J, Chandy BR, Tharion G, Devasahayam SR.


Objectives To demonstrate reduction in detrusor overactivity using surface electrical stimulation of posterior tibial nerve (PTN) or dorsal penile nerve (DPN) in patients with spinal cord injury (SCI). Design Patients with SCI with symptoms of urinary urgency/leaks, with cystometrogram (CMG) proven detrusor overactivity were recruited in this study. Ten persons with observable F-wave from tibial nerve were included in the PTN group. Five persons who had F-wave absent but preserved bulbocavernous reflex were included in the DPN group. Stimulation was given at 20 Hz, 10-40 mA for 20 minutes/session/day for 14 consecutive days. Detrusor overactivity was recorded using CMG on days 1 and 15. Settings Rehabilitation Institute, Department of Physical Medicine and Rehabilitation, Christian Medical College and Hospital, Vellore, TN, India. Participants Patients with SCI. Interventions Surface stimulation of peripheral nerves for reduction of detrusor overactivity. Outcome measures Qualitative analysis using voiding diary data and quantitative analysis using CMG data comparing pre- and post-intervention. Results P value obtained from voiding chart was 0.021 for PTN and 0.062 for DPN. P value obtained from CMG data was not significant in both groups. In one subject, treatment was extended to 4 weeks and further improvement in voiding diary was seen. Conclusions In this pilot study of 15 patients, voiding chart data showed statistically significant improvement following PTN stimulation and trend of improvement following DPN stimulation. However, the CMG data were not statistically significant in this sample population. Further studies with larger, appropriately powered sample size would be helpful to demonstrate the associations of symptoms with CMG data. Trial registration CTRI no.; CTRI/2012/12/003234; CMCH Approval no.: CMC/IRB/6735/2008/12/18.

Ojha R, George J, Chandy BR, Tharion G, Devasahayam SR.


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Paul A(1), Babji S(1), Sowmyanarayanan TV(1), Dhingra MS(2), Ramani S(1), Kattula D(1), Kang G(3).

Human and bovine rotavirus strain antigens for evaluation of immunogenicity in a randomized, double-blind, placebo-controlled trial of a single dose live attenuated tetravalent, bovine-human-reassortant, oral rotavirus vaccine in Indian adults.


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A single dose of live attenuated tetravalent (G1-G4) bovine human reassortant rotavirus vaccine (BRV-TV) was administered to healthy Indian adult volunteers, who were assessed for safety and immunogenicity of the vaccine with 3:1 randomization to vaccine or placebo. All 20 adult male volunteers in the study had rotavirus specific serum IgA at baseline. There were no side effects or adverse events reported. Administration of BRV-TV was not associated with fever, diarrhea, or altered liver transaminases. Rotavirus IgA seroconversion post single dose administration was 27%. This study shows that BRV-TV is non-reactogenic, safe and immunogenic in adults. The IgA units estimated for the same sample using human G1P[8] rotavirus strain as the antigen were consistently higher than with the bovine G6P[5] WC3 strain and the human G2P[4] DS-1 strain antigen. The use of different human and bovine rotavirus strains as antigens in a quantitative rotavirus specific serum IgA assay resulted in different estimations of IgA antibody in the same sample.

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Suction assisted pulse lavage: randomised controlled studies comparing its efficacy with conventional dressings in healing of chronic wounds.

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Chronic, open, non-healing wounds pose a continual challenge in medicine as the treatment is variable and there are no documented consistent responses. Although wound aetiologies vary and there are a number of factors that affect chronic wound pathogenesis, wound ischaemia and bacterial colonisation of wounds are the chief concerns among them. Conventionally, pulse lavage has been used primarily as a wound debriding device. To address both the critical factors of wound ischaemia and bacterial burden, a couple of technical points were proposed and applied in this study. The objective of our study was to evaluate pulse lavage therapy’s ability to improve the healing rate of chronic wounds compared to that of the traditional saline-wet-to-moist dressings. The study period was from 1 August 2010 to 31 January 2012 and was conducted in our institution. Thirty patients with 31 chronic, non-healing wounds were enrolled in the study after obtaining proper consent. Subjects were randomised (15 patients each) to the pulse lavage group and the control group. Patients in the test group were subjected to irrigation of their wounds with pulsed lavage at 10 to 15 psi pressure. In the control group, wound was closed by applying moist betadine saline gauze dressings after cleaning with saline. Wounds treated with pulse lavage system significantly reduced in size, had better control of bacterial contamination and had overall faster healing rates. Efficacy of pulse lavage can be increased by correct method of administration of the irrigant.

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Immune response and intestinal permeability in children with acute gastroenteritis treated with Lactobacillus rhamnosus GG: a randomized, double-blind, placebo-controlled trial.


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BACKGROUND: Probiotics have a possible role in the treatment of pediatric acute gastroenteritis. We report the effect of the probiotic Lactobacillus rhamnosus GG (LGG) on intestinal function, immune response, and clinical outcomes in Indian children with cryptosporidial or rotavirus diarrhea.

METHODS: Children with gastroenteritis aged 6 months to 5 years, testing positive for either rotavirus or Cryptosporidium species in stool (coinfections were excluded), were randomized to LGG (ATCC 53103) or placebo, once daily for 4 weeks. Baseline demographic and clinical details were obtained. Sera were tested for immunoglobulin G (IgG) and immunoglobulin A (IgA) antibodies to Cryptosporidium and rotavirus, and the lactulose to mannitol ratio for intestinal permeability was determined at baseline and at the end of follow-up.

RESULTS: Of the 124 children enrolled, 82 and 42 had rotavirus and cryptosporidial diarrhea, respectively. Median diarrheal duration was 4 days; one-third of the children had severe diarrhea. Baseline and clinical parameters were comparable between children receiving LGG and placebo. At the end of follow-up, fewer children with rotavirus diarrhea on LGG had repeated diarrheal episodes (25% vs 46%; P = .048) and impaired intestinal function (48% vs 72%; P = .027). Significant increase in IgG levels postintervention (456 vs 2215 EU; P = .003) was observed in children with rotavirus diarrhea receiving LGG. Among children with cryptosporidial diarrhea,
those receiving LGG showed significant improvement in intestinal permeability.

**CONCLUSIONS:** LGG has a positive immunomodulatory effect and may be useful in decreasing repeated episodes of rotavirus diarrhea. Improvement in intestinal function in children with rotavirus and cryptosporidial gastroenteritis emphasizes the role of probiotics in treating intestinal impairment after infection.

**CLINICAL TRIALS REGISTRATION:** CTRI/2010/091/000339.

**PMCID:** PMC3967829 [Available on 2015/4/15]  
**PMID:** 24501384 [PubMed - in process]

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**Background:** Cervical cancer is the most common gynecological cancer in Indian women. This study was initiated to assess whether the combination of paclitaxel and cisplatin with radiation was feasible in Indian women.

**Aims and Objectives:** The aim of this study was to assess the immediate tumor response and toxicity of weekly cisplatin and paclitaxel along with radiotherapy in the treatment of cervical cancer.

**Materials and Methods:** Women with primary untreated squamous cell carcinoma of the cervix with FIGO stages IB2 to IIB were treated with weekly injections of cisplatin 30 mg/m2 and paclitaxel 40 mg/m2 for 4 weeks along with radiotherapy. A total of 25 patients were enrolled in this study. Disease was assessed prior to treatment by pelvic examination and contrast enhanced computed tomography scan of the abdomen and pelvis. Response was assessed 6 weeks after completion of treatment using the same parameters. Clinical and radiological response was documented. The toxicity was assessed and was graded using the common toxicity criteria Version 3.0.

**Intention to treat analysis was used when reporting results.** Results: A total of 23 patients completed the intended treatment. There was a complete response rate of 88%, 12% were not available for response assessment. The major toxicity was Grade 3 diarrhea (48%). The mean duration of treatment was 58 days.

**Conclusions:** Combination chemotherapy with cisplatin and paclitaxel along with radiotherapy in patients with locally advanced squamous cell carcinoma of cervix had a high incidence of acute toxicity. There was no increase in immediate tumor response and progression free survival with this treatment regimen. Hence, this regimen offers no added benefit when compared to the chemo radiation with cisplatin alone.

**PMCID:** 25022387 [PubMed - in process]

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Warlick ED(1), Paulson K(2), Brazauskas R(3), Zhong X(3), Miller AM(4), Camitta BM(5), George B(6), Savani BN(7), Ustun C(8), Marks D(9), Waller EK(10), Baron F(11), Freytes CO(12), Socie G(13), Akpek G(14), Schouten HC(15), Lazarus HM(16), Horwitz EM(17), Koreth J(18), Cahn JY(19), Bornhauser M(20), Seftel M(2), Cairo MS(21), Laughlin MJ(22), Sabloff M(23), Ringdén O(24), Gale RP(25), Kamble RT(26), Vij R(27), Gergis U(28), Mathews V(7), Saber W(3), Chen YB(29), Liesveld JL(30), Cutler CS(18), Ghobadi A(31), Uy GL(25), Eapen M(3), Weisdorf DJ(8), Litzow MR(32).

**Effect of postremission therapy before reduced-intensity conditioning allogeneic transplantation for acute myeloid leukemia in first complete remission.**


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The impact of pretransplant (hematopoietic cell transplantation [HCT]) cytarabine consolidation therapy on post-HCT outcomes has yet to be evaluated after reduced-intensity or nonmyeloablative conditioning. We analyzed 604 adults with acute myeloid leukemia in first complete remission (CR1) reported to the Center for International Blood and Marrow Transplant Research who received a reduced-intensity or nonmyeloablative conditioning HCT from an HLA-identical sibling, HLA-matched unrelated donor, or umbilical cord blood donor from 2000 to 2010. We compared transplant outcomes based on exposure to cytarabine postremission consolidation. Three-year survival rates were 36% (95% confidence interval [CI], 29% to 43%) in the no consolidation arm and 42% (95% CI, 37% to 47%) in the cytarabine consolidation arm (P = .16). Disease-free survival was 34% (95% CI, 27% to 41%) and 41% (95% CI, 35% to 46%; P = .15), respectively. Three-year cumulative incidences of relapse were 37% (95% CI, 30% to 44%) and 38% (95% CI, 33% to 43%), respectively (P = .80). Multivariate regression confirmed no effect of consolidation on relapse, disease-free survival, and survival. Before reduced-intensity or nonmyeloablative
conditioning HCT, these data suggest pre-HCT consolidation cytarabine does not significantly alter outcomes and support prompt transition to transplant as soon as morphologic CR1 is attained. If HCT is delayed while identifying a donor, our data suggest that consolidation does not increase transplant treatment-related mortality and is reasonable if required.

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INTRODUCTION AND OBJECTIVE: Congenital anterior urethral diverticulum is a rare entity. This teaching video shows the scrotal pop-off mechanism for an anterior urethral diverticulum and the unique voiding pattern of a boy who empties his bladder by compression of his scrotum. The findings during urethroscopy and open reconstruction are also demonstrated.

PATIENT AND METHODS: A four-year-old boy presented to the clinic with a poor urinary stream and scrotal swelling during voiding. Physical examination during voiding revealed a dumbbell-shaped anterior urethral diverticulum with scrotal pop off and preserved renal function.

RESULTS: Open excision of the scrotal part of diverticulum was performed. Urethroplasty was conducted using a de-epithelialised diverticular wall flap from the penobulbar urethra. On follow up the boy voided with a good flow and resolution of symptoms.

CONCLUSION: Scrotal pop off with completion of voiding by manual compression of the diverticulum may preserve bladder and renal function. The preferred treatment of anterior urethral diverticulum is open excision of the diverticulum and reconstruction. The wall of the diverticulum may be used to reinforce the repair ventrally, where the corpus spongiosum is deficient.

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INTRODUCTION AND OBJECTIVE: Scrub typhus is endemic in large parts of India and can cause multi-organ failure and death. Acute pancreatitis as a complication is very rare and is potentially fatal. This case series describes seven adult patients who presented with an acute febrile illness and were diagnosed to have scrub typhus with acute pancreatitis. The mean age of the seven patients with acute pancreatitis was 49.4 years, and mean duration of fever prior to presentation was 7.7 days. All seven patients had abdominal pain, and three had a pathognomonic eschar. The mean serum lipase level was 1,509 U/L (normal value: <190 U/L) and the mean serum amylase level was 434 U/L (normal value: <200 U/L). Six patients had evidence of multi-organ dysfunction. Hematological and respiratory system...
dysfunction was seen in five patients, hepatic and renal dysfunction in four, and central nervous system dysfunction in three patients. Three patients who had 4 organs involved, died (mortality rate: 42.8%). Our case series shows that pancreatitis in scrub typhus is an extremely rare complication and when present, is associated with increased mortality (42.8%). Physicians may be familiar with the various complications of scrub typhus but less so with acute pancreatitis and hence may be underdiagnosed.

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Alexander S(1), Fleming DH, Mathew BS, Varughese S, Jeyaseelan V, Tamilarasi V, Jacob CK, John GT.
Pharmacokinetics of concentration-controlled mycophenolate mofetil in proliferative lupus nephritis: an observational cohort study.
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BACKGROUND: Mycophenolate mofetil (MMF) has variable pharmacokinetics. This study examines the pharmacokinetic and clinical correlations in proliferative lupus nephritis.

METHODS: Thirty-four patients were started on MMF, and the area under the concentration-time curve (AUC) was measured by limited sampling strategies, and dosing was adjusted to achieve an AUC of 30-60 mg·h·L. Twenty-seven patients had at least 2 measurements, and renal response was assessed within 1 year.

RESULTS: About 61.8% of patients had mycophenolic acid (MPA) AUC <30 mg·h·L with an empiric starting dose of 30 mg/kg. About 79.4% of patients achieved renal response by 1 year, and the median time to renal response was 111 days. MMF dose per body weight had a weak correlation with the AUC and did not correlate with trough concentrations. The median dose was 1.5 g/d at entry and 2 g/d after dose modification during the induction phase. Trough concentrations had a weak correlation with AUC. Patients with serum albumin ≤35 g/L had a greater chance of having an AUC ≤30 mg·h·L. The between-patient coefficient of variability for dose-normalized AUC was 37.9% at entry and 31% within 1 year, whereas repeated measurements over time in an individual had a good intraclass correlation of 0.78. Infections occurred in 11.8% and toxicities in 5.9%. MPA exposure was not significantly associated with adverse events. Patients with an AUC ≤30 mg·h·L had greater renal response at 1 year.

CONCLUSIONS: Lupus nephritis patients induced with concentration-controlled MMF had excellent renal response and fewer adverse events with lower than usual dosing. MPA exposure had high interpatient variability, requiring measurements for personalized dosing, and fewer adverse events. Long-term cost reduction is achievable with lower doses and good renal response in the majority of patients.


Aparanji G(1), Agarwal I(2), Chaturvedi S(3).
Quiz Page JULY 2014: Bilateral Abdominal Masses in an Infant.
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Ophthalmic masquerades of the atherosclerotic carotids.
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Patients with carotid atherosclerosis can present with ophthalmic symptoms. These symptoms and signs can be due to retinal emboli, hypoperfusion of the retina...
and choroid, opening up of collateral channels, or chronic hypoperfusion of the globe (ocular ischemic syndrome). These pathological mechanisms can produce many interesting signs and a careful history can bring out important past symptoms pointing toward the carotid as the source of the patient’s presenting symptom. Such patients are at high risk for an ischemic stroke, especially in the subsequent few days following their first acute symptom. It is important for clinicians to be familiar with these ophthalmic symptoms and signs caused by carotid atherosclerosis for making an early diagnosis and to take appropriate measures to prevent a stroke. This review elaborates the clinical features, importance, and implications of various ophthalmic symptoms and signs resulting from atherosclerotic carotid artery disease.


Cytokine network in scrub typhus: high levels of interleukin-8 are associated with disease severity and mortality.


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BACKGROUND: Scrub typhus, caused by Orientia tsutsugamushi, is endemic in the Asia-Pacific region. Mortality is high if untreated, and even with treatment as high as 10-20%, further knowledge of the immune response during scrub typhus is needed. The current study was aimed at comparing plasma levels of a variety of inflammatory mediators in scrub typhus patients and controls in South India in order to map the broader cytokine profile and their relation to disease severity and clinical outcome.

METHODOLOGY/PRINCIPAL FINDINGS: We examined plasma levels of several cytokines in scrub typhus patients (n = 129) compared to healthy controls (n = 31) and infectious disease controls (n = 31), both in the acute phase and after recovery, by multiplex technology and enzyme immunoassays. Scrub typhus patients were characterized by marked changes in the cytokine network during the acute phase, differing not only from healthy controls but also from infectious disease controls. While most of the inflammatory markers were raised in scrub typhus, platelet-derived mediators such as RANTES were markedly decreased, probably reflecting enhanced platelet activation. Some of the inflammatory markers, including various chemokines (e.g., interleukin-8, monocyte chemoattractant peptide-1 and macrophage inflammatory protein-1α) and downstream markers of inflammation (e.g., C-reactive protein and pentraxin-3), were also associated with disease severity and mortality during follow-up, with a particular strong association with interleukin-8.

CONCLUSIONS/SIGNIFICANCE: Our findings suggest that scrub typhus is characterized by a certain cytokine
profile that includes dysregulated levels of a wide range of mediators, and that this enhanced inflammation could contribute to disease severity and clinical outcome.

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Comment in


OBJECTIVE: To implement a neonatal hearing screening program using automated auditory brainstem response audiometry in a tertiary care set-up and assess the prevalence of neonatal hearing loss.

DESIGN: Descriptive study.

SETTING: Tertiary care hospital in Southern India.

PARTICIPANTS: 9448 babies born in the hospital over a period of 11 months.

INTERVENTION: The neonates were subjected to a two stage sequential screening using the BERAphone. Neonates suspected of hearing loss underwent confirmatory testing using auditory steady state response audiometry. In addition, serological testing for TORCH infections, and connexin 26 gene was done.

MAIN OUTCOME MEASURES: Feasibility of the screening program, prevalence of neonatal hearing loss and risk factors found in association with neonatal hearing loss.

RESULTS: 164 babies were identified as suspected for hearing loss, but of which, only 58 visited the audiovestibular clinic. Among 45 babies who had confirmatory testing, 39 were confirmed to have hearing loss and were rehabilitated appropriately. 30 babies had one or more risk factors; 6 had evidence of TORCH infection and 1 had connexin 26 gene mutation.

CONCLUSION: Neonatal hearing screening using BERAphone is a feasible service. The estimated prevalence of confirmed hearing loss was comparable to that in literature. Overcoming the large numbers of loss to follow-up proves to be a challenge in the implementation of such a program.

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Primary epithelioid angiosarcoma of the bone is very rare. We report a rare case of epithelioid angiosarcoma of the calcaneum and the difficulties we had in diagnosing this condition. A 22-year-old woman presented with complaints of pain and swelling of the left ankle of 8 years’ duration. Examination revealed swelling and tenderness over the lateral aspect of calcaneum. Plain radiographs showed an osteolytic lesion of the calcaneum. She underwent curettage and bone grafting, with bone substitutes. Histopathologic examination showed epithelioid angiosarcoma in contrast to the needle biopsy, which had showed an aneurismatic bone cyst. The patient was counseled about the need for amputation. She refused limb ablative surgery, and the likelihood of local recurrence and systemic spread and the need for close follow-up were explained. At the end of 3 years of follow-up, she was pain free and had no evidence of recurrence. We present this case because of the rare site, histopathologic challenges in diagnosing the condition, and unique presentation of the disease.
Balaji V(1), Sharma A, Ranjan P, Kapil A. Revised ciprofloxacin breakpoints for Salmonella Typhi: its implications in India.
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The rise of multidrug resistant strains of Salmonella Typhi in the last decade of the previous century led to the use of fluoroquinolones as the drug of choice. However, over the past few years fluoroquinolone resistance has been increasingly reported. In accordance with the revised Clinical and Laboratory Standards Institute (CLSI) breakpoints, only 3% of the isolates were susceptible to ciprofloxacin in comparison to 95% as per the earlier guidelines when 488 isolates collected between 2010 and 2012 were re-interpreted. Interestingly, re-emergence of strains susceptible to chloramphenicol, ampicillin and cotrimoxazole is being seen. Amidst the changing susceptibility profile, azithromycin remains a promising alternative.

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BACKGROUND: Fibro-calcful pancreatic diabetes is an indigenous disorder present in populations largely in tropical regions. Energy expenditure through indirect calorimetry has not been studied in this disorder and may provide important clues as to the pathogenesis of diabetes in these patients.

METHODS: A total of 51 males in three groups comprising fibro-calcful pancreatic diabetes (FCPD) (group 1; n =24), type 2 diabetes (group 2; n = 15) and healthy controls (group 3; n = 12) were studied. The body composition was measured using Dual Energy X-ray Absorptiometry (DEXA) and the REE was estimated using indirect calorimetry. The predicted energy expenditure (PEE) was calculated using three different equations.

RESULTS: Patients in both groups with diabetes had a higher mean waist-hip ratio than the controls (P = 0.002). However patients with type 2 diabetes alone had a significantly higher mean body mass index (P = 0.012), percentage of fat (P = 0.016) and total fat content (P = 0.031). There was no significant difference in REE among the three groups. After adjustment of body mass index (BMI), the REE was significantly higher in patients with FCPD than in those patients with Type 2 diabetes. PEE correlated poorly with indirect calorimetry.

CONCLUSIONS: Energy expenditure in patients with diabetes varies according to the composition and distribution of body fat and is lower in patients with FCPD. Standard predictive equations were not accurate for the assessment of energy expenditure in patients with FCPD. Further research is required to recommend specific nutritional therapy for this group of patients.

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Reducing multiple births in assisted reproduction technology.
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Multiple pregnancy, a complication of assisted reproduction technology, is associated with poorer maternal and perinatal outcomes. The primary reason behind this is the strategy of replacing more than one embryo during an assisted reproduction technology cycle to maximise pregnancy rates. The solution to this problem is to reduce the number of embryos transferred during in-vitro fertilisation. The transition from triple- to double-embryo transfer, which decreased the risk of triplets without compromising pregnancy rates, was easily implemented. The adoption of a single embryo transfer policy has been slow because of concerns about impaired pregnancy rates in a fresh assisted reproduction technology cycle. Widespread availability of effective cryopreservation programmes means that elective single embryo transfer, along with subsequent frozen embryo transfers, could provide a way forward. Any such strategy will need to consider couples’ preferences and existing funding policies, both of which have a profound influence on decision making around embryo transfer.

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A rare presentation of subacute progressive ascending myelopathy secondary to cement leakage in percutaneous vertebroplasty.
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Percutaneous vertebroplasty is used to manage osteoporotic vertebral body compression fractures. Although it is relatively safe, complications after vertebroplasty ranging from minor to devastatingly major ones have been described. Cement leakage into the spinal canal is one such complication. Subacute progressive ascending myelopathy is an infrequent neurologic complication after spinal cord injury, typically presenting as ascending neurologic deficit within weeks after the initial insult. The precise cause of subacute progressive ascending myelopathy still remains an enigma, considering the rarity of this disorder. The authors present the case of a 62-yr-old woman with osteoporotic vertebral fracture who underwent percutaneous vertebroplasty and developed T6 complete paraplegia because of cement leakage. A few weeks later, the neurologic level ascended to higher cervical level (C3). To date, no case of subacute progressive ascending myelopathy secondary to cement leakage after percutaneous vertebroplasty has been reported. Literature is reviewed regarding subacute progressive ascending myelopathy, and the rehabilitation challenges in the management of this patient are discussed.
Boopalan PR(1), Sait A, Jepegnanam TS, Matthai T, Varghese VD.  
The efficacy of single-stage open intramedullary nailing of neglected femur fractures.  
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BACKGROUND: Neglected femur fractures are not rare in the developing world. Treatment options include single-stage open reduction and intramedullary nailing, or open release, skeletal traction, and then second-stage open intramedullary nailing, with bone grafting. Single-stage procedures have the potential advantage of avoiding neurovascular complications secondary to acute lengthening, but they require a second operation, with potentially increased resource use and infection risk.  
QUESTIONS/PURPOSES: We sought to determine the (1) likelihood of union, (2) complications and reoperations, and (3) functional results with single-stage open intramedullary nailing without bone grafting in patients with neglected femur fractures.  
METHODS: Between January 2003 and December 2007, 17 consecutive patients presented to our practice with neglected femoral shaft fractures. All were treated with single-stage nailing without bone grafting. There were 15 men and two women with a median age of 27 years. The average time from fracture to treatment was 13 weeks (range, 4-44 weeks). Eleven patients underwent open nailing with interlocked nails and six were treated with cloverleaf Kuntscher nails. Patients were followed for a minimum of 6 months (mean, 33 months; range, 6-72 months). The mean preoperative ROM of the knee was 28° (range, 10°-150°) and femoral length discrepancy was 3.1 cm (range, 1-5 cm).  
RESULTS: All fractures united and the mean time to union was 16 weeks (range, 7-32 weeks). There were no neurologic complications secondary to acute lengthening. The mean postoperative ROM of the knee was 130° (range, 60°-150°). All patients were able to return to preinjury work. Sixteen patients regained their original femoral length.  
CONCLUSIONS: One-stage open intramedullary nailing of neglected femoral diaphyseal fractures without bone grafting was safe and effective, and obviated the need for a two-stage approach. Although the findings need to be replicated in larger numbers of patients, we believe this technique may be useful in treating patients with this injury, and may offer advantages in resource-constrained environments.  
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Boorugu H(1), Chrispal A, Gopinath KG, Chandy S, Prakash JJ, Abraham AM, Abraham OC, Thomas K.  
Central nervous system involvement in scrub typhus.  
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Scrub typhus is an emerging infectious disease in India. Among its protean clinical manifestations, central nervous system involvement is common. In this prospective observational study, altered sensorium, headache, seizures and aseptic meningitis were found to be common central nervous system manifestations. Prompt treatment with doxycycline reduces morbidity and mortality.  
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Chacko AG(1), Turel MK, Sarkar S, Prabhu K, Daniel RT.  
Clinical and radiological outcomes in 153 patients undergoing oblique corpectomy for cervical spondylotic myelopathy.  
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OBJECTIVE: To document the clinical and radiological outcomes in a large series of patients undergoing the oblique cervical corpectomy (OCC) for spondylotic myelopathy.  
MATERIALS AND METHODS: We retrospectively analyzed our series of 153 patients undergoing OCC for cervical spondylotic myelopathy (CSM) over the
last 10 years. A mean clinical follow-up of 3 years was obtained in 125 patients (81.7%), while 117 patients (76.5%) were followed up radiologically. Neurological function was measured by the Nurick grade and the modified Japanese Orthopedic Association score (JOA). Plain radiographs and magnetic resonance images (MRI) were reviewed.

RESULTS: Ninety-two percent were men with a mean age of 51 years and a mean duration of symptoms of 18 months. Sixty-one had a single level corpectomy, 66 had a 2-level, 24 had a 3-level, and two had a 4-level OCC. There was statistically significant improvement (p < 0.05) in both the Nurick grade and the JOA score at mean follow-up of 34.6 ± 25.4 months. Permanent Horner’s syndrome was seen in nine patients (5.9%), postoperative C5 radiculopathy in five patients (3.3%), dural tear with CSF leak in one patient (0.7%), and vertebral artery injury in one patient (0.7%). Of the 117 patients who were followed up radiologically, five patients (4.3%) developed an asymptomatic kyphosis of the cervical spine while 22 patients (25.6%) with preoperative lordotic spines had a straightening of the whole spine curvature.

CONCLUSIONS: The OCC is a safe procedure with good outcomes and a low morbidity for treating cervical cord compression due to CSM. This procedure avoids graft-related complications associated with the central corpectomy, but is technically demanding.

OBJECTIVES: To describe atypical ultrasound features of parathyroid lesions and correlate them with clinical presentation and histopathology.

MATERIALS AND METHODS: Retrospective review of 264 patients with primary hyperparathyroidism who underwent ultrasound imaging prior to parathyroidectomy was performed. Patients with atypical ultrasound findings (n = 26) were identified; imaging findings were correlated with clinical presentation and histopathology.

RESULTS: Twenty-one (80%) lesions were adenomas, two (8%) were adenomas with cellular atypia, and three (11.5%) were carcinomas. Seventeen (65%) lesions showed cystic change; five (19%) of them had >50% cystic change. These lesions were adenomas with cystic degeneration. Cystic degeneration had significant positive correlation with the lesion size and PTH level, but cystic adenomas correlated negatively with lesion weight. Six (23%) lesions were isoechoic and one (4%) was hyperechoic; histology predominantly revealed haemorrhage, hyalinisation and fibrosis; one lesion showed fat deposition and another had multiple granulomas within the adenoma. Twenty (83%) lesions had heterogeneous echotexture and showed combinations of acinar dilatation, necrosis, haemorrhage and fibrosis. Heterogeneous lesions tended to be significantly larger and heavier, and they were associated with higher PTH levels. Four (15%) lesions had calcifications. Scintigraphy was concordant in 22 (96%), n = 23. One scintigraphy-negative lesion was a cystic parathyroid adenoma.

CONCLUSION: Atypical ultrasound features of parathyroid lesions pose a diagnostic challenge. Awareness of these features would help improve lesion detection.

TEACHING POINTS: 1. Cystic change is significantly related to the size, weight and measured parathyroid hormone levels. 2. Cystic change in parathyroid tumours indicated a slightly higher risk of malignancy. 3. Heterogeneous parathyroid adenomas are larger in size and heavier, and they have higher PTH levels. 4. Awareness of atypical ultrasound features will improve preoperative clinical prediction.
INTRODUCTION: Antibiotic pressure contributes to rising antibiotic resistance. Policy guidelines encourage rational prescribing behavior, but effectiveness in containing antibiotic use needs further assessment. This study therefore assessed the patterns of antibiotic use over a decade and analyzed the impact of different modes of guideline development and dissemination on inpatient antibiotic use.

METHODS: Antibiotic use was calculated monthly as defined daily doses (DDD) per 100 bed days for nine antibiotic groups and overall. This time series compared trends in antibiotic use in five adjacent time periods identified as ‘Segments,’ divided based on differing modes of guideline development and implementation: Segment 1—Baseline prior to antibiotic guidelines development; Segment 2—During preparation of guidelines and booklet dissemination; Segment 3—Dormant period with no guidelines dissemination; Segment 4—Booklet dissemination of revised guidelines; Segment 5—Booklet dissemination of revised guidelines with intranet access. Regression analysis adapted for segmented time series and adjusted for seasonality assessed changes in antibiotic use trend.

RESULTS: Overall antibiotic use increased at a monthly rate of 0.95 (SE = 0.18), 0.21 (SE = 0.08) and 0.31 (SE = 0.06) for Segments 1, 2 and 3, stabilized in Segment 4 (0.05; SE = 0.10) and declined in Segment 5 (-0.37; SE = 0.11). Segments 1, 2 and 4 exhibited seasonal fluctuations. Pairwise segmented regression adjusted for seasonality revealed a significant drop in monthly antibiotic use of 0.401 (SE = 0.089; p<0.001) for Segment 5 compared to Segment 4. Most antibiotic groups showed similar trends to overall use.

CONCLUSION: Use of overall and specific antibiotic groups showed varied patterns and seasonal fluctuations. Containment of rising overall antibiotic use was possible during periods of active guideline dissemination. Wider access through intranet facilitated significant decline in use. Stakeholders and policy makers are urged to develop guidelines, ensure active dissemination and enable accessibility through computer networks to contain antibiotic use and decrease antibiotic pressure.
Tropical fevers were defined as infections that are prevalent in, or are unique to tropical and subtropical regions. Some of these occur throughout the year and some especially in rainy and post-rainy season. Concerned about high prevalence and morbidity and mortality caused by these infections, and overlapping clinical presentations, difficulties in arriving at specific diagnoses and need for early empiric treatment, Indian Society of Critical Care Medicine (ISCCM) constituted an expert committee to develop a consensus statement and guidelines for management of these diseases in the emergency and critical care. The committee decided to focus on most common infections on the basis of available epidemiologic data from India and overall experience of the group. These included dengue hemorrhagic fever, rickettsial infections/scrub typhus, malaria (usually falciparum), typhoid, and leptospira bacterial sepsis and common viral infections like influenza. The committee recommends a ‘syndromic approach’ to diagnosis and treatment of critical tropical infections and has identified five major clinical syndromes: undifferentiated fever, fever with rash / thrombocytopenia, fever with acute respiratory distress syndrome (ARDS), fever with encephalopathy and fever with multi organ dysfunction syndrome. Evidence based algorithms are presented to guide critical care specialists to choose reliable rapid diagnostic modalities and early empiric therapy based on clinical syndromes.


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BACKGROUND: We have reported A disintegrin and metalloprotease with thrombospondin type 1 motif, member 13 (ADAMTS13) deficiency in noncirrhotic intrahepatic portal hypertension (NCIPH) patients of European origin with preserved liver function. We aimed to study ADAMTS13-von Willebrand factor (vWF) imbalance in Indian patients with NCIPH.

METHODS: Twenty-nine cases with NCIPH [22 males; 29 years (13-58); Child’s A, 23; B, 6], 22 disease controls with cryptogenic chronic liver disease [15 males; 46 years (18-74); Child’s A, 9; B, 9; C, 4] and 17 healthy controls [14 males; 32 years (27-45)] were enrolled in the study. We measured ADAMTS13 antigen and activity (by collagen binding assay (CBA) and by fluorescence resonance energy transfer [FRET] assay), and vWF antigen levels in plasma of study patients.

RESULTS: ADAMTS13 activity by CBA in NCIPH patients (32 %, 5 % to 100 %; median, range; p-value <0.001) and disease controls (36 %, 5 % to 144 %; p = 0.001) was significantly lower than in healthy controls (87 %; 60 % to 148 %). ADAMTS13 antigen and activity by FRET assay were also lower in cases and disease controls. ADAMTS13 activity (by CBA) to antigen ratio was lower in NCIPH and disease controls than in healthy controls. Of 29 NCIPH patients, 3 (all in Child’s A) had severe ADAMTS13 deficiency (<10 % ADAMTS13 activity), and 8 (Child’s A; 7; B, 1) had moderate ADAMTS13 deficiency (10 % to 25 % activity). Conversely, vWF antigen and vWF:ADAMTS13 ratio were higher in patients with NCIPH and in disease controls than in healthy controls.

CONCLUSIONS: This study validates the finding of ADAMTS13 deficiency in NCIPH despite preserved liver functions in an Indian population suggesting its involvement in pathogenesis of NCIPH.

Goel R(1), Kumar TS(1), Danda D(2), Joseph G(1), Jeyaseelan V(1), Surin AK(1), Bacon P(1).
Childhood-onset Takayasu arteritis — experience from a tertiary care center in South India.

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OBJECTIVE: To study the clinical profile and outcome of Asian Indian children with childhood-onset Takayasu arteritis (c-TA).

METHODS: Records were studied of patients with c-TA onset prior to age 16. Disease Extent Index-Takayasu (DEI.TAK), Indian Takayasu Arteritis Score 2010, and Takayasu Arteritis Damage Score (TADS) were calculated retrospectively from electronic records. Cumulative incidence of sustained remission was estimated using the Kaplan-Meier curve.

RESULTS: There were 40 patients with c-TA, with median age of onset of 12.5 years (range 1-16) and median diagnostic delay of 11.3 months (range 1-60). The most common presenting features were hypertension, headache, malaise, and fever. Pulseless disease was observed in 25 cases (62.5%). The majority (n = 28) had active disease with raised inflammatory markers, high baseline median DEI.TAK score of 10 (range 3-24), and high median TADS of 7 (range 1-14). Of the 34 patients followed for 21.5 months (range 3-192), remission was attained in 30. However, cumulative sustained remission was achieved in only 29% of them at 5 years. Median period of sustained remission was 22.5 months (95% CI 17.1-26.8). New areas of vessel involvement were observed in 13 patients (38%). Disease progression was arrested in the majority (n = 22, 66%) through aggressive medical management and endovascular intervention. All 11 patients with an increment in TADS of ≥ 4 during followup had persistently active or relapsing disease. There was a single fatality.

CONCLUSION: Despite aggressive immunosuppression, damage progressed in one-third of patients with c-TA in association with persistent inflammation, warranting surveillance with clinical instruments and followup imaging.

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Gopinath KG(1), Chrispal A, Boorugu H, Chandy S, Prakash JJ, Abraham AM, Abraham OC, Thomas K.
Clinico-epidemiological profile of seven adults with spotted fever from a tertiary care hospital in South India.

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Spotted fever (SF), a tick-borne rickettsial infection, is being increasingly reported from mainly northern Indian states. A lack of awareness and confirmatory laboratory tests underestimate the incidence of this infection which, in India, is predominantly seen during the rainy season. Many patients diagnosed with viral exanthematous illnesses may be suffering from SF, which is treatable if detected early. There is very little data on SF in adults in southern India. We present seven patients with SF treated between January 2007 and January 2008 in a tertiary care hospital in South India. We present seven patients with SF treated between January 2007 and January 2008 in a tertiary care hospital in South India. All presented during the rainy season, with rash (100%) and generalized oedema (71%) being the most
common features. There was one death due to type I respiratory failure. Renal failure, shock, aseptic meningitis and hepatitis were other significant abnormalities detected in these patients. Clinicians need to be aware of SF and suspect it in appropriate patients.

METHODS: A case-cohort study (N = 411) was nested within a randomized cART trial of 1571 cART-naive adults in 8 resource-limited settings and the United States. The primary outcome (WHO stage 3/4 disease or death within 96 weeks of cART initiation) was met by 192 cases, and 152 and 29 cases met secondary outcomes of virologic and immunologic failure. We studied prevalence and risk factors for baseline low 25(OH)D (<32 ng/mL) and examined associated outcomes using proportional hazard models.

RESULTS: Low 25(OH)D prevalence was 49% and ranged from 27% in Brazil to 78% in Thailand. Low 25(OH)D was associated with high body mass index (BMI), winter/spring season, country-race group, and lower viral load. Baseline low 25(OH)D was associated with increased risk of human immunodeficiency virus (HIV) progression and death (adjusted hazard ratio (aHR) 2.13; 95% confidence interval [CI], 1.09-4.18) and virologic failure (aHR 2.42; 95% CI, 1.33-4.41).

CONCLUSIONS: Low 25(OH)D is common in diverse HIV-infected populations and is an independent risk factor for clinical and virologic failure. Studies examining the potential benefit of vitamin D supplementation among HIV patients initiating cART are warranted.

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Molecular epidemiology and genetic characterization of hepatitis B virus in the Indian subcontinent.
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BACKGROUND: Hepatitis B virus (HBV) is a gradually evolving virus. The aim of this study was to characterize the distribution pattern of HBV genotypes and subgenotypes and HBsAg subtypes in chronic hepatitis B subjects from the Indian subcontinent. We also sought to investigate the genetic diversity of HBV genotypes and its influence on the therapeutic response.

METHODS: A total of 295 chronic hepatitis B subjects were studied. HBV genotypes and subgenotypes were determined using the generated HBV reverse transcriptase (rt) sequences. HBsAg subtypes were predicted using a newly developed automated program in Microsoft Visual Basic (VB6). Genetic diversity was characterized by calculating the mean genetic distance (d), the number of synonymous substitutions per synonymous site (dS), and the number of non-synonymous substitutions per non-synonymous site (dN). The virological response was measured by HBV DNA levels.

RESULTS: In southern India, the predominant HBV subgenotype/subtype was D2/ayw3 (79.1%). In eastern India, C1/adr (28.2%) was found to be the predominant subgenotype/subtype, followed by A1/adw2 (25.4%). In the north-eastern region, C2/adr, D2/ayw3, and D5/ayw3 were predominant and were each identified in 20.8% of subjects. In treatment-naïve subjects, the d, dS, and dN of genotype D sequences were higher compared to genotypes C and A. Additionally, the d, dS, and dN of HBV rt sequence were higher in subjects who subsequently showed a virological response to nucleos(t)ide analogues as compared to non-responders, irrespective of the genotypes tested (p=0.014 to p<0.0001).

CONCLUSIONS: We have described the distribution of HBV genotypes and subgenotypes and HBsAg subtypes in three major regions of the Indian subcontinent. HBV genetic diversity may play a pivotal role in the clinical outcome of chronic hepatitis B.

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Ismail AM(1), Samuel P, Ramachandran J, Eapen CE, Kannangai R, Abraham P.
Lamivudine monotherapy in chronic hepatitis B patients from the Indian subcontinent: antiviral resistance mutations and predictive factors of treatment response.
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BACKGROUND AND OBJECTIVE: Management of chronic hepatitis B is a global public health challenge. There are several updated guidelines proposed based on treatment outcome data from the respective study populations. In this study, we aim to characterize the antiviral resistance mutations to lamivudine monotherapy in patients diagnosed with chronic hepatitis B from the Indian subcontinent.

METHODS: A total of 147 lamivudine-treated patients with a median treatment duration of 13 (interquartile range 8-24) months were studied. Virological response was measured by hepatitis B virus (HBV) DNA levels. Antiviral resistance mutations were identified by sequencing HBV reverse transcriptase domains. Factors associated with virological response and antiviral resistance mutations were analyzed.

RESULTS: Virological response was observed in 50 (35 %) patients while 84 (57 %) were non-responders. The virological response for the remaining 13 (9 %) patients was undetermined. Forty patients (27 %) developed lamivudine-resistant mutations. HBV genotypes, subgenotypes and hepatitis B surface antigen subtypes did not show significant association with virological response or lamivudine-resistant
mutations. High HBV DNA levels and increased treatment duration were strongly associated with the development of lamivudine-resistant mutations (p = 0.002 and p < 0.001). Patients who continued to be positive for hepatitis B e antigen have an increased risk for treatment failure (p = 0.010). High baseline aspartate transaminase levels were significantly associated with subsequent lamivudine response (p = 0.037).

CONCLUSION: Considering the limited potency and high resistance rates to lamivudine therapy, our study emphasizes the use of more potent drugs in the management of chronic hepatitis B in the Indian subcontinent.

Antiviral efficacy of adefovir dipivoxil in the treatment of chronic hepatitis B subjects from Indian subcontinent.
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Adefovir is one of the therapeutic options for the treatment of chronic hepatitis B. A total of 30 adefovir-experienced subjects with the median treatment duration of 12 (interquartile range (IQR) 6-18) months were studied. Virological response was measured by hepatitis B virus deoxyribonucleic acid (HBV DNA) levels. HBV reverse transcriptase (rt) domains were sequenced for the identification of resistance mutations. Among the 30 subjects, two (7%) showed virological response and 19 (63%) were non-responders. The virological response for the remaining nine (30%) subjects was not determined. On sequence analysis, two subjects were identified with rt169L and rtA181V mutation after 9 months and 18 months of adefovir treatment, respectively. Though the frequencies of adefovir resistance mutations are low, a large majority of subjects showed non-response. Therefore, adefovir in the management of HBV should be used judiciously.

Tibiocalcaneal arthrodesis has been a salvage option for conditions with extensive loss of the talar body. In conditions that preclude the use of internal fixation, external compression arthrodesis has been the preferred technique to achieve fusion about the hindfoot. Since Sir John Charnley elucidated the technique of compression arthrodesis using compression clamps, various modifications and techniques of external compression arthrodesis have been described. Various clinical and biomechanical studies have established the superiority of triangular transfixation in external compression arthrodesis. We have described a simple technique of compression arthrodesis after the principle of triangular transfixation using easily available hardware from Ilizarov instrumentation. This technique is relatively inexpensive in terms of the cost of the materials, uses a modular construct, and allows multiplanar correction of the hindfoot. It can be used intraoperatively to distract the hindfoot joints, especially in the presence of fibrosis and poor skin conditions. We believe this device can be a reasonable alternative to the conventional external fixation techniques for tibiocalcaneal arthrodesis.

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Tibiocalcaneal arthrodesis using a simple external fixator.
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Abstract
Background. Organophosphate (OP) poisoning results in significant toxicity while pyrethroid poisoning is associated with extremely low fatality. OPs can inhibit the detoxification of pyrethroid and increase the toxicity of the combination. We assessed whether mixed OP-pyrethroid poisoning impacted outcome in human poisoning. Methods. Patients were identified from a prospectively collected institutional poisoning database that incorporates demographic and outcome data of patients presenting with poisoning. Results. Of the 1177 poisoned patients admitted over 2 years, 32 presented with OP-pyrethroid (50% chlorpyrifos-5% cypermethrin mixture) poisoning (Group 1), 26 consumed 20% chlorpyrifos (Group 2), and 32 took 15% cypermethrin (Group 3). Seizures occurred in 15.6% (n = 5) with chlorpyrifos-cypermethrin poisoning, 18.8% (n = 6) with cypermethrin poisoning, and 3.9% (n = 1) with chlorpyrifos poisoning. Ventilatory requirements were 53.5% (17/32), 42.3% (11/26), and 15.7% (5/32) in Groups 1-3, respectively. Ventilator-free days (Mean ± SD) was significantly lower (p <0.006) in Group 1 (20.9 ± 9.3 days) than those in Group 2 (26.1 ± 4.4 days) or 3 (27.8 ± 0.6). The median (inter-quartile range) hospital stay was 5.5 (4-19.5), 5 (5-6), and 1 (0.65-1.5) days, respectively, in the three groups. Four patients died in Group 1 (13%). None died in the other groups. Conclusion: Although confounded by the varying quantity of chlorpyrifos and cypermethrin in the different formulations, patients with mixed poisoning appear to have shorter ventilator-free days than patients poisoned by either of the pesticides alone. Further studies are required comparing patients poisoned by formulations with similar quantities of OP and pyrethroid or with analysis of blood pesticide concentration on admission.

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The universal models employed by psychiatry de-emphasise the role of context and culture. Despite highlighting the impact of culture on psychiatric diagnosis and management in the Diagnostic and Statistical Manual of Mental Disorders-5, most of the changes suggested remain in the introduction and appendices of the manual. Nevertheless, clinical and biological heterogeneity within phenomenological categories mandates the need to individualise care. However, social and cultural context, patient beliefs about causation, impact, treatment and outcome expectations are never systematically elicited, as they were not essential to diagnosis and classification. Patient experience and narratives are trivialised and the biomedical model is considered universal and transcendental. The need to elicit patient perspectives, evaluate local reality, assess culture, educate patients about possible interventions, and negotiate a shared plan of management between patient and clinician is cardinal for success. The biopsychosocial model, which operates within a paternalistic physician-patient relationship, needs to move towards a shared approach, within a more equal patient-clinician partnership.

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Diagnostic and Statistical Manual-5 and dementia: Fine print, finer points.
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Jasper A(1), Harshe G, Keshava SN, Kulkarni G, Stephen E, Agarwal S.
Evaluation of normal abdominal aortic diameters in the Indian population using computed tomography.
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OBJECTIVES: The aim of this study was to establish normal diameters for the suprarenal and infrarenal abdominal aorta measured at T12 and L3 vertebral levels in the Indian population and to study the variation in aortic diameters with age, sex, height, weight, body mass index (BMI), and body surface area (BSA).

MATERIALS AND METHODS: One hundred and forty-two patients who underwent helical contrast-enhanced computed tomography (CT) scans of the abdomen for non-cardiovascular reasons were recruited. The mean internal diameters of the suprarenal and infrarenal abdominal aorta (maximum anteroposterior and transverse diameter) were measured at T12 and L3 vertebral levels and tabulated according to various age groups for both men and women. Pearson correlation coefficient was used to evaluate the correlation between aortic diameters, height, weight, BSA, and BMI.

RESULTS: The mean diameters of the suprarenal and infrarenal abdominal aorta measured at T12 and L3 vertebral levels, in men were 19.0 ± 2.3 and 13.8 ± 1.9 mm and in women 17.1 ± 2.3 and 12.0 ± 1.6 mm, respectively. The aortic diameter progressively increased in caliber with increasing age of the patients and was smaller in women than men. A significant positive correlation was found in men between the suprarenal and infrarenal aortic diameters and weight, BSA, and BMI. In women, this correlation was significant in the infrarenal aorta but not in the suprarenal aorta.

CONCLUSION: We obtained a set of normal values for the abdominal aorta in the Indian population. The aortic diameters correlated with age, gender, and body size of the patients as seen with previously published data in the Western population. A brief comparison of data between Indian and Western population showed that the values obtained were less than published elsewhere and hence, this should be considered while formulating intervention protocols.

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Personality disorders in geriatric inpatients in a tertiary hospital.
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OBJECTIVE: To assess the prevalence of personality disorders in general medical geriatric admissions.

METHODS: Forty of 508 general medical geriatric admissions screened at a large tertiary hospital, who were eligible as defined by a Mini-Mental State Examination score of over 23 and capable of informed consent, were assessed by direct interview and discussion with the patient’s family or close contact to determine personality traits.

RESULTS: Eight (20%) of these patients were found to satisfy DSM-IV criteria for a personality disorder. They were found to have significantly lower global assessments of functioning, impaired overall functioning and lower quality of life compared with non-personality disordered patients. None of their
personality disorders had been recognised by their treating teams.

CONCLUSIONS: This study supports the need for systematic research into the area and the need for increased clinical awareness of the issues.

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Our experience with papillary thyroid microcancer.


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BACKGROUND: Papillary thyroid microcarcinoma (PTMC) describes a focus of papillary thyroid cancer that is less than 1 cm in size. These tumors are frequently found on histopathological examination of thyroid specimens, operated upon for an indication other than suspected malignancy.

MATERIALS AND METHODS: From 2005 to 2012, 94 of 1300 thyroidectomy specimens in our institution were found to have PTMC. Of these, 77 were isolated PTMC while the others were associated with other differentiated cancers. We studied their clinicopathologic features, treatment and long-term outcome.

RESULTS: There were 18 men and 59 women (the male: female ratio was 1:3), their mean age was 44 ± 10.5 years (range: 18-72 years). Multinodular goiter was the most common indication for surgery. Malignancy was suspected in only 31.4% cases. The mean tumor size was 4.1 ± 2.3 mm. Nearly 17% cases had slightly larger tumors measuring >6 but <10 mm. Multifocal disease restricted to a single lobe was found in 19.5%. Eleven patients (14.2%) had cervical lymph node metastasis, 3 (3.9%) had extra thyroid tumor extension and 2 (2.6%) had evidence of vascular invasion. One patient (1.3%) presented with bone metastasis. Majority of the patients (79.2%) underwent total thyroidectomy with or without lymph node dissection. Sixteen patients (20.7%) who had initially undergone hemithyroidectomy went on to have completion thyroidectomy. Twenty nine patients (36.8%) also received radioactive iodine. The mean duration of follow-up was 20.2 ± 13.5 months. On follow-up one patient developed cervical lymph node recurrence and one died due to a second malignancy.

CONCLUSIONS: PTMC is often found as an incidental finding on the thyroidectomy specimen. Sometimes they present with regional lymph node metastasis and very rarely with distant metastasis. They have a good prognosis similar to papillary thyroid carcinoma.

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[PubMed] CO

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Predictors of disability: a 5-year cohort study of first-episode schizophrenia.


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BACKGROUND: There is a dearth of information about the predictors of disability in schizophrenia from low and middle-income countries. This study attempted to investigate the impact of socio-demographic and clinical variables on disability in a cohort of first episode schizophrenia.

METHOD: Patients diagnosed to have DSM IV schizophrenia (n=131) were assessed prospectively for psychopathology, functioning, insight and explanatory models of illness at baseline, 6, 12 and 60 months using standard instruments. Disability was assessed at 5 years. Multiple linear regression was employed to adjust for common confounders.
RESULTS: We could follow-up 95 (72.5%) patients. Sixty-five of these patients (68.4%) achieved remission. Disability scores at 5 years were associated negatively with episodic nature of illness at baseline, functional assessments at 6 and 12 months and return to pre-morbid level function. Disability correlated positively with psychopathology at 6 and 12 months and time spent in psychotic episodes. It was also associated with psychopathology, remission, insight and patient perspectives at the 5th year cross-sectional evaluation. While employment status at recruitment was not associated with disability, it was associated with unemployment at follow-up.

CONCLUSIONS: Disability at 5 years was associated with illness variables - episodic nature of illness at baseline, psychopathology and functioning, duration in psychotic episode and return to pre-morbid function. Patient perspectives about their illness (insight and patient explanatory models) were only associated cross-sectionally at 60 months but not earlier and are more suggestive of a coping response rather than being predictive of outcome. The relationship between unemployment and disability suggests that they are products of the same disease process.

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GnRH analogues are commonly used before hysteroscopic myomectomy to make surgery easier and safer, but they are expensive, have potential side effects and lack a robust evidence base to support this practice. We undertook a systematic review of the literature to determine whether, in women with submucous fibroids, pre-operative GnRH analogues were more effective than placebo/no treatment in terms of symptom relief, complications and ease of surgery. The outcomes were patient-reported relief of symptoms, complete resection of the fibroids, operative time and complications. Meta-analysis was performed where appropriate. Two trials including 86 women were identified. The assessment of symptom relief differed in the two trials: hence it was not possible to combine these data. The relative risk for completion of surgery and mean differences (95% confidence intervals) for operating time and fluid deficit were [0.94 (0.68-1.31); -5.34 min, (-7.55 min to -3.12 min) and -176.2 ml, (-281.05 ml to -71.5 ml)] respectively. Our results suggest that GnRHa may improve some outcomes but there is insufficient evidence to support their routine use prior to hysteroscopic resection of submucous fibroids. More randomised trials are needed to inform definitive conclusions.

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To establish normative data of vestibular evoked myogenic potential in different age groups among a heterogeneous Indian population. Prospective study design using a sample of convenience. Eighty five normal controls ranging between the ages 7 and 71 years were asked to provide a written signed consent for the study. Demographic characteristics of the patients were summarized using descriptive statistical methods using SPSS-17 analysing software. The outcome variable (VEMP recording) was...
expressed in percentiles as function of age. In all patients the stimulus which gave the best response was 95 dB (97.7 %) and 100 dB (95 %). The mean of wave latencies (p1 & n1) for 95-VEMP were, 11.2 ± 3.2 and 17.3 ± 4.7 ms on the right and 11.0 ± 2.8 and 17.0 ± 4.2 ms on the left respectively. The amplitude was 45.1 ± 54 mV on right and 46.9 ± 61.6 mV on the left. The mean of latency difference was 0.87 ms. The VEMP is a relatively simple test. The VEMP response rate was maximum in the younger age group; the optimum intensity was 95 dB. The asymmetry ratio interpretation should be done according to the age specific values.

CONCLUSION: We recommend the rectovestibular fistula be used as the neoanus and not as the neovagina. Delayed bowel vaginal replacement has excellent results and allows for optimal assessment of functioning uterine body or remnants.


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BACKGROUND/PURPOSE: Takayasu Arteritis (TA) is a chronic granulomatous vasculitis of autoimmune etiology characterized by narrowing of aorta and its main branches. It is one of the rarest diseases but the third common cause of vasculitis in pediatric age group. Mortality in juvenile onset TA has been reported to range from 8% to 35%. The outcome of disease has improved recently with interdisciplinary treatment including immunosuppressants and cardiovascular interventional procedures. We aimed to study the clinical features, angiographic findings and outcome of children with TA referred to a single centre in South India over a 9 year period.

METHODS: Records of TA patients, with symptom onset prior to 16 years of age were studied. Disease Extent Index-Takayasu (DEI.TAK), Indian Takayasu Arteritis Score 2010, and Takayasu Arteritis Damage Score (TADS) were calculated retrospectively using clinical information in electronic records. Cumulative incidence of sustained remission was estimated using Kaplan Meir curve

RESULTS: Forty patients with childhood onset TA with median age of onset of 12.5 (range 1-16) years presented at a median diagnostic delay of 11.3 (range 1-60) months. Commonest presenting features were hypertension, headache, malaise and fever. Pulse-less disease was observed in 25 (62.5%) cases. Majority (n = 28) had active disease with raised inflammatory markers, high baseline DEI.TAK score of 10 (3-24) and high median TADS of 7 (3-14). Of the 34 patients, followed up for 21.5 (range 3-192) months, remission was attained in 30, however cumulative sustained remission was achieved in only 29% of them at 5
years. Median period of sustained remission was 22.5 months (95% CI 17.1-26.8). New areas of vessel involvement were observed in 13 patients. Disease progression was arrested in majority (n= 20) with aggressive medical management and endovascular intervention. All 11 patients with an increment in TADS of >4 units during follow up had persistently active or relapsing disease. There was single case with fatality.

CONCLUSION: Corticosteroids and immunosuppressive therapy were effective in the control of disease activity. Progression of damage was associated with persistent inflammation. Continued surveillance by clinical instruments and imaging is warranted.

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L wave in echo Doppler.

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OBJECTIVE: Right ventricular (RV) dysfunction in isolated severe mitral stenosis (MS) patients have prognostic significance. Study aim was to assess RV function in these subjects by strain and strain rate analysis, pre and post-balloon mitral valvuloplasty (BMV).

METHODS: Twenty five patients with isolated severe MS in sinus rhythm were assessed for RV function by two dimensional (2D) longitudinal strain & strain rate imaging before and after BMV and compared with that from twelve healthy age matched controls.

RESULTS: Patients with severe MS had significantly lower global RV systolic strain; segmental strain at basal, mid, apical septum and basal RV free wall; but similar strain at mid and apical RV free wall as compared to controls. The systolic strain rate was significantly lower only at mid septum. In addition, they had higher estimated pulmonary artery systolic pressure and RV myocardial performance index; lower tricuspid annular plane systolic excursion (TAPSE), peak systolic velocity at lateral tricuspid annulus, isovolumic acceleration and fractional area change (FAC). Global RV systolic strain as well as, segmental strain at basal, mid and apical septum showed a statistically significant rise after BMV. TAPSE and FAC also increased significantly post BMV.

CONCLUSIONS: RV systolic function is impaired in patients with severe MS and can be assessed by global and segmental RV strain before the appearance
of clinical signs of systemic venous congestion. Impaired global and segmental RV strain values in these patients are primarily due to increased afterload and improve after BMV with reduction in RV afterload.


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Rotaviruses (RVs) are leading causes of severe diarrhea and vomiting in infants and young children. RVs with G10P[11] genotype specificity have been associated with symptomatic and asymptomatic neonatal infections in Vellore, India. To identify possible viral genetic determinants responsible for differences in symptomology, the genome sequences of G10P[11] RVs in stool samples of 19 neonates with symptomatic infections and 20 neonates with asymptomatic infections were determined by Sanger and next-generation sequencing. The data showed that all 39 viruses had identical genotype constellations (G10-P[11]-I2-R2-C2-A1-N1-T1-E2-H3), the same as the previously characterized symptomatic Vellore isolate N155. The data also showed that the RNA and deduced protein sequences of all the Vellore G10P[11] viruses were nearly identical; no nucleotide or amino acid differences were found that correlated with symptomatic versus asymptomatic infection. Next-generation sequencing data revealed that some stool samples, both from neonates with symptomatic and asymptomatic infections, also contained one or more positive-strand RNA viruses (Aichi virus, astrovirus, or salivirus/klassevirus) suspected of being potential causes of pediatric gastroenteritis. However, none of the positive-strand RNA viruses could be causally associated with the development of symptoms. These results indicate that the diversity of clinical symptoms in Vellore neonates does not result from genetic differences among G10P[11] RVs; instead, other undefined factors appear to influence whether neonates develop gastrointestinal disease symptoms. IMPORTANCE: Rotavirus (RV) strains have been identified that preferentially replicate in neonates, in some cases, without causing gastrointestinal disease. Surveillance studies have established that G10P[11] RVs are a major cause of neonatal infection in Vellore, India, with one-half of infected neonates exhibiting symptoms. We used Sanger and next-generation sequencing technologies to contrast G10P[11] RVs...
recovered from symptomatic and asymptomatic neonates. Remarkably, the data showed that the RNA genomes of the viruses were virtually indistinguishable and lacked any differences that could explain the diversity of clinical outcomes among infected Vellore neonates. The sequencing results also indicated that some symptomatic and asymptomatic Vellore neonates were infected with other enteric viruses (Aichi virus, astrovirus, salivirus/klassevirus); however, none could be correlated with the presence of symptoms in neonates. Together, our findings suggest that other poorly-defined factors, not connected to the genetic make-up of the Vellore G10P[11] viruses, influence whether neonates develop gastrointestinal disease symptoms.

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Lionel KR(1), John J(2), Sen N(1).
Glycated hemoglobin A: A predictor of outcome in trauma admissions to intensive care unit.
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BACKGROUND AND AIM: Although large studies have demonstrated the association between hyperglycemia and adverse intensive care unit (ICU) outcomes, it is yet unclear which subset of patients benefit from tight sugar control in ICU. Recent evidence suggests that stress induced hyperglycemia (SIH) and co-incidentally detected diabetes mellitus are different phenomena with different prognoses. Differentiating SIH from diabetic hyperglycemia is challenging in ICU settings. We followed a cohort of trauma patients admitted to a surgical intensive care unit (SICU) to evaluate if initial glycated hemoglobin A (HbA1c) level predicts the outcome of admission.

MATERIALS AND METHODS: A cohort of 120 consecutive admissions to SICU following trauma were recruited and admission blood sugar and HbA1c were measured. Outcomes were prospectively measured by blinded ICU doctors. A logistic regression model was developed to assess if HbA1c predicts poor outcomes in these settings.

RESULTS: Nearly 24% of the participants had HbA1c ≥ 6. Those with HbA1c ≥ 6 had 3.14 times greater risk of poor outcome at the end of hospital stay when compared to those with HbA1c < 6 and this risk increased to an odds ratio of 4.57 on adjusting for other significant predictors: Acute Physiology and Chronic Health Evaluation II, injury severity score, admission blood sugar and age at admission.

CONCLUSIONS: Substantial proportion of trauma admissions has underlying diabetes. HbA1c, a measure of pre admission glycaemic status is an important predictor of ICU outcome in trauma patients.

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Mascarenhas M(1), Habeebullah S(2), Sridhar MG(3).
Revisiting the role of first trimester homocysteine as an index of maternal and fetal outcome.
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AIM: To revisit the role of first trimester homocysteine levels with the maternal and fetal outcome.

METHODS: This was a cohort study comprising 100 antenatal women between 8 and 12 weeks of gestation. Serum homocysteine levels were checked after overnight fasting.

RESULTS: There were significantly elevated homocysteine levels among women with prior history of hypertensive disorders of pregnancy and prior second or third trimester pregnancy losses. There was no significant difference in homocysteine levels among women with previous gestational diabetes mellitus, preterm deliveries, or fetal malformations. Homocysteine levels were significantly elevated in
those who developed hypertensive disorder of pregnancy, oligohydramnios, and meconium stained amniotic fluid, had a pregnancy loss, or delivered a low birth weight baby. There was no significant difference in homocysteine levels for those who developed gestational diabetes mellitus.

**CONCLUSIONS:** Increased first trimester serum homocysteine is associated with history of pregnancy losses, hypertensive disorders of pregnancy, and preterm birth. This is also associated with hypertensive disorders of pregnancy, pregnancy loss, oligohydramnios, meconium stained amniotic fluid, and low birth weight in the current pregnancy. This trial is registered with ClinicalTrials.gov CTRI/2013/02/003441.

**Mathew MA(1), Paulose A, Chitralekha S, Nair MK, Kang G, Kilgore P.**

Prevalence of rotavirus diarrhea among hospitalized under-five children.

Indian Pediatr. 2014 Jan;51(1):27-31. Epub 2013 Sep 5. Author information:

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**OBJECTIVE:** To estimate the prevalence of rotavirus diarrhea among hospitalized children less than 5 years of age in Kerala State and to determine the circulating strains of rotavirus in Kerala.

**DESIGN:** Multicenter, cross-sectional study.

**SETTING:** Eight representative hospitals in Kunnathunadu Thaluk, Ernakulam district, Kerala.

**PARTICIPANTS:** Children in the age group under 5 years.

**METHODS:** Hospitalized children admitted with acute diarrhea were examined and standardized case report form was used to collect demographic, clinical and health outcome. Stool specimens were collected and ELISA testing was done. ELISA rotavirus positive samples were tested by reverse transcription PCR for G and P typing (CMC Vellore).

**RESULTS:** Among the 1827 children, 648 (35.9%) were positive for rotavirus by the Rotaclone ELISA test. The prevalence of rotavirus diarrhea in infants less than 6 months of age was 24.7%; 6- 11 months 31.9%; 12-23 months 41.9%; 24- 35 months 46.9%; and 33.3% in 36- 59 months. Rotavirus infections were most common during the dry months from January through May. G1P[8] (49.7%) was the most common strain identified followed by G9P[8] (26.4%), G2P[4] (5.5%), G9P[4] (2.6%) and G12P[6] (1.3%).

**CONCLUSIONS:** The prevalence of rotavirus diarrhea among hospitalized children less than 5 years is high in Ernakulam district, Kerala State.

**Mathews V(1), Savani BN(2).**

Conditioning regimens in allo-SCT for thalassemia major.

Bone Marrow Transplant. 2014 May;49(5):607-10. doi: 10.1038/bmt.2013.216. Epub 2014 Jan 20. Author information:

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Allogeneic hematopoietic SCT remains the only treatment that can correct the hematological manifestations in patients with thalassemia major. Improving the clinical outcomes of high-risk, heavily transfused patients with liver fibrosis and inadequate iron chelation remains a challenge. Because of the relatively high probability of graft rejection and regimen-related toxicity in many patients receiving SCT for advanced thalassemia major, further development of new treatment regimens is warranted. This review addresses the reported clinical studies in patients with advanced thalassemia major and we have summarized our suggested conditioning approach to improve the outcome after SCT.

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OBJECTIVES: This study attempted to follow up a cohort of women who presented to a tertiary hospital to investigate the effect of domestic violence on maternal and neonatal outcomes.

MATERIALS AND METHODS: Women, between 26-34 weeks of gestation, attending the obstetrics outpatient department, were recruited and followed up until delivery. They were assessed at recruitment and after delivery using the Edinburgh Postnatal Depression Scale, the Abuse Assessment Screen, and a pro forma to assess socio-demographic and clinical characteristics. Bivariate and multivariate statistics were employed to assess statistical significance.

RESULTS: One hundred and fifty women were recruited, 132 delivered in the hospital and were followed up. Domestic violence was associated with antenatal and postnatal depression, spouse’s insistence of a boy baby, medical complications during pregnancy, preterm delivery, and lower birth-weight.

CONCLUSION: Domestic violence has a significant impact on maternal and neonatal outcomes. Screening for domestic violence and interventions should be part of all antenatal programs. India should also employ public health approaches to change its patriarchal culture.


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OBJECTIVES: Scrub typhus is endemic in the Asia-Pacific region. Mortality is high even with treatment, and further knowledge of the immune response during this infection is needed. This study was aimed at comparing plasma levels of monocyte/macrophage and endothelial related inflammatory markers in patients and controls in South India and to explore a possible correlation to disease severity and clinical outcome.

METHODS: Plasma levels of ALCAM, VCAM-1, sCD163, sCD14, YKL-40 and MIF were measured in scrub typhus patients (n = 129), healthy controls (n = 31) and in infectious disease controls (n = 31), both in the acute phase and after recovery, by enzyme immunoassays.

RESULTS: Patients had markedly elevated levels of all mediators in the acute phase, differing from both healthy and infectious disease controls. During follow-up levels of ALCAM, VCAM-1, sCD14 and YKL-40 remained elevated compared to levels in healthy controls. High plasma ALCAM, VCAM-1, sCD163, sCD14, and MIF, and in particular YKL-40 were all associated with disease severity and ALCAM, sCD163, MIF and especially YKL-40, were associated with mortality.

CONCLUSIONS: Our findings show that scrub typhus is characterized by elevated levels of monocyte/macrophage and endothelial related markers. These inflammatory markers, and in particular YKL-40, may contribute to disease severity and clinical outcome.

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Acquired methemoglobinemia is an uncommon blood disorder induced by exposure to certain oxidizing agents and drugs. Although parents may not give any history of toxin ingestion; with the aid of pulse-oximetry and blood gas analysis, we can diagnose methemoglobinemia. Prompt recognition of this condition is required in emergency situations to institute early methylene blue therapy. We report an unusual case of severe toxic methemoglobinemia, which did not respond to methylene blue, but was successfully managed with exchange transfusion.

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Pendergast LL(1), Scharf RJ(2), Rasmussen ZA(3), Seidman JC(3), Schaefer BA(4), Svensen E(5), Toft JF(6), Koshy B(7), Kosek M(8), Rasheed MA(9), Roshan R(7), Maphula A(10), Shrestha R(11), Murray-Kolb LE(4); The MAL-ED Network Investigators. Postpartum depressive symptoms across time and place: Structural invariance of the Self-Reporting Questionnaire among women from the international, multi-site MAL-ED study. J Affect Disord. 2014 Jun 12;167C:178-186. doi: 10.1016/j.jad.2014.05.039. [Epub ahead of print]

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BACKGROUND: The Self-Reporting Questionnaire (SRQ) is a screening instrument that has been shown to be an effective measure of depression in postpartum women and is widely used in developing nations.

METHODS: The SRQ was administered to 2028 mothers from eight nations at two time points: one
and six months postpartum. All data were obtained from the Interactions of Malnutrition and Enteric Infections: Consequences for Child Health and Development (MAL-ED) study. The sample included women from MAL-ED sites in Bangladesh, Brazil, India, Nepal, Pakistan, Peru, South Africa, and Tanzania. This study examined three aspects of validity of SRQ scores including (a) structural validity, (b) cross-cultural invariance, and (c) invariance over time.

RESULTS: A 16-item, one-factor structure with items reflecting somatic symptoms removed was deemed to be superior to the original structure in this postpartum population. Although differential item functioning (DIF) across sites was evident the one-factor model was a good fit to the data from seven sites, and the structure was invariant across the one- and six-month time points.

LIMITATIONS: Findings are based on data from self-report scales. No information about the clinical status of the participants was available.

CONCLUSIONS: Overall, findings support the validity of a modified model of the SRQ among postpartum women. Somatic symptoms (e.g., headaches, not sleeping well) may not reflect internalizing problems in a postpartum population. Implications for researchers and practitioners are discussed.

Peter JV(1), Mani RK(2).
Association between glycemic variability and mortality: How robust is the evidence?
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Philip SS(1), Dutton GN.
Identifying and characterising cerebral visual impairment in children: a review.
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Cerebral visual impairment (CVI) comprises visual malfunction due to retro-chiasmal visual and visual association pathway pathology. This can be isolated or accompany anterior visual pathway dysfunction. It is a major cause of low vision in children in the developed and developing world due to increasing survival in paediatric and neonatal care. CVI can present in many combinations and degrees. There are multiple causes and it is common in children with cerebral palsy. CVI can be identified easily, if a structured approach to history-taking is employed. This review describes the features of CVI and describes practical management strategies aimed at helping affected children. A literature review was undertaken using ‘Medline’ and ‘Pubmed’. Search terms included cerebral visual impairment, cortical visual impairment, dorsal stream dysfunction and visual function in cerebral palsy.

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Predicting the impact of vaccination on the transmission dynamics of typhoid in South Asia: a mathematical modeling study.
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(2)Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, United States of America; Department of Ecology and Evolutionary Biology, Princeton University, Princeton, New Jersey, United States of America.
BACKGROUND: Modeling of the transmission dynamics of typhoid allows for an evaluation of the potential direct and indirect effects of vaccination; however, relevant typhoid models rooted in data have rarely been deployed.

METHODOLOGY/PRINCIPAL FINDINGS: We developed a parsimonious age-structured model describing the natural history and immunity to typhoid infection. The model was fit to data on culture-confirmed cases of typhoid fever presenting to Christian Medical College hospital in Vellore, India from 2000-2012. The model was then used to evaluate the potential impact of school-based vaccination strategies using live oral, Vi-polysaccharide, and Vi-conjugate vaccines. The model was able to reproduce the incidence and age distribution of typhoid cases in Vellore. The basic reproductive number ($R_0$) of typhoid was estimated to be 2.8 in this setting. Vaccination was predicted to confer substantial indirect protection leading to a decrease in the incidence of typhoid in the short term, but (intuitively) typhoid incidence was predicted to rebound 5-15 years following a one-time campaign.

CONCLUSIONS/SIGNIFICANCE: We found that model predictions for the overall and indirect effects of vaccination depend strongly on the role of chronic carriers in transmission. Carrier transmissibility was tentatively estimated to be low, consistent with recent studies, but was identified as a pivotal area for future research. It is unlikely that typhoid can be eliminated from endemic settings through vaccination alone.

Pond GR(1), Di Lorenzo G(2), Necchi A(3), Eigl BJ(4), Kolinsky MP(5), Chacko RT(6), Dorff TB(7), Harshman LC(8), Milowsky MI(9), Lee RJ(10), Galsky MD(11), Federico P(2), Bolger G(12), DeShazo M(12), Mehta A(12), Goyal J(13), Sonpavde G(14).

Prognostic risk stratification derived from individual patient level data for men with advanced penile squamous cell carcinoma receiving first-line systemic therapy.


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BACKGROUND: Prognostic factors in men with penile squamous cell carcinoma (PSCC) receiving systemic therapy are unknown. A prognostic classification system in this disease may facilitate interpretation of outcomes and guide rational drug development. We
performed a retrospective analysis to identify prognostic factors in men with PSCC receiving first-line systemic therapy for advanced disease.

PATIENTS AND METHODS: Individual patient level data were obtained from 13 institutions to study prognostic factors in the context of first-line systemic therapy for advanced PSCC. Cox proportional hazards regression analysis was conducted to examine the prognostic effect of these candidate factors on progression-free survival (PFS) and overall survival (OS): age, stage, hemoglobin, neutrophil count, lymphocyte count, albumin, site of metastasis (visceral or nonvisceral), smoking, circumcision, regimen, ECOG performance status (PS), lymphovascular invasion, precancerous lesion, and surgery following chemotherapy. The effect of different treatments was then evaluated adjusting for factors in the prognostic model.

RESULTS: The study included 140 eligible men. Mean age across all men was 57.0 years. Among them, 8.6%, 21.4%, and 70.0% of patients had stage 2, 3, and 4 diseases, respectively; 40.7% had ECOG PS $\geq 1$, 47.4% had visceral metastases, and 73.6% received cisplatin-based chemotherapy. The multivariate model of poor prognostic factors included visceral metastases ($P<0.001$) and ECOG PS $\geq 1$ ($P<0.001$) for both PFS and OS. A risk stratification model constructed with 0, 1, and both poor prognostic factors was internally validated and demonstrated moderate discriminatory ability (c-statistic of 0.657 and 0.677 for OS and PFS, respectively). The median OS for the entire population was 9 months. Median OS was not reached, 8, and 7 months for those with 0, 1, and both risk factors, respectively. Cisplatin-based regimens were associated with better OS ($P = 0.017$) but not PFS ($P = 0.37$) compared with noncisplatin-based regimens after adjusting for the 2 prognostic factors.

CONCLUSIONS: In men with advanced PSCC receiving first-line systemic therapy, visceral metastases and ECOG PS $\geq 1$ were poor prognostic factors. A prognostic model including these factors exhibited moderate discriminatory ability for outcomes and warrants external validation. Patients receiving cisplatin-based regimens exhibited better outcomes compared with noncisplatin-based regimens after adjusting for prognostic factors.

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PURPOSE: To determine whether the ISNT rule (Inferior>Superior>Nasal>Temporal) or the “IST” rule (Inferior>Superior>Temporal) can be applied to the peripapillary retinal nerve fiber layer (RNFL) thickness as measured using Heidelberg Retinal Tomography (HRT) and Optical Coherence Tomography (OCT).

MATERIALS AND METHODS: This was a cross-sectional study of 189 normal and 42 glaucomatous eyes. RNFL thicknesses measured in different quadrants using HRT and OCT were compared to determine the percentage of eyes obeying the ISNT and IST rule.

RESULTS: The HRT-measured mean RNFL thickness in normal eyes showed that 25.9% obeyed the ISNT rule and 70.4% conformed to the “IST” rule. The “IST” rule was able to identify normal eyes better ($P=0.040$), but had a poor sensitivity (45%) and specificity (70%) to diagnose glaucoma. The OCT-measured average RNFL thickness showed that 47.1% of normal eyes obeyed the ISNT rule and 58.7% conformed to the “IST” rule. Exclusion of the nasal sector also increased the number of glaucomatous eyes conforming to the IST rule (31% obeyed the ISNT rule and 50% obeyed the IST rule). Sensitivities and specificities of the ISNT and the IST rules for OCT-quantified RNFL ranged from 42% to 77%.

CONCLUSIONS: A larger number of normal eyes obeyed the IST rule compared with the ISNT rule for the RNFL thickness measured by HRT and OCT. Exclusion of the nasal sector from the analysis (IST rule) marginally improved the specificity in diagnosing glaucoma at the cost of the sensitivity, making neither of these parameters (ISNT and IST) likely to be useful clinically.
Pradhan ZS(1), Mittal R, Jacob P.
Rigid gas-permeable contact lenses for visual rehabilitation of traumatized eyes in children.

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PURPOSE: The aim of this study was to investigate the usefulness and tolerance of rigid gas-permeable (RGP) contact lenses in the visual rehabilitation of children postocular trauma.

METHODS: In this retrospective case series, children below 15 years of age with ocular trauma were included. The best-corrected visual acuity with RGP contact lenses was compared with that of spectacle correction. The factors affecting visual improvement were analyzed, and problems caused by contact lens use were identified.

RESULTS: Twelve eyes of 12 boys were included. The mean best-corrected visual acuity was 0.81 ± 0.29 (LogMar equivalent) with spectacles and 0.47 ± 0.27 (LogMar equivalent) with contact lenses (P < 0.001). Seven of the 12 eyes achieved a >2 line increase in visual acuity with contact lens correction as compared with that using spectacle correction. The mean astigmatism in eyes that achieved this improvement in vision was 5.45 ± 1.6 diopters, whereas the mean astigmatism in the eyes that did not improve was 2.6 ± 1.2 diopters, which was statistically significant (P = 0.009). No other factors (age, corneal scar location/density, grade/zone of injury, lens status, and occlusion) seemed to affect visual improvement with contact lenses. The mean follow-up duration was about 15 months during which 91% of the patients continued their contact lens usage.

CONCLUSIONS: RGP contact lenses offer a useful refractive treatment alternative in traumatized eyes of children. Eyes with high degrees of astigmatism were found to benefit the most. RGP contact lenses were found to be well tolerated in this population.

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BACKGROUND: Improvement of transcranial electrical motor-evoked potentials (TeMEPs) following untethering during tethered cord surgery (TCS) and its clinical significance have not been analyzed in the literature.

METHODS: Forty-five consecutive cases of tethered cord were operated on with multimodality intraoperative neurophysiological monitoring (IONM) between February 2005 and January 2012. Intraoperative TeMEP change was classified as improvement, worsening or no change. Motor, sensory, bladder and bowel symptoms and signs were evaluated preoperatively, in the first week post-surgery and at the last follow-up (maximum of 2 years).

RESULTS: Patient age ranged from 5 to 44 years (mean, 16 ± 10 years), with 30 children. Intraoperative MEPs improved in 23 (51 %), remained the same in 21 (46.7 %) and worsened in 1 (2 %) patient. Motor improvement occurred in 7 patients and clinical improvement in 17 patients in the immediate postoperative period. Postoperative neurological worsening occurred in one patient (2.2 %). Improved and stable MEPs correlated with the motor (p = 0.002) and clinical improvement (p= 0.02) in the immediate postoperative period. Follow-up was available in 35 patients (77.7 %), ranging from 5 to 24 months (median, 21 months; mean, 17.7 ± 6.8 months). There was late clinical improvement in 73.5 % of the patients in whom the intraoperative MEP had remained the same or improved. However, there was no statistically significant correlation between MEP change and long-term outcome.

CONCLUSIONS: Intraoperative MEP improvement occurs in about 50 % of the patients following successful untethering. This finding probably provides support to the ischemic theory of tethered cord syndrome.

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BACKGROUND: Schatzker type V and VI tibial fractures are complex injuries, usually treated with open reduction and internal fixation (ORIF) using dual plates or ring fixators. ORIF has the advantage of not requiring pin tract care, but has a higher infection rate, especially in open fractures. We have combined the advantages of these two methods to treat these difficult fractures.

MATERIALS AND METHODS: Ten Schatzker type V and 11 Schatzker type VI fractures were treated between 2006 and 2010. ORIF with dual plates was performed, only if there was marked articular displacement (> 2 mm) in a closed fracture. All other fractures including open fractures and closed fractures with soft tissue compromise or minimal articular displacement were treated with ring fixators. The outcomes were analyzed and documented using the Honkonen and Jarvinen subjective, clinical, functional, and radiological criteria and the Western Ontario and McMaster Universities Arthritis Index (WOMAC).

RESULTS: Nine closed fractures with marked articular displacement (> 2 mm) were treated with dual plates. Eight closed fractures with minimal articular displacement (< 2 mm) and poor skin condition and four open fractures were treated with ring fixators. The mean follow-up period was 2 ½ years. The mean postoperative knee flexion was 128°. All patients could walk, jump, and climb steps. 90% could squat, though only 50% could duck walk properly. Radiologically, 85% had a plateau tilt of less than 5°, 92% had an articular step of less than 2 mm, and a residual articular widening of less than 5 mm. There were no major infections. Two patients had minor pin tract infections and two requested that their plates be removed subsequently.

CONCLUSION: The protocol used to treat Schatzker type V and VI tibial plateau fractures has had excellent results and we suggest that all open fractures be treated with ring fixators and that ORIF should be...
done only for closed fractures with marked displacement.

NAT PMCID: PMC3931151 PMID: 24600061 [PubMed] CO

Rajesh V.
Stereotactic biopsy of brain stem masses: A safe and useful procedure.

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INTL PMCID: PMC3985370 PMID: 24741240 [PubMed - as supplied by publisher] CO

Ralph R(1), Peter JV, Chrispal A, Zachariah A, Dian J, Sebastian T, Venkatesh B, Thomas K.
Supraphysiological 25-hydroxy vitamin D3 level at admission is associated with illness severity and mortality in critically ill patients.
J Bone Miner Metab. 2014 Apr 22. [Epub ahead of print]

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We studied the association between admission serum 25-hydroxy vitamin D3 level and in-hospital mortality in a prospective cohort of critically ill patients admitted to the medical intensive care unit of a tertiary care referral center. Of the 180 patients enrolled, 129 were included. Vitamin D3 deficiency was observed in 37 % (n = 48) and supra-physiological levels (e”250 nmol/L) in 15.5 % (n = 20). Patients with supraphysiological vitamin D3 levels were grouped as outliers. There was no difference in mortality (p = 0.41) between vitamin D3 deficient (21/48) and non-deficient (36/81) patients in analysis with and without outliers. Patients with vitamin D3 e”250 nmol/L had a significantly higher (p = 0.02) Simplified Acute Physiology Score (SAPS) II and mortality (p = 0.003) [mean (SD) 60.1 ± 17.1 and 75 % (15/20), respectively] when compared with the rest [45.6 ± 18 and 38.5 % (42/109), respectively]. The sensitivity, specificity and SAPS II independent odds ratio to predict mortality in patients with supraphysiological vitamin D3 levels were 26.3, 93.1 and 3.7 % (95 % confidence interval 1.2-11.4; p = 0.03), respectively. In conclusion, vitamin D3 deficiency in our cohort was not associated with mortality. A patient subset with supra-physiological vitamin D levels had higher illness severity scores and mortality. Extrinsic factors interfering with test results were ruled out. A biological hypothesis to explain this observation is proposed. Further clarification of mechanisms leading to this observation is warranted.

INTL PMID: 24752822 CO

Ramachandran J(1), Ismail AM, Chawla G, Fletcher GJ, Goel A, Eapen CE, Abraham P.
Serum HBsAg quantification in treatment-naïve Indian patients with chronic hepatitis B.

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BACKGROUND AND AIMs: There is paucity of Indian data regarding serum HBsAg levels (qHBsAg) in treatment-naïve chronic hepatitis B (CHB). This study was done to determine correlation of qHBsAg with hepatitis B e antigen (HBeAg) and hepatitis B virus (HBV) DNA levels and its ability to independently categorize subgroups of CHB.

METHODS: We studied 131 treatment-naïve CHB patients and initially classified them based on HBeAg status. The HBeAg-positive group was further classified into immune tolerance (IT) and immune clearance (IC) phases based on serum alanine aminotransferase. HBeAg-negative patients were classified into low replicators (LR) and HBeAg-negative chronic hepatitis (ENH) based on DNA levels. HBsAg quantification was performed using the Architect chemiluminescence system.

RESULTS: HBeAg-positive patients had higher DNA (7.89 vs. 2.69 log10 IU/mL) and higher qHBsAg (4.60 vs. 3.85 log10 IU/mL) compared to the HBeAg-negative group. Good correlation between qHBsAg and DNA was seen in HBeAg-positive (r = 0.6, p < 0.001) but not in HBeAg-negative CHB (r = 0.2). A qHBsAg level greater than 4.39 log10IU/mL predicted HBeAg-positive state with 81 % sensitivity and 85 % specificity.
However, among HBeAg-negative CHB, qHBsAg failed to discriminate between LR and ENH.

CONCLUSIONS: A single point estimation of qHBsAg in treatment-naïve patients could predict replicative HBeAg-positive CHB, but was not helpful in defining replicative status in the HBeAg-negative CHB.


Efficacy and safety of hepatitis C antiviral therapy in moderate and severe chronic kidney disease.
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Hepatitis C virus (HCV) infection is an important cause of liver-related morbidity and mortality in patients with end-stage renal disease (ESRD). Though indicated, antiviral therapy adds to the existing financial burden and is poorly tolerated in these patients. We studied HCV treatment outcomes in patients with moderate and severe chronic kidney disease (CKD) between June 2010 and June 2012. Out of 46 patients with CKD, only 16 (genotype 1:6, 3:9, indeterminate 1) received interferon treatment (conventional 9, pegylated 7; with low-dose ribavirin 5). End of treatment response was achieved in 50 % and sustained viral response in 44 %. Adverse effects such as tuberculosis, anemia, and cardiac failure resulting in discontinuation of therapy were seen in three. The dropout rate was 38 %. Though interferon therapy was efficacious and safe, it was received by only 35 % of patients with CKD. We suggest that antiviral therapy be offered under close monitoring in the absence of contraindications in patients with moderate and severe CKD.

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Association between heat shock protein 70 gene polymorphisms and clinical outcomes in intensive care unit patients with sepsis.
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OBJECTIVE: The objective of the following study is to evaluate the associations between single nucleotide polymorphisms (SNPs) in the Heat Shock Protein 70 (HSP70) gene, gene expression of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) and medical intensive care unit (MICU) stay and organ failure in sepsis.

MATERIALS AND METHODS: MICU patients with sepsis were genotyped for rs1061581, rs2227956, rs1008438 and rs1043618 polymorphisms in HSP70 gene using polymerase chain reaction (PCR)-restriction fragment length polymorphism analysis or allele-specific PCR. Messenger ribonucleic acid (mRNA) expression of IL-6 and TNF-α were quantitated in peripheral blood lymphocytes. Outcomes were recorded.

RESULTS: 108 patients (48 male) aged 40.7 ± 16.0 (mean ± standard deviation) years included H1N1 infection (36), scrub typhus (29) and urosepsis (12). Seventy-one (65.7%) had dysfunction of three or more organ systems, 66 patients (61.1%) were treated by mechanical ventilation, 21 (19.4%) needed dialysis. ICU stay was 9.3 ± 7.3 days. Mortality was 38.9%. One or more SNPs were noted in 101/108 (93.5%) and organ failure was noted in only 1/7 patients without a single SNP. The A allelotypes of rs1061581 and rs1008438 were associated with hematological
CONCLUSIONS: HSP70 genotypes may determine some adverse outcomes in patients with sepsis.
of age using linear splines. We incorporated the longitudinal prevalence of diarrhea in both current and previous periods into the model. Diarrhea during the current period was associated with slower linear and ponderal growth. Faster (catch-up) growth in length was observed in children with no diarrhea in age groups immediately after an age group in which diarrhea was experienced [age group >6-12 mo: 0.03 mm/mo for each percentage diarrhea prevalence in the previous period (95% CI: 0.007, 0.06) relative to 11.3 mm/mo mean growth rate; age group >12-18 mo: 0.04 mm/mo (95% CI: 0.02, 0.06) relative to 8.9 mm/mo mean growth rate; age group >18-24 mo: 0.04 mm/mo (95% CI: 0.003, 0.09) relative to 7.9 mm/mo mean growth rate]. The associations were stronger in boys than in girls when separate models were run. Similar results were observed when weight was the outcome variable. When diarrheal episodes are followed by diarrhea-free periods in the first 2 y of life, catch-up growth is observed that may allow children to regain their original trajectories. The finding of a greater effect of diarrhea on linear growth in boys than in girls was unexpected and requires additional study. Diarrhea burdens are high throughout the first 2 y of life in these study sites, therefore reducing the likelihood of catch-up growth. Extending diarrhea-free periods may increase the likelihood of catch-up growth and decrease the prevalence of stunting.

SUBJECTS AND METHODS: The case records of 11 patients (12 ears) treated for congenital perilymph fistula presenting with recurrent meningitis were reviewed to ascertain their clinical, radiological, and intraoperative features and outcome following surgery.

RESULTS: Most patients presented after at least 3 episodes of meningitis (range, 2-10 episodes). Ipsilateral hearing loss was present in 9 of 12 ears, with normal hearing in 3 patients. High-resolution computed tomography and/or magnetic resonance imaging scanning of the temporal bone contributed to the diagnosis in 75% of cases but was normal in 3 cases (25%). Oval window and round window defects were the most common (66.7% and 63.6%, respectively). Four ears (33.3%) had more than 1 defect. The unusual presentations included 2 patients who presented in adulthood, a patient with a defect in the medial wall of the attic, and 3 patients with normal radiological findings. Follow-up ranged from 1 to 11 years (median, 2 years). There were 2 failures following simple fistula closure with cessation of symptoms after vestibular obliteration. No patient was readmitted with recurrent meningitis after definitive surgery.

CONCLUSION: Up to 25% of patients with recurrent meningitis secondary to congenital perilymph fistula may have normal audiological and radiological assessment necessitating exploratory tympanotomy. Vestibular obliteration, rather than simple fistula closure, prevents recurrence.

Rupa V(1), Agarwal I, Rajshekhar V.
Congenital perilymph fistula causing recurrent meningitis: lessons learnt from a single-institution case series.
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(1)Department of ENT, Christian Medical College, Vellore, India.

OBJECTIVE: To study the steps involved in definitive evaluation and successful management of patients with congenital perilymph fistula presenting with recurrent meningitis.

STUDY DESIGN: Case series with chart review.

SETTING: Tertiary care center.

Sajith KG(1), Dutta AK, Sahni RD, Esakimuthu S, Chacko A.
Is empiric therapy with fluconazole appropriate for esophageal candidiasis?
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We studied the prevalence of fluconazole resistance in esophageal candidiasis. Patients with suspected esophageal candidiasis during gastroscopy underwent culture of white plaques. Minimum inhibitory
concentration (MIC) >64 µg/mL of fluconazole for Candida was indicative of resistance. Sensitivity of itraconazole was tested in a subset of resistant strains. Sixty-five patients were included. Mean (SD) age was 50.03 (13.5) years and 67.7 % were males. Predisposing factors for candidiasis were found in 42 (64.6 %) patients. C. albicans was identified in 64 (97.4 %) patients and C. glabrata in one patient. Fluconazole resistance was seen in 38 (59.4 %) patients with C. albicans and also in the one patient with C. glabrata. All the fluconazole resistant isolates of C. albicans had MIC >128 µg/mL suggesting very high resistance. Twelve patients with fluconazole resistance had itraconazole resistance as well. The study shows a high rate of fluconazole resistance in patients with esophageal candidiasis.


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Immune mechanisms alone cannot directly account for exocrine gland dysfunction and extraglandular features such as renal tubular acidosis, neuropathy, hearing loss and fatigue in Sjögren’s syndrome (SS). Absence of Vacuolar ATPase (V-ATPase) has been reported in SS related renal tubular acidosis (RTA). We hypothesise how defect in V-ATPase could account for decreased neurotransmitter release leading onto exocrine dysfunction, neuroendocrine manifestations and hearing loss which are well described manifestations in SS. S-phase-kinase-associated protein-1 (Skp1) is a constituent of RAVE which is involved in V-ATPase assembly. It is also a component of SCF ligase which is crucial in NFκB signalling. SKP1 also interacts with TRIM 21/Ro 52 which is an autoantigen in SS. By virtue of these interactions, we postulate how a defective skp1 could fit into the existing pathogenesis of SS and also account for increased risk of lymphoma in SS as well as congenital heart block in fetus of mothers with SS.

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Sarkar S(1), Jacob KS, Pratheesh R, Chacko AG.
Transsphenoidal surgery for acromegaly: predicting remission with early postoperative growth hormone assays.

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BACKGROUND: Early detection of residual disease may benefit management strategies in patients undergoing transsphenoidal surgery for acromegaly. This requires establishing objective thresholds for early postoperative growth hormone (GH) assays, and incorporating these parameters into a scale for outcome prediction.

METHOD: We analyzed a database containing the records of 86 patients who had undergone gross total transsphenoidal resection of GH-secreting pituitary adenomas. Early postoperative biochemical testing included a morning fasting basal GH assay on the first postoperative day (POD1) and a second GH assay following suppression with 100 g of oral glucose on the seventh postoperative day (POD7). Remission was defined as a normal IGF-1 with either a GH nadir <0.4 ng/ml following suppression with oral glucose or a basal fasting GH <1 ng/ml on follow-up dated >3 months after surgery. Receiver operator characteristic (ROC) curves identified optimal thresholds for all biochemical parameters. Logistic regression analysis assessed the statistical significance of factors associated with cure. A point system was developed, employing regression coefficients obtained from the multivariate statistical model to quantify the impact of each predictor on cure.

RESULTS: Remission was achieved in 34.6 % of patients and was associated with smaller, non-invasive tumors with lower preoperative, POD1 and POD7 GH levels. Optimal thresholds obtained from the ROC analysis suggested that lower POD1 and POD7 GH values provided good sensitivity and specificity for cure, despite modest predictive values.
The model with the best ability to predict outcome included size, POD1 GH and POD7 GH levels, with a score of $\geq 95$ demonstrating high specificity for prediction of remission.

**CONCLUSION:** Early postoperative GH assays are highly sensitivity and specific. The scoring system that we propose provided excellent predictive value and requires further validation in larger cohorts and in different populations. The model may help guide the intensity of follow-up and enable early identification of residual disease.

**Novel use of tendon tunneler to create space with minimal dissection in endoscopic head and neck operations.**
Sathya RK, Thomas RJ, Kisku S, Jehangir S, Singh DS, Kurien JJ.


**Lumbosacral transition vertebra: prevalence and its significance.**
Sekharappa V, Amritanand R, Krishnan V, David KS.

INTL PMCID: PMC3939369 PMID: 24596605 [PubMed] CO

**The impact of the Hologic vs the ICMR database in diagnosis of osteoporosis among South Indian subjects.**
Shetty S(1), Kapoor N, Naik D, Asha HS, Thomas N, Paul TV.

INTL PMCID: PMC3939369 PMID: 24596605 [PubMed] CO

METHODS: The study involved examining the radiological images of 3 groups of patients. Group A consisted of kidney urinary bladder (KUB) X-rays of patients attending urology outpatient clinic. Group B consisted of X-rays with or without magnetic resonance images (MRIs) of patients attending a spine outpatient clinic, and group C consisted of X-rays and MRI of patients who had undergone surgery for lumbar disc herniation. One thousand patients meeting the inclusion criteria were selected to be in each group. LSTV was classified by Castellvi’s classification and disc degeneration was assessed by Pfirrmann’s grading on MRI scans.

**RESULTS:** The prevalence of LSTV among urology outpatients, spine outpatients and discectomy patients was 8.1%, 14%, and 16.9% respectively. LSTV patients showed a higher Pfirrmann’s grade of degeneration of the last mobile disc. Results were found to be significant statistically.

**CONCLUSIONS:** The prevalence of LSTV in spinal outpatients and discectomy patients was significantly higher as compared to those attending the urology outpatient clinic. There was a definite causal relationship between the transitional vertebra and the degeneration of the disc immediately cephalad to it.

**BACKGROUND AND OBJECTIVES:** Recently, the Indian Council of Medical Research (ICMR) has published normative data for bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (DXA) scanning. However, the impact this has had on the diagnosis of osteoporosis when compared to currently used Caucasian databases has not been analysed. Hence, this study was undertaken to look at agreement between the Hologic Database (HD) based on BMD
normative data in Caucasians and the ICMR database (ICMRD) in defining osteoporosis in subjects with or without hip fracture.

MATERIALS AND METHODS: It is a cross-sectional study of 2976 subjects (men 341, women 2757) (mean age ± SD = 62.2 ± 7.2 years), including 316 subjects with low impact hip fracture: 2199 were from the hospital database, and 461 were healthy postmenopausal women from the community who underwent (DXA) scanning between January 2010 and March 2013. Recalculated T scores from ICMRD were used for the diagnosis of osteoporosis and compared with HD.

RESULTS: An almost perfect agreement existed between the two databases for the diagnosis of osteoporosis at the hip (κ -0.82, P < 0.0001) in all subjects, and a moderate relationship existed in those with hip fracture (κ -0.65, P < 0.0001). Seventy-three of 316 hip fracture subjects (23.5%) defined as osteoporosis according to HD were classified as osteopenia according to ICMRD.

CONCLUSION: The threshold of hip BMD T score for treating osteoporosis may have to be redefined if the ICMR reference database is used. Initiation of treatment in these subjects must be based on multiple fracture risk factor assessment in addition to looking at BMD. Further studies with a larger sample size of subjects with fracture are needed to validate our findings.

INTL PMID: 24821494

Sinha A(1), Gulati A(1), Saini S(1), Blanc C(2), Gupta A(1), Gurjar BS(3), Saini H(1), Kothresh ST(2), Ali U(4), Bhatia D(1), Ohri A(4), Kumar M(5), Agarwal I(6), Gulati S(7), Anand K(8), Vijayakumar M(9), Sinha R(10), Sethi S(1), Salona M(2), George A(3), Bal V(3), Singh G(11), Dinda AK(11), Hari P(1), Rath S(3), Dragon-Durey MA(2), Bagga A(1); Indian HUS Registry.

Prompt plasma exchanges and immunosuppressive treatment improves the outcomes of anti-factor H autoantibody-associated hemolytic uremic syndrome in children.


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Comment in


Antibodies to complement factor H are an uncommon cause of hemolytic uremic syndrome (HUS). Information on clinical features and outcomes in children is limited. In order to explore this we studied a multicenter cohort of 138 Indian children with anti-complement factor H antibody associated HUS, constituting 56% of patients with HUS. Antibody titers were high (mean 7054 AU/ml) and correlated inversely with levels of complement C3, but not complement factor H. Homozygous deletion of the CFHR1 gene was found in 60 of 68 patients. Therapies included dialysis in 119 children, 105 receiving plasma exchanges and 26 intravenous immunoglobulin. Induction immunosuppression consisted of 87 children receiving prednisolone with or without intravenous cyclophosphamide or rituximab. Antibody titers fell significantly following plasma exchanges and increased during relapses. Adverse outcome (stage 4-5 CKD or death) was seen in 36 at 3 months and 41 by last follow up, with relapse in 14 of 122 available children. Significant independent risk factors for adverse outcome were an antibody titer over 8000 AU/ml, low C3 and delay in plasma exchange. Combined plasma exchanges and induction immunosuppression resulted in significantly improved renal survival: one adverse outcome prevented for every 2.6 patients
treated. Maintenance immunosuppressive therapy, of prednisolone with either mycophenolate mofetil or azathioprine, significantly reduced the risk of relapses. Thus, prompt use of immunosuppressive agents and plasma exchanges are useful for improving outcomes in pediatric patients with anti-complement factor H-associated HUS.

INTRODUCTION AND AIM: Tibial plateau fractures (TPFs) are an independent, non-modifiable risk factor for surgical site infections (SSIs). Current antero-lateral approaches to the knee dissect through the anterior tibial angiosome (ATA), which may contribute to a higher rate of SSIs. The aim of this study was to develop an angiosome-sparing antero-lateral approach to allow reduction and fixation of lateral TPFs and to investigate its feasibility in a consecutive cohort.

METHODS: Twenty cadaveric knees were dissected to define the position of the vessels supplying the ATA from the lateral tibial condyle to the skin perforators. Based on these results, an angiosome-sparing surgical approach to treat lateral TPFs was developed. Fifteen consecutive patients were subsequently treated through this approach. Clinical outcomes included assessment of SSI and Lysholm score. Fracture healing and stability were assessed using the Rasmussen score and radiostereometric analysis (RSA).

RESULTS: At the latest follow-up between 1 and 4 years, there was no report of SSI. Nine patients (60%) had good or excellent Lysholm scores. The mean Rasmussen score at final follow-up was 17 (median 18, range 14-18) with 10 patients (66%) graded as excellent. Fracture fragment migration measured using RSA was below 2mm in all cases.

DISCUSSION: This study has demonstrated that an angiosome-sparing antero-lateral approach to the lateral tibial plateau is feasible. Adequate stability of these fracture types was achieved by positioning a buttress plate away from the bone and superficial to the regional fascial layer as an ‘internal-external fixator’.

CONCLUSION: The angiosome-sparing approach developed was able to be used in a prospective cohort and the clinical results to date are encouraging. Future clinical studies need to investigate the potential benefits of this surgical approach when compared with the previously described antero-lateral approaches.

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This retrospective study was done to determine the incidence of neonatal Group B streptococcal (GBS) sepsis among newborn between 1998 and 2010. Among 107,692 babies born during this period, the overall incidence of GBS sepsis was 0.76 / 1000 live births with the incidence of early onset sepsis (EOS) being 0.68 (95%CI 0.52-0.83)/1000 live births. The overall rate of EOS decreased to 0.55/1000 live births with introduction of intrapartum antibiotic policy.

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Sun HY(1), Munoz P(2), Torre-Cisneros J(3), Aguado JM(4), Lattes R(1), Montejo M(5), Garcia-Reyne A(4), Bouza E(2), Valero M(2), Lara R(6), Wagener MM(7), John GT(8), Bruno D(9), Singh N(7).


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We determined the characteristics of posttransplant tuberculosis and the impact of rifampin-based antituberculosis regimens on outcomes in the current era. Patients comprised 64 transplant recipients with tuberculosis, divided into 2 consecutive cohorts: an earlier cohort (cases occurring from 2003 to 2007) and a later cohort (cases from 2008 to 2011). Patients from the later versus earlier era had tuberculosis develop later after transplant (odds ratio, 1.01; 95% CI, 1.00-1.02; P= .05), were more likely to be liver transplant recipients (odds ratio, 4.52; 95% CI, 1.32-15.53; P= .02), and were more likely to receive tacrolimus-based immunosuppression (odds ratio, 3.24; 95% CI, 1.14-9.19; P= .03). Mortality rate was 10% in the later cohort and 21% in the earlier cohort (P= .20). Rifampin-based treatment was less likely to be used in patients with prior rejection (P= .04). However, neither rejection rate (P=. .71) nor mortality (P= .93) after tuberculosis differed between recipients who received rifampin and recipients who did not. Thus, notable changes have occurred in the epidemiological characteristics of tuberculosis in transplant recipients. Overall mortality rate has improved, with about 90% of the patients now surviving after tuberculosis.

INTL PMID: 24598564


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(3)Department of Physical Medicine and Rehabilitation, Christian Medical College, Vellore, Tamil Nadu, India.
OBJECTIVE: To assess the survival in persons with traumatic spinal cord injury (SCI) receiving structured follow-up in South India.

DESIGN: Retrospective study.

SETTING: Rehabilitation center.

PARTICIPANTS: Persons with traumatic SCI (N=490) residing within a 100-km radius of the institute who were managed and regularly followed up by the rehabilitation center between the years 1981 and 2011.

INTERVENTIONS: Not applicable.

MAIN OUTCOME MEASURES: Survival rates and mortality risk factors. Measures were estimated using the product limit (Kaplan-Meier) method and the Cox model.

RESULTS: The survival rate after SCI was 86% after 5 years, 71% after 15 years, and 58% after 25 years. Survival of persons with complete high cervical injury is substantially low compared with other levels of SCI. Level of injury and extent of lesion (Frankel classification and/or American Spinal Injury Association Impairment Scale) play a significant role in predicting survival of this population.

CONCLUSIONS: Survival rates of regularly followed-up persons with SCI from this study show promising results, though survival rates are lesser when compared with studies from developed countries. Better understanding of the predictors, causes of deaths, comprehensive rehabilitation, community integration, and regular follow-up could possibly assist in improving survival rates.

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OBJECTIVE: The aim of this study was to assess vitamin D status of preterm babies at birth and adequacy of daily supplementation with vitamin D.

METHODS: This prospective cohort study recruited 111 preterm babies, 25 to 32 weeks' gestation from a tertiary care perinatal center in south India. Cord blood was assayed for serum calcium, phosphate, alkaline phosphatase, and 25-hydroxyvitamin D (25(OH)D). All of the babies were fed unfortified breast-milk and supplemented daily with calcium, phosphate, and 400 IU of vitamin D. At 6 weeks serum calcium, phosphate, alkaline phosphatase, parathyroid hormone, and 25(OH)D levels were estimated.

RESULTS: Of 111 preterm babies recruited, a total of 90 (81%) of the preterm babies were followed up until 6 weeks. The median (interquartile range) vitamin D level in the preterm group was 34.7 (25.6-50.1) and 19.3 (13.9-27.1) ng/mL at birth and 6 weeks, respectively. Using a cutoff value of <20 ng/mL to determine vitamin D insufficiency (VDI), it was observed that 12.6% of the babies were vitamin D insufficient at birth. This increased to 52.2% at 6 weeks despite the recommended supplementation with vitamin D (P < 0.001).

CONCLUSIONS: The prevalence of VDI was not high at birth; however, a large proportion of preterm babies were vitamin D insufficient at 6 weeks despite being supplemented with vitamin D 400 IU/day. The recommended vitamin D supplementation of 400 IU appears to be inadequate to prevent VDI, and hence randomized controlled trials looking at higher doses of vitamin D supplementation are needed.

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Turel MK(1), Babu KS, Singh G, Chacko AG.
The utility of facial nerve amplitude and latency ratios in predicting postoperative facial nerve function after vestibular schwannoma surgery.
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(1)Department of Neurological Sciences, Christian Medical College, Vellore, Tamil Nadu, India.

BACKGROUND: Despite advances in vestibular schwannoma (VS) surgery and intraoperative electrophysiological monitoring, immediate and delayed facial nerve outcomes are difficult to accurately predict consistently.

OBJECTIVE: To determine the utility of proximal to distal facial nerve amplitude and latency ratios in predicting the long-term postoperative facial nerve function in patients undergoing excision of VS.

MATERIALS AND METHODS: One hundred consecutive patients undergoing surgery for VS with intraoperative facial nerve monitoring were included. Clinical, radiological, electrophysiological, and postoperative outcome data were prospectively entered into a database. Other parameters such as brainstem distance, size of the porus acousticus, and facial nerve length were also analyzed.

RESULTS: Of the 100 patients, 53 were women. The mean age was 42.5 ± 14.1 years (range, 14-71 years) and the average tumor size was 4.1 ± 0.8 cm (range, 2.4-6.5 cm). Total excision was done in 89% of patients. Intraoperatively, the facial nerve was anatomically preserved in 86 patients, but electrophysiological responses were obtained from the root entry zone (REZ) in only 77 patients at the end of surgery, 75% of which had good facial function at long-term follow-up. In nine patients where no responses were obtained but the facial nerve was anatomically intact, 50% had good facial function at long-term follow-up. Proximal and distal amplitude and latency ratios, size or consistency of the tumor, brainstem distance, size of the porus acousticus, and length of the facial nerve were not useful in predicting long-term functional outcome.

CONCLUSIONS: While a positive response to facial nerve stimulation at the end of VS surgery is a good predictor of long-term postoperative function, the absence of responses in an anatomically intact nerve does not preclude good function in the long term. Proximal to-distal amplitude and latency ratios did not correlate with the final facial function.

Valson AT(1), Kakde ST, Mohanraj P, Basu G, Mohapatra A, Varughese S.
Resolution of Acremonium kiliense subcutaneous abscess in a renal allograft recipient without antifungal therapy.

Valson AT(1), Sundaram M(1), David VG(1), Deborah MN(1), Varughese S(1), Basu G(1), Mohapatra A(1), Alexander S(1), Jose J(2), Roshan J(2), Simon B(3), Rebekah G(4), Tamilarasi V(1), Jacob CK(1).
Profile of incident chronic kidney disease related-mineral bone disorders in chronic kidney disease Stage 4 and 5: A hospital based cross-sectional survey.

Chronic kidney disease related-mineral bone disorder (CKD-MBD) has been poorly studied in pre-dialysis Indian CKD patients. We aimed to study the clinical, biochemical and extra skeletal manifestations of untreated CKD-MBD in pre-dialysis Stage 4 and 5 CKD patients attending nephrology out-patient clinic at a tertiary care hospital in South India. A hospital based cross-sectional survey including, demographic profile, history of CKD-MBD symptoms, measurement of serum calcium, phosphate, parathyroid hormone, 25 hydroxy vitamin D (25(OH) D) and alkaline phosphatase; lateral
abdominal X-rays for abdominal aortic calcification (AAC) and echocardiography for valvular calcification (VC) was carried out. Of the 710 patients surveyed, 45% had no CKD-MBD related symptom. Prevalence of hypocalcemia, hyperphosphatemia, hyperparathyroidism (>150 pg/mL) and 25(OH) D levels <30 ng/mL was 66.3%, 59%, 89.3% and 74.7% respectively. Echocardiography was carried out in 471 patients; 96% of whom had VC (calcification score e”1). Patients with VC were older and had lower 25(OH) D levels than those without. Lateral abdominal X-rays were obtained in 558 patients, 6.8% of whom were found to have AAC, which was associated with older age. Indian patients with incident CKD-MBD have a high prevalence of hypocalcemia, 25(OH) D deficiency and VC even prior to initiating dialysis while AAC does not appear to be common. The association between 25(OH) D deficiency and VC needs further exploration.

NAT
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Clinical profile and improving mortality trend of scrub typhus in South India.

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BACKGROUND: Scrub typhus, a bacterial zoonosis caused by Orientia tsutsugamushi, may cause multiorgan dysfunction syndrome (MODS) and is associated with significant mortality. This study was undertaken to document the clinical and laboratory manifestations and complications and to study time trends and factors associated with mortality in patients with scrub typhus infection.

METHODS: This retrospective study, done at a university teaching hospital, included 623 patients admitted between 2005 and 2010 with scrub typhus. The diagnosis was established by a positive IgM ELISA and/or pathognomonic eschar with PCR confirmation where feasible. The clinical and laboratory profile, course in hospital, and outcome were documented. Factors associated with mortality were analyzed using multivariate logistic regression analysis.

RESULTS: The most common presenting symptoms were fever (100%), nausea/vomiting (54%), shortness of breath (49%), headache (46%), cough (38%), and altered sensorium (26%). An eschar was present in 43.5% of patients. Common laboratory findings included elevated transaminases (87%), thrombocytopenia (79%), and leukocytosis (46%). MODS was seen in 34% of patients. The overall case-fatality rate was 9.0%. Features of acute lung injury were observed in 33.7%, and 29.5% required ventilatory support. On multivariate analysis, shock requiring vasoactive agents (relative risk (RR) 10.5, 95% confidence interval (CI) 4.2-25.7, p<0.001), central nervous system (CNS) dysfunction (RR 5.1, 95% CI 2.4-10.7, p<0.001), and renal failure (RR 3.6, 95% CI 1.7-7.5, p=0.001) were independent predictors of mortality. Over 4 years, a decreasing trend was observed in the mortality rate.

CONCLUSIONS: Scrub typhus can manifest with potentially life-threatening complications such as lung injury, shock, and meningoencephalitis. MODS occurred in a third of our patients. The overall case-fatality rate was 9%, with shock, renal failure, and CNS associated with a higher mortality. Copyright © 2014 The Authors. Published by Elsevier Ltd. All rights reserved.

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Familial hypercholesterolemia (FH) is a genetic disorder of lipoprotein metabolism resulting in elevated serum low-density lipoprotein (LDL) cholesterol levels leading to increased risk for premature cardiovascular diseases (CVDs). The diagnosis of this condition is based on clinical features, family history, and elevated LDL-cholesterol levels aided more recently by genetic testing. As the atherosclerotic burden is dependent on the degree and duration of exposure to raised LDL-cholesterol levels, early diagnosis and initiation of treatment is paramount. Statins are presently the mainstay in the management of these patients, although newer drugs, LDL apheresis, and other investigational therapies may play a role in certain subsets of FH, which are challenging to treat. Together these novel treatments have notably improved the prognosis of FH, especially that of the heterozygous patients. Despite these achievements, a majority of children fail to attain targeted lipid goals owing to persistent shortcomings in diagnosis, monitoring, and treatment. This review aims to highlight the screening, diagnosis, goals of therapy, and management options in patients with FH.

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OBJECTIVES: To evaluate preoperative neck resorption and postoperative valgus orientation as predictors of union and functional outcome after valgus intertrochanteric osteotomy for treatment of neglected femoral neck fractures and nonunions.

DESIGN: Retrospective cohort study.

SETTING: Tertiary care center.

PATIENTS/PARTICIPANTS: Forty consecutive patients with neglected femoral neck fracture and nonunions were treated with valgus intertrochanteric osteotomy, and follow-up was available in 32 patients (average age, 43 years; range, 14-60 years; average nonunion duration, 6 ± 7 months; range, 1-36 months).

INTERVENTION: Valgus intertrochanteric osteotomy.

MAIN OUTCOME MEASUREMENTS: Clinical outcome was assessed with Harris hip score. Plain radiographs were evaluated for union, avascular necrosis, preoperative bone deficiency (neck resorption ratio), and postoperative femoral head fragment alignment (head-shaft angle).

RESULTS: Follow-up at 5 ± 3 years (range, 2-12 years) after surgery showed union in 29 patients (91%), and Harris hip score was 82 ± 13 points (range, 63-100 points). The 3 patients with persistent nonunion at the neck of femur had neck resorption ratio <0.52. Increased postoperative head-shaft angle was associated with lower follow-up Harris hip score; postoperative valgus alignment >15 degrees compared with the contralateral side was associated with poor functional outcome. The presence of avascular necrosis did not affect the outcome.

CONCLUSIONS: Valgus intertrochanteric osteotomy resulted in union and satisfactory functional outcome in most patients who had neglected femoral neck fractures and nonunions. Preoperative neck resorption ratio <0.5 was a risk factor for nonunion, and excessive valgus alignment was a risk factor for poor functional outcome after osteotomy.

LEVEL OF EVIDENCE: Prognostic Level II. See Instructions for Authors for a complete description of levels of evidence.

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Vedantam A(1), Rajeshkhar V.
Change in Morphology of Intramedullary T2-Weighted Increased Signal Intensity Following Anterior Decompressive Surgery for Cervical Spondylotic Myelopathy.
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(2)2Department of Neurological Sciences, Christian Medical College, Vellore India.
Study Design. Retrospective studyObjective. To study the change in morphology of T2-weighted (T2W) increased signal intensity (ISI) and its association with functional outcome after central corpectomy for cervical spondylotic myelopathy (CSM) and ossified posterior longitudinal ligament (OPLL).
Summary of Background Data. There are limited data on change in T2W ISI morphology after anterior decompressive surgery. It is unclear whether change in T2W ISI carries prognostic significance in patients with CSM/OPLL.
Methods. We reviewed patients who underwent central corpectomy for CSM/OPLL between 1996 and 2010, and had a follow up MRI at e” 6 months postoperatively. T2W ISI on sagittal images was classified as type 0- no ISI; type 1- predominantly (>50%) faint with an indistinct border; and type 2 - predominantly (>50%) intense with a sharp border. The length of T2W ISI and the presence of T1W hypointensity was also recorded on preoperative and follow-up images. Functional outcomes as measured by the Nurick grade were correlated with change in morphology of MR signal changes.
Results. Sixty-four patients (60 males, mean age = 50±1.1 years) were reviewed. The mean follow up duration was 29±3.5 months. The majority of patients (71.9%) had no change in the type of ISI at follow up. The type of ISI improved in 13 patients (20.3%), and worsened in 5 patients (7.8%). The mean length of ISI was 26.2±3.4 mm preoperatively and 13.7±1.8 mm at follow up in 53 patients (p = 0.002). Change in ISI grade or length was not associated with change in Nurick grade or length at follow up (p = 0.74, p = 0.5). Conclusions. The type of T2W ISI does not change, but the length of T2W ISI decreases for the majority of patients undergoing anterior cervical decompression for CSM/OPLL. In our series, change in morphology of T2W ISI did not correlate with functional outcome as measured by Nurick grade.
INTL PMID: 24859579

Venkatramani V(1), Shanmugasundaram R, Kekre NS.
Urogenital fistulae in India: results of a retrospective analysis.
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OBJECTIVE: To review our experience with urogenital fistulae with respect to etiology and management.
DESIGN: Retrospective analysis of electronic records from January 2004 to June 2011.
METHODS: A retrospective analysis of electronic records of all urogenital fistulae presenting to our institution from January 2004 to June 2011 was undertaken. Etiology, presentation, management, and outcome of these cases were noted and analyzed.
RESULTS: A total of 210 cases were identified, with vesicovaginal fistulae being the most common. The etiology was predominantly gynecological (58.6%) with laparoscopic assisted hysterectomy seeming to play an increasingly important role. Success rates of more than 90% were achieved in all cases, even in complex fistulae. No factors predicting successful repair were identified. Laparoscopic repair was successful in well-selected cases.
CONCLUSIONS: The etiology of urogenital fistulae in India seems to be changing to one in line with developed countries. High success rates are possible even in complex cases.
INTL PMID: 24368482  

Verghese A.
A fresh look at homosexuality.
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NAT PMCID: PMC4040081 PMID: 24891721  

Verghese VP(1), Robinson JL(2).
A Systematic Review of Hepatitis E Virus Infection in Children.
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A systematic review was conducted, seeking all literature relevant to the epidemiology, clinical and laboratory features, and outcome of hepatitis E virus (HEV) infection in children. Transmission is thought to be primarily from fecal-oral transmission, with the role of transmission from animal reservoirs not being clear in children. Worldwide, seroprevalence is <10% up to 10 years of age, with the exception of 1 of 5 studies from India and the sole study from Egypt. Seroprevalence increases with age, but it is not clear if it is increasing over time. The clinical presentation of HEV infection has broad similarities to hepatitis A virus (HAV) infection, with most cases being subclinical. However, HEV differs from HAV in that infectivity is lower, perinatal transmission can result in neonatal morbidity and even mortality, and a chronic carrier state exists, accounting for chronic hepatitis in some pediatric solid organ transplant recipients.
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[PubMed - as supplied by publisher]

Distribution of serotypes and antibiotic susceptibility patterns among invasive pneumococcal diseases in Saudi Arabia.
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BACKGROUND: Streptococcus pneumoniae causes life-threatening infections such as meningitis, pneumonia, and febrile bacteremia, particularly in young children. The increasing number of drug-resistant isolates has highlighted the necessity for intervening and controlling disease. To achieve this, information is needed on serotype distribution and patterns of antibiotic resistance in children.
METHODS: All cases of invasive pneumococcal disease (IPD) in children aged less than 15 yr recorded at King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia, were reviewed for serotyping and antibiotic susceptibility. Isolates were collected from 78 consecutive patients with IPD between 2009 and 2012. All collected isolates were subjected to serotyping by co-agglutination, sequential multiplex PCR, and single PCR sequotyping as previously described.
RESULTS: The most frequently isolated IPD serotypes were 23F, 6B, 19F, 18C, 4, 14, and 19A, which are listed in decreasing order and cover 77% of total isolates. The serotype coverage for the pneumococcal conjugate vaccine (PCV)7, PCV10, and PCV13 was 77%, 81%, and 90%, respectively. Results from sequential multiplex PCR agreed with co-agglutination results. All serotypes could not be correctly identified using single PCR sequotyping. Minimum inhibitory concentration showed that 50 (64%) isolates were susceptible to penicillin, whereas 70 (90%) isolates were susceptible to cefotaxime.
CONCLUSIONS: The most common pneumococcal serotypes occur with frequencies similar to those found in countries where the PCV has been introduced. The most common serotypes in this study are included in the PCVs. Addition of 23A and 15 to the vaccine would improve the PCV performance in IPD prevention.
INTL
PMCID: PMC3999319
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[PubMed - in process]
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Brinda EM, Rajkumar AP(1), Enemark U, Attermann J, Jacob KS.
Cost and burden of informal caregiving of dependent older people in a rural Indian community. BMC Health Serv Res. 2014 May 7;14:207. doi: 10.1186/1472-6963-14-207.
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BACKGROUND: Lack of state supported care services begets the informal caregiving by family members as the mainstay of care provided to the dependent older people in many Low and Middle Income Countries (LMICs), including India. Little is known about the time spent on caregiving, its cost and the burden experienced by these informal caregivers. We aimed to estimate the costs of informal caregiving and to evaluate the nature as well as correlates of caregivers’ burden in a rural Indian community.

METHODS: We assessed 1000 people aged above 65 years, among whom 85 were dependent. We assessed their socioeconomic profiles, disability, health status and health expenditures. Their caregivers’ socio-demographic profiles, mental health, and the time spent on caregiving were assessed using standard instruments. Caregiver’s burden was evaluated using Zarit Burden Scale. We valued the annual informal caregiving costs using proxy good method. We employed appropriate non-parametric multivariate statistics to evaluate the correlates of caregivers’ burden.

RESULTS: Average time spent on informal caregiving was 38.6 (95% CI 35.3-41.9) hours/week. Estimated annual cost of informal caregiving using proxy good method was 119,210 US$ in this rural community. Mean total score of Zarit burden scale, measuring caregivers’ burden, was 17.9 (95% CI 15.6-20.2).

Prevalence of depression among the caregivers was 10.6% (95% CI 4.1-17.1%). Cerebrovascular disease, Parkinson’s disease, higher disability, insomnia and incontinence of the dependent older people as well as the time spent on helping Activities of Daily Living and on supervision increased caregiver’s burden significantly.

CONCLUSIONS: Cost and burden of informal caregiving are high in this rural Indian community. Many correlates of burden, experienced by caregivers, are modifiable. We discuss potential strategies to reduce this burden in LMICs. Need for support to informal caregivers and for management of dependent older people with chronic disabling diseases by multidisciplinary community teams are highlighted.

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OBJECTIVE: To determine the relationship between birth weight and the evolution of obesity in adult life in women from a rural developmental block in southern India.

DESIGN: Non-concurrent cohort.

SETTING: General community- a rural developmental block in southern India.

PARTICIPANTS: Two hundred and seventy one young healthy females were recruited from a birth cohort. The study subjects were 98 women in the age group of 19-23 years who had been born with low birth weight (LBW) and 173 women in the same age group who had been born with normal birth weight (NBW).

MATERIALS AND METHODS: Data collection involved interview using a structured questionnaire and anthropometric measurements.

ANALYSIS: Chi-square test to assess significance of association, independent sample t test to assess the
difference between means, odds ratios for measuring magnitude of association, stratified analysis to identify various interactions and confounders, and multiple logistic regression models to identify the relationship between birth weight and young adult obesity (BMI > 25).

RESULTS: A crude odds ratio of 0.564 (95% CI 0.262 - 1.214) was obtained for the association between LBW and development of obesity later in life. In the final logistic regression model, it was found that a young adult female with low birth weight who belonged to a higher socio-economic group had a higher risk of developing obesity (Adjusted odds for the interaction term between LBW and high SES 6.251; 95% CI 1.236 - 31.611).

CONCLUSION: The study could not find any significant association between LBW and development of obesity later in life, but it found a higher probability of developing obesity later in life among low birth weight female children born in high socio-economic status families.

Cherian A(1), Syam UK(1), Sreevidya D(1), Jayaraman T(2), Oommen A(2), Rajshekhar V(2), Radhakrishnan K(1), Thomas SV(3).
Low seroprevalence of systemic cysticercosis among patients with epilepsy in Kerala - South India.
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PURPOSE: Neurocysticercosis (NCC) is considered to be rare in Kerala state, India, although it is an important cause of epilepsy in many other parts of India. Our objective was to test this notion by determining the seroprevalence of cysticercosis (CC) in an unselected sample of persons with epilepsy and comparing it to that of persons without epilepsy living in Kerala.

METHODS: Individuals with active epilepsy (AE) who had never resided outside Kerala state for more than one month and were attending our center for epilepsy care constituted the cases. Sex-matched persons without epilepsy who had never resided outside Kerala state for more than one month constituted the controls. The demographic details, occupation, and food habits (for the cases and controls), as well as clinical characteristics and imaging (for cases only) were recorded. Sera separated from blood drawn by venipuncture from the cases and controls were assayed for cysticercal antibodies by enzyme-linked immunoelectrotransfer blot (EITB).

RESULTS: Of the 80 persons with AE, 12 were seropositive for cysticercus antibodies (15%; 95% CI: 8.8-24.4); among the 68 controls, 7 were seropositive (10.3%; 95% CI: 5.1-19.8). The odds ratio (OR) for seropositivity in the epilepsy group (1.54) was not statistically significant (95% CI: 0.6-4.2). Among the 69 patients who had a brain computed tomography (CT) scan or magnetic resonance imaging (MRI), none had features diagnostic of NCC. Gender, diet (vegetarian vs non-vegetarian, consumption of raw vegetables), drinking water status (clean vs unclean), residence (rural vs urban), exposure to manure, and animal rearing including pigs did not have any association with seropositivity.

CONCLUSION: Among the residents of Kerala, most epilepsy is not related to cysticercosis.

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Jennifer MS(1), Kattula D, Sowmyanarayanan TV, Sarkar R, Kang G.
Health Utilization for Childhood Gastroenteritis in Southern India.
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Eradicating poliomyelitis: India’s journey from hyperendemic to polio-free status.


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India’s success in eliminating wild polioviruses (WPVs) has been acclaimed globally. Since the last case on January 13, 2011 success has been sustained for two years. By early 2014 India could be certified free of WPV transmission, if no indigenous transmission occurs, the chances of which is considered zero. Until early 1990s India was hyperendemic for polio, with an average of 500 to 1000 children getting paralysed daily. In spite of introducing trivalent oral poliovirus vaccine (tOPV) in the Expanded Programme on Immunization (EPI) in 1979, the burden of polio did not fall below that of the pre-EPI era for a decade. One of the main reasons was the low vaccine efficacy (VE) of tOPV against WPV types 1 and 3. The VE of tOPV was highest for type 2 and WPV type 2 was eliminated in 1999 itself as the average per-capita vaccine coverage reached 6. The VE against types 1 and 3 was the lowest in Uttar Pradesh and Bihar, where the force of transmission of WPVs was maximum on account of the highest infant-population density. Transmission was finally interrupted with sustained and extraordinary efforts. During the years since 2004 annual pulse polio vaccination campaigns were conducted 10 times each year, virtually every child was tracked and vaccinated - including in all transit points and transport vehicles, monovalent OPV types 1 and 3 were licensed and applied in titrated campaigns according to WPV epidemiology and bivalent OPV (bOPV, with both types 1 and 3) was developed and judiciously deployed. Elimination of WPVs with OPV is only phase 1 of polio eradication. India is poised to progress to phase 2, with introduction of inactivated poliovirus vaccine (IPV), switch from tOPV to bOPV and final elimination of all vaccine-related and vaccine-derived polioviruses. True polio eradication demands zero incidence of poliovirus infection, wild and vaccine.
RESULTS: Of 807 residents evaluated, 73 (9.0%) had significant psychological morbidity. Such morbidity was associated with being older, female, poorer, illiterate, currently employed and being a spouse of the older person. A diagnosis of depression, neuropsychiatric symptoms and greater disability in older people were also associated with psychological morbidity among co-residents.

CONCLUSION: Co-residents living with older people have significant psychological morbidity, which needs to be recognised and treated.

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Mallath MK(1), Taylor DG(2), Badwe RA(3), Rath GK(4), Shanta V(5), Pramesh CS(3), Dugumarti R(6), Sebastian P(7), Borthakur BB(8), Kalwar A(9), Kapoor S(10), Kumar S(11), Gill JL(2), Kuriakose MA(12), Malhotra H(13), Sharma SC(14), Shukla S(15), Viswanath L(16), Chacko RT(17), Pau, IJ(18), Reddy KS(19), Sharma KS(3), Purushotham AD(20), Sullivan R(21).

The growing burden of cancer in India: epidemiology and social context.


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Cancer can have profound social and economic consequences for people in India, often leading to family impoverishment and societal inequity. Reported age-adjusted incidence rates for cancer are still quite low in the demographically young country. Slightly more than 1 million new cases of cancer are diagnosed every year in a population of 1.2 billion. In age-adjusted terms this represents a combined male and female incidence of about a quarter of that recorded in western Europe. However, an estimated 600,000-700,000 deaths in India were caused by cancer in 2012. In age-standardised terms this figure is close to the mortality burden seen in high-income countries. Such figures are partly indicative of low rates of early-stage detection and poor treatment outcomes. Many cancer cases in India are associated with tobacco use, infections, and other avoidable causes. Social factors, especially inequalities, are major determinants of India’s cancer burden, with poorer people more likely to die from cancer before the age of 70 years than those who are more affluent. In this first of three papers, we examine the complex epidemiology of cancer, the future burden, and the dominant sociopolitical themes relating to cancer in India.

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Mallath MK(1), Taylor DG(2), Badwe RA(3), Rath GK(4), Shanta V(5), Pramesh CS(3), Dugumarti R(6), Sebastian P(7), Borthakur BB(8), Kalwar A(9), Kapoor S(10), Kumar S(11), Gill JL(2), Kuriakose MA(12), Malhotra H(13), Sharma SC(14), Shukla S(15), Viswanath L(16), Chacko RT(17), Pau, IJ(18), Reddy KS(19), Sharma KS(3), Purushotham AD(20), Sullivan R(21).

The growing burden of cancer in India: epidemiology and social context.


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Nair M(1), Chacko D(1), Rajaraman V(2), George B(1), Samraj L(1), Russell PS(2).

The diagnostic accuracy and validity of the teen screen questionnaire-mental health for clinical and epidemiological studies in primary-care settings.


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BACKGROUND: To validate a brief, self-reported, Teen Symptom Questionnaire-Mental Health (TSQ-M), for identifying adolescents with mental ill-health, designed for conducting epidemiological studies and clinical work in primary-care settings.

MATERIALS AND METHODS: In this prospective, cross-sectional study of 146 adolescents, recruited six rural and urban schools, the newly developed TSQ-M as the measure for validation and General Health Questionnaire-12 item (GHQ-12) as the gold standard measure were administered by independent trained raters. Tests for diagnostic accuracy and validity were conducted.

RESULTS: A TSQ-M score of ≥29 (Sn=75.68%, Sp=68.06, +LR=2.37, -LR=0.36, PPV=70.9, NPV=73.1) with the AUC of 0.79, is suggested for screening use in Indian populations. Besides the adequate face and content validity, TSQ-M has moderate internal consistency (Cronbach’s α = .64) suggesting that the construct of mental ill-health as conceptualized by TSQ-M has multiple sub-constructs. The presence of sub-constructs was demonstrated by an 8-factor structure, which explained 60% of variance.

CONCLUSION: The TSQ-M is a psychometrically adequate, yet a brief measure, for clinical and research work in identifying mental ill-health among adolescents in primary-care settings in India.

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Philip M, Alex RG, Sunny SS, Alwan A, Guzzula D, Srinivasan R.

A study on morbidity among automobile service and repair workers in an urban area of South India.


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INTRODUCTION: Service sector in Indian industrial growth has obtained significant numbers. Automobile service industry is one of the largest in the world with a majority of the workers in unorganized sector of the industry. This study was carried out among auto service industry workers in Vellore urban area to assess possible occupation related morbidity.

MATERIALS AND METHODS: A cross-sectional observation study was carried out among 106 automobile repair shop workers.

RESULTS: Half (47%) suffered work related stress, 32 (30.2%) reported exposure to dust, 81 (76%) to heat, and 50 (17%) to hazardous chemicals and heavy metals. More than 90% reported over exposure to petroleum products. A third reported cough for more than 2 weeks, more than a quarter reported gastrointestinal symptoms associated with work. Half of them reported musculoskeletal complaints associated with work with a quarter reporting unintentional work place injuries. A tenth of them were found to have reduced pulmonary function on testing and nearly half had impaired sensory functions in peripheries. Reduced pulmonary function was found to be significantly associated with heavy metal exposure (P = 0.001). Peripheral neuropathy was significantly associated with years of occupation (P = 0.001), exposure to petroleum products (P = 0.03) and exposure to heavy metals (P = 0.018).

DISCUSSION: Half of the workers were unaware of health problems associated with their occupational exposures and thereby the use of personal protection is abysmally low. A very high proportion of workers had symptoms of cough, breathlessness, abdominal pain, abdominal discomfort and muscle aches. Almost a quarter of the workers had un-intentional occupational injuries in the last 6 months. Though they work in a high-risk environment with chances of fire hazard, falls and chemical exposures, none of the workshops had fire-extinguishers, first aid kits or any such safety devices.

PMCID: PMC4083523 PMID: 25006310 [PubMed] EPH
Determinants of postpartum anemia among women from a rural population in southern India.

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BACKGROUND: Even though the problem of anemia during pregnancy has been adequately emphasized, very little attention has been paid to postpartum anemia. The objective of the current study was to estimate the mean change in maternal hemoglobin from 36 weeks’ gestation to 6 weeks postpartum and to identify the factors associated with anemia during the postpartum period among women in a rural development block in Tamil Nadu, India.

METHODS: Ninety-three pregnant women were interviewed using a structured questionnaire at 36 weeks’ gestation and then at 2 and 6 weeks postpartum. Blood samples were collected from the participants at 36 weeks’ gestation and at 6 weeks postpartum. Paired t-tests assessing the difference in mean hemoglobin prepartum and postpartum, univariate analysis, and multiple logistic regression to identify factors associated with postpartum anemia were done using Statistical Package for the Social Sciences version 12 for Microsoft Windows software.

RESULTS: The proportion of study subjects who were anemic (hemoglobin <11 g/dL) at 36 weeks’ gestation was 26.8% and at 6 weeks postpartum was 47.3% (hemoglobin <12 g/dL). The mean hemoglobin at 36-38 weeks’ gestation was 11.70±1.43 g/dL and at 6 weeks postpartum was 12.10±1.27 g/dL. Anemia at 36 weeks’ gestation (odds ratio [OR] 10.47, 95% confidence interval [CI] 2.37-42.34), heavy blood loss perceived by the mother during delivery (OR 12.91, 95% CI 2.01-61.25), younger maternal age (<21 years, OR 2.45, 95% CI 1.28-23.86), and inadequate iron supplementation during the postpartum period (OR 3.53, 95% CI 1.18-11.37) were identified as significant factors associated with anemia at 6 weeks postpartum.

CONCLUSION: Anemia during the third trimester of pregnancy, heavy bleeding perceived by the mother during delivery, younger maternal age, and inadequate iron supplementation during the postpartum period were associated with postpartum anemia.

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Survey of ethical issues reported by Indian medical students: basis for design of a new curriculum.

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Education in ethics is now a formal part of the undergraduate medical curriculum. However, most courses are structured around principles and case studies more appropriate to western countries. The cultures and practices of countries like India differ from those of western countries. It is, therefore, essential that our teaching should address the issues which are the most relevant to our setting. An anonymised, questionnaire-based, cross-sectional survey of medical students was carried out to get a picture of the ethical problems faced by students in India. The data were categorised into issues related to professional behaviour and ethical dilemmas. Unprofessional behaviour was among the issues reported as a matter of concern by a majority of the medical students. The survey highlights the need to design the curriculum in a way that reflects the structure of medical education in India, where patients are not always considered socio-culturally equal by students or the medical staff. This perspective must underpin any further efforts to address education in ethics in India.
Vasan SK(1), Ramachandran P(2), Mathew M(2), Natraj CV(2), Antonisamy B(3), Thomas N(4).
Post-absorptive glucose lowering in normal healthy individuals: an epidemiological observation.
Author information:
(1)Rolf Luft Centre for Diabetes, Department of Molecular Medicine & Surgery, Karolinska Institutet, Stockholm, Sweden; Department of Endocrinology, Diabetes & Metabolism, Christian Medical College, Vellore, India.
(2)Indian Institute of Science, Bangalore, India.
(3)Department of Biostatistics, Christian Medical College, Vellore, India.
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Electronic address: nihal_thomas@yahoo.com.
Post-absorptive glucose lowering (PALG) is observed in individuals with glucose intolerance and in healthy individuals. We report a prevalence of about 23% among healthy Asian Indians. Individuals with PALG are characterized by leaner phenotype, low body fat percentage, increased insulin sensitivity and higher fasting glucose levels.
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Agarwal I.
A Case of Liddle Syndrome: Author’s Reply.
Indian J Pediatr. 2014 May 15. [Epub ahead of print]
Author information:
Pediatric Nephrology Division, Department of Pediatrics Unit II, Christian Medical College, Vellore, 632 004, South India, indiraagarwal@cmcvellore.ac.in.

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Alex R(1), Mathew M(2), Arul S(2), Kundavaram A(1).
Overdose of mycophenolate mofetil managed in a secondary care hospital in South India.
Author information:
(1)Department of Medicine 4, Christian Medical College, Vellore, Tamil Nadu, India.
(2)Department of Community Medicine, Christian Medical College, Vellore, Tamil Nadu, India.
Mycophenolate mofetil (MMF) is a commonly used immunosuppressive agent and is considered relatively safe with minimal side-effects in therapeutic doses. However, data regarding the effects of an overdose is sparse and therefore, concerns remain regarding its safety. Here, we report the case of a 24-year-old young woman who consumed high dose (10 g) of MMF with suicidal intent. We did not observe any complications related to MMF overdose.

Bal HS(1), Kisku S, Sen S, Masih D.
A retroperitoneal enteric duplication cyst communicating with the right upper ureter in an infant.
Author information:
(1)Department of Paediatric Surgery, Christian Medical College, Vellore, Tamil Nadu, India.
We report an extremely rare case of isolated retroperitoneal enteric duplication cyst with gastric mucosa causing haematuria and dysuria by communicating with the urinary system. A 9-month-old male child was admitted to our hospital with persistent haematuria, dysuria and anaemia. Investigations revealed a retroperitoneal cyst abutting the hydronephrotic non-functioning right kidney. At surgery an isolated retroperitoneal cyst communicating with the right pelviureteric junction was found. The kidney and associated cyst were excised. Histology of the cystic lesion revealed an enteric duplication cyst lined by ectopic gastric mucosa. Isolated retroperitoneal enteric duplication cyst communicating with the urinary tract has not been previously reported in the English literature. We propose that acid secretion into the right renal system
was the cause of the haematuria-dysuria syndrome which promptly resolved postoperatively.

**Bhageerathy PS(1), Cecilia M(2), Sebastian A(2), Raghavendran A(3), Abraham P(3), Thomas A(2), Peedicayil A(2).**

Human papilloma virus-16 causing giant condyloma acuminata.


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(3)Department of Clinical Virology, Christian Medical College Hospital, Vellore, Tamil Nadu, India.

A 28-year-old multiparous lady presented to the Gynaecology outpatient department with a 12 × 5 cm warty growth in the vulva. A biopsy of the growth revealed condyloma acuminata of the vulva. Simple vulvectomy was done. A PCR of the specimen detected the presence of human papilloma virus (HPV)-16 which is usually considered as a high-risk HPV type for carcinogenesis.

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Chandrasekharan R(1), Varghese AM, Mathew J, Ashish G.
A rare case of bilateral nasolabial cysts in a postpartum lady.
Author information:
(1)Department of ENT, Christian Medical College, Vellore, Tamilnadu, India.

Nasolabial cyst, also known as Klestadt’s cyst is an uncommon nonodontogenic cyst. Bilateral nasolabial cysts are rarer and less than 10 cases have been reported in the literature. Diagnosis is usually clinical and they present as slow-growing swellings in the nasolabial region causing cosmetic deformity and nasal obstruction. A postpartum lady presented with bilateral swelling of the cheeks. Excision was done via a sublabial approach. She is asymptomatic one year after surgery. Nasolabial cysts are developmental but usually noticed after a trauma. There is no data relating the cysts to pregnancy.

DATA COLLECTION AND ANALYSIS: Two authors independently selected relevant studies, extracted data and assessed risk of bias. We summarised data, where possible, using a random-effects model. Formal assessment of heterogeneity was not possible because of insufficient data.

OBJECTIVES: To determine the dose-related effects of different classes of antihypertensive medications, as monotherapy compared to placebo; as combination therapy compared to placebo or a single medication; or in comparisons of various doses within the same class, on systolic or diastolic blood pressure (or both) in children with hypertension.

SEARCH METHODS: We searched the Cochrane Hypertension Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (2013, Issue 9), Ovid MEDLINE (1946 to October 2013), Ovid EMBASE (1974 to October 2013) and bibliographic citations.

SELECTION CRITERIA: The selection criteria were deliberately broad due to there being few clinical trials in children. We included randomised controlled trials (RCTs) of at least two weeks duration comparing antihypertensive agents either as monotherapy or combination therapy with either placebo or another medication, or comparing different doses of the same medication, in children with hypertension. Hypertension was defined as an average (over a minimum of three readings) systolic or diastolic blood pressure (or both) on the 95(th) percentile or above for age, height and gender.
blood pressure by 6.50 mmHg (95% confidence interval (CI) -9.44 to -3.56) and diastolic blood pressure by 5.50 mmHg (95% CI -9.62 to -1.38) (low-quality evidence). High dose telmisartan (one trial, n = 76), when compared to placebo, reduced systolic blood pressure by -8.50 (95% CI -13.79 to -3.21) but not diastolic blood pressure (-4.80, 95% CI -9.50 to 0.10) (low-quality evidence). Beta blocker (metoprolol, one trial, n = 140), when compared with placebo, significantly reduced systolic blood pressure by 4.20 mmHg (95% CI -8.12 to -0.28) but not diastolic blood pressure (-3.20 mmHg 95% CI -7.12 to 0.72) (low-quality evidence). Beta blocker/diuretic combination (Bisoprolol/hydrochlorothiazide, one trial, n = 94) when compared with placebo, did not result in a significant reduction in systolic blood pressure (-4.0 mmHg, 95% CI -8.99 to 0.19) but did have an effect on diastolic blood pressure (-4.50 mmHg, 95% CI -8.26 to -0.74) (low-quality evidence). Calcium channel blocker (extended-release felodipine, one trial, n = 133) was not effective in reducing systolic blood pressure (-0.62 mmHg, 95% CI -2.97 to 1.73) or diastolic blood pressure (-1.86 mmHg, 95% CI -5.23 to 1.51) when compared with placebo. Further, there was no consistent dose response observed among any of the drug classes. The adverse events associated with the antihypertensive agents were mostly minor and included headaches, dizziness and upper respiratory infections.

**AUTHORS’ CONCLUSIONS:** Overall, there are sparse data informing the use of antihypertensive agents in children, with outcomes reported limited to blood pressure and not end organ damage. The most data are available for candesartan, for which there is low-quality evidence of a modest lowering effect on blood pressure. We did not find evidence of a consistent dose response relationship for escalating doses of angiotensin receptor blockers, calcium channel blockers or angiotensin-converting enzyme inhibitors. All agents appear safe, at least in the short term.


**Acute pancreatitis and hyperparathyroidism: a case series.**


**Author information:**

(1)Department of Gastrointestinal Sciences, Christian Medical College, Vellore, 632 004, India, sudipto.d.c@gmail.com.

Primary hyperparathyroidism is a rare cause of acute pancreatitis. Five consecutive patients with acute or recurrent acute pancreatitis and primary hyperparathyroidism were included. All patients had elevated serum calcium on admission and high levels of circulating parathyroid hormone. Both ultrasonography and Sestamibi scan was used to localize parathyroid adenoma. Except for one, all patients underwent parathyroidectomy and postoperative histology was consistent with parathyroid adenoma. One patient died while on treatment. Metabolic causes of acute pancreatitis, though uncommon, are important as early recognition helps management and prevents recurrence.

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**Danda D.**

**Cost of publication - who pays for it?**


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**INTL PMID: 24848286 [PubMed - in process]**  

**Ekbote AV(1), Danda S, Zankl A, Mandal K, Maguire T, Ungerer K.**

**Patient with mutation in the matrix metalloproteinase 2 (MMP2) gene - a case report and review of the literature.**


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(1)Christian Medical College, Clinical Genetics Unit, Vellore, India. E-mail: alkasethi@cmcvellore.ac.in.

Torg and Winchester syndromes and patients reported by Al-AqeelSawairi as well as nodulosis-arthropathy-
osteolysis (NAO) patients, patients with multicentric NAO share autosomal recessive inheritance. The common presenting symptomatology includes progressive osteolysis chiefly affecting the carpal, tarsal and interphalangeal joints. Here, we report a patient with Torg syndrome. Torg syndrome is caused by homozygous or compound heterozygous mutations in the matrix metalloproteinase 2 (MMP2) gene. MMP2 codes for a gelatinase that cleaves type IV collagen, a major component of basement membrane. The clinical presentation of our patient included moderate osteolysis of the small joints of the hands and knees, hirsutism, nodulosis sparing the palms and soles, corneal opacities and mild facial dysmorphism without gum hypertrophy. Genetic analysis showed that the patient was homozygous for a novel base variant c538 G>A (p.D180N) in the MMP2 gene. Both parents were carriers of the same mutated variant. Our patient had some previously unreported endocrine manifestations such as premature thelarche and elevated follicle-stimulating hormone levels.

George T(1), Shaikh AI(1), Thomas L(2), Kundavaram AP(1).
Severe methemoglobinemia due to insecticide poisoning.
Author information:
(1)Department of Medicine 4, Christian Medical College, Vellore, Tamil Nadu, India.
(2)Department of Medical Intensive Care Unit, Christian Medical College, Vellore, Tamil Nadu, India.

Methemoglobinemia is an altered state of hemoglobin resulting in impaired oxygen delivery to the tissues. Deliberate ingestion of certain insecticides and pesticides may result in this condition. We report a case of severe methemoglobinemia after deliberate ingestion of an insecticide marketed to be safe and containing only biological extracts and fillers. Methemoglobinemia should be suspected with low oxygen saturation on pulse oxymetry and the presence of chocolate colored blood. The methemoglobin level of 91% in our patient is the highest level reported among methemoglobinemia survivors.

Ghosh U(1), Thomas M, Mathai S.
 Syndrome of Insulin Resistance with Acanthosis Nigricans, Acral Hypertrophy and Muscle Cramps in an Adolescent - A Rare Diagnosis Revisited.
Author information:
(1)Department of Pediatrics, Christian Medical College, Vellore, Tamil Nadu, India.
The authors report a 14-y-old boy with insulin resistance, acanthosis nigricans, acral hypertrophy and muscle cramps. While there was a dramatic response of the muscle cramps to phenytoin therapy, some other features of metabolic syndrome did not respond to phenytoin therapy alone.

Giri S(1), Kindo AJ(2), Kalyani J(3).
Fatal Case of Candidemia due to Candida glabrata.
Author information:
(1)Department of Gastrointestinal Sciences, Christian Medical College, Vellore, Tamil Nadu, India.
(2)Department of Microbiology, Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu, India.
(3)Department of Microbiology, Sri Muthukumaran Medical College, Chennai, Tamil Nadu, India.

Govind B(1), Tete PI, Thomas N.
Percutaneous central line extravasation masquerading as an abscess.
Author information:
(1)Department of Neonatology, Christian Medical College, Vellore, Tamil Nadu, India.
Correspondence to: Dr Niranjan Thomas, Professor, Department of Neonatology, Christian Medical College Hospital, Vellore 632 004, Tamilnadu, India. niranjan@cmcvellore.ac.in.

BACKGROUND: Percutaneous central line insertion is a common procedure in the neonatal intensive care unit.
CASE CHARACTERISTICS: A preterm baby, who had a percutaneous central line inserted developed an erythematous swelling over the infraclavicular area.

OBSERVATION: A diagnosis of abscess was made, and an incision and drainage done that revealed a white fluid with high triglyceride content, confirming lipid extravasation.

OUTCOME: The lesion healed completely few days after removal of the catheter.

MESSAGE: This case highlights the importance of proper placement and confirmation of central line position.

Gupta A, Nair BR, Joseph V(1).
Mickey Mouse aneurysms: a rare case of bilateral superior cerebellar artery origin aneurysms.
Author information:
(1)Department of Neurological Sciences, Christian Medical College, Vellore, Tamil Nadu, India.

Gupta M(1), Shah J, Manipadam MT, Rao VM.
Case of pulmonary pneumocytoma: A probable cytological diagnosis with histopathological confirmation.
Author information:
(1)Assistant Professor, Department of General Pathology, Christian Medical College, Vellore, India.

Gupta M, Kandasamy S.
Coexisiting adenoma and granuloma involving the right inferior parathyroid gland with adjacent ectopic thymic tissue.
Author information:
Department of General Pathology, Christian Medical College, Vellore, Tamil Nadu, India.

Inflammatory lesions, particularly granulomas, involving adenoma of the parathyroid gland are rare. Ectopic thymic tissue is commonly associated with the thyroid and/or parathyroid gland due to their close embryonic relationship. We report a rare case of coexisting adenoma and granuloma of the parathyroid gland with adjacent ectopic thymic tissue.

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Gupta RD(1), Shetty S(1), Asha HS(2), Albert S(3), Paul TV(4).
Images in medicine - bisphosphonate induced atypical fracture.
Author information:
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(2)Associate Professor, Department of Endocrinology, Diabetes & Metabolism, Christian Medical College, Vellore - 632 004, Tamil Nadu, India.
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(4)Professor, Department of Endocrinology, Diabetes & Metabolism, Christian Medical College, Vellore - 632 004, Tamil Nadu, India.
Gupta V(1), Kumar M, Tete PI, Thomas N.
Simple Procedure-Serious Problems: Story of a Misplaced Nasogastric Tube.
Author information:
(1)Department of Neonatology, Christian Medical College, Vellore, 632004, Tamil Nadu, India.
NAT PMID: 24633951 [PubMed - as supplied by publisher] MISC

Jahan A(1), Agarwal I, Chaturvedi S.
An unusual cause of severe rickets.
Author information:
(1)Paediatric Nephrology unit, Department of Paediatrics, Christian Medical College, Vellore, Tamilnadu, 632004, India.

Jasper A(1), Sudhakar SV, Sridhar GV.
The multiple associations of Klippel-Feil syndrome.
Acta Neurol Belg. 2014 Jun 21. [Epub ahead of print]
Author information:
(1)Department of Radiology, Christian Medical College, Vellore, 632004, Tamil Nadu, India, anithapjp@gmail.com.
INTL PMID: 24950730 [PubMed - as supplied by publisher] MISC

Jegaraj KA(1), Saurabh RS, Rakesh PS.
Spider bite from South India.
Author information:
(1)Department of Family Medicine, Christian Medical College, Vellore, Tamil Nadu, India.
NAT PMID: 24823536 [PubMed - in process] MISC

Joel A, Bhatt AD, Samuel A, Chacko RT.
Cutaneous metastasis from testicular germ cell tumour.
Author information:
Department of Medical Oncology, Christian Medical College and Hospital, Vellore, India.
The skin is an unusual site of metastases from solid organ malignancies. We report the case of a patient with a malignant mixed non-seminomatous germ cell tumor of the testis, presenting with cutaneous metastasis, which was treated with salvage chemotherapy.
NAT PMID: PMC3897063 PMID: 24497691 [PubMed] MISC

Kapoor N, Shetty S, Shetty S, Paul TV.
Dysphagia in a patient with Addison’s disease.
Author information:
Christian Medical College, Vellore, Tamil Nadu, India.
INTL PMID: 24980997 [PubMed - in process] MISC

Kota AA(1), Nayak S(2), Mukha RP(3), Kekre NS(3).
Acute jejunal obstruction following laparoscopic nephrectomy.
Author information:
(1)Department of Surgery IV, Christian Medical College and Hospital, Vellore, Tamil Nadu. 632004, India. albertkota@cmcvellore.ac.in.
(2)Department of Surgery IV, Christian medical college and hospital, Vellore, India.
(3)Department of Urology, Christian medical college and hospital, Vellore, India.
INTL PMID: 25015624 [PubMed - in process] MISC
Kundavaram A(1), Francis NR, Jude AP, Varghese GN.
Acute infectious purpura fulminans due to probable spotted fever.
Author information:
(1)Department of Medicine, Christian Medical College, Vellore, Tamilnadu, India.

Purpura fulminans (PF) is associated with several infections, most notably with meningococcus, staphylococcus, and streptococcus infections. However, there are few reports of association of this entity with spotted fever from India. We report the case of a 55-year-old man who presented with fever, headache, and myalgia. On the seventh day of fever he developed nonblanching purple hemorrhagic purpura on the trunk and most prominently on the extremities consistent with purpura fulminans. Immunofluorescent assay confirmed the diagnosis of spotted fever. PF though common with rocky mountain spotted fever (RMSF) is rarely seen in association with Indian tick typhus, the usual cause of spotted fever in India.

PMID: 24823524 [PubMed - in process] MISC

Kundavaram AP(1), Das S(2), George VM(2).
Scrub typhus presenting as an acute abdomen.
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(1)Department of Medicine 4, Christian Medical College, Vellore, Tamil Nadu, India.
(2)Department of Medicine 1, Christian Medical College, Vellore, Tamil Nadu, India.

Scrub typhus is a mite-borne infectious disease caused by Orientia tsutsugamushi, which presents as an acute febrile illness with headache, myalgia, breathlessness, and an eschar, a pathognomonic sign, in a varying proportion of patients. However, this illness can present unusually with fever and severe abdominal pain mimicking acute abdomen. A careful search for an eschar in all patients with an acute febrile illness would provide a valuable diagnostic clue and avoid unnecessary investigations and surgical exploration.

PMCID: PMC3982349 PMID: 24741225 [PubMed] MISC

Kunder S, Pillai R, Sahajanandan R.
Dontukurthy et al: Large ascending aortic and arch aneurysm: an unusual cause of preoperative airway compromise.
Comment on
Author information:

Christian Medical College, Tamil Nadu, Vellore, India

PMID: 24508376 [PubMed - in process] MISC

Lionel AP(1), Joseph LK, Simon A.
Pierson Syndrome - A Rare Cause of Congenital Nephrotic Syndrome.
Author information:
(1)Department of Pediatrics Unit 1, Christian Medical College and Hospital, Vellore, Tamil Nadu, 632004, India, arulpremanand@gmail.com.

PMID: 24944146 [PubMed - as supplied by publisher] MISC

Mahajan R(1), Zachariah U.
Images in clinical medicine. Wing-beating tremor.
Author information:
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PMCID: 24988588 [PubMed - indexed for MEDLINE] MISC

Mahajan R, Simon EG.
Urinary retention as a cause of hyponatremia in an elderly man.
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Hyponatremia is a common disorder in elderly and can result in changes in cognition, seizures, coma or even respiratory arrest if not recognised and treated. Syndrome of inappropriate anti diuretic hormone secretion (SIADH) is the most common cause of
hyponatremia in elderly hospitalised patients and in most cases the etiology cannot be determined on routine investigations. We present a 76 year old male with symptomatic hyponatremia who had chronic urinary retention due to a urethral stricture. His sodium levels improved with catheterisation and worsened again after the catheter was removed. This supports the hypothesis that urinary retention and bladder distension can stimulate ADH release from the posterior pituitary, producing a picture similar to SIADH.


Naik D(1), Asha HS(2), Mathews SS(3), Paul TV(2).
Two siblings with Paget’s disease of bone.
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Paget’s disease of bone (PDB) is a chronic disorder characterised by focal areas of excessive osteoclastic bone resorption with a secondary increase in osteoblastic bone formation. First-degree relatives of patients with PDB are at seven times higher risk of developing this disorder, with a tendency towards earlier age at onset. We report two siblings who presented with features of polyostotic Paget’s disease. They presented with features of non-inflammatory back pain. Biochemical evaluation was unremarkable except for elevated serum alkaline phosphatase. Subsequently, radiology and bone scans were diagnostic of polyostotic PDB. They were treated with bisphosphonates with which they improved.

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Nair BR, Joseph V(1), Chacko G, Keshava SN.
Giant solid hemangioblastoma of the cerebellopontine angle: a technically challenging case.
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NAT  PMID: 24823754 [PubMed - in process]  MISC

Nair BR, Prabhu K(1), Chacko G, Chacko AG.
Calcified cavernous malformation of the lower cranial nerves.
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(1)Department of Neurosurgery, Christian Medical College, Vellore, Tamil Nadu, India.

NAT  PMID: 24608484 [PubMed - indexed for MEDLINE]  MISC

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(2)Department of Neurosurgery, Christian Medical College, Vellore, Tamil Nadu, India.

Prabhu SM(1), Irodi A(1), George PP(1), Sundaresan R(2), Anand V(2).
Missed intranasal wooden foreign bodies on computed tomography. Indian J Radiol Imaging. 2014 Jan;24(1):72-4. doi: 10.4103/0971-3026.130703. Author information:

(1)Department of Radiology, Christian Medical College, Vellore, Tamil Nadu, India.

(2)Department of Oto-Rhino-Laryngology, Christian Medical College, Vellore, Tamil Nadu, India.

We report a case of post traumatic impacted intranasal wooden foreign body in a 16 year old boy, which was undetected on Computed Tomography in the acute stage. Intranasal wooden foreign body may be missed on CT in the acute stage because of apparent air attenuation of the foreign body and lack of contrast with the surrounding intranasal air. Radiologists need to be aware of the CT imaging appearances of wood in various stages for early detection and management.

Prabhu SM(1), Yadav V(1), Irodi A(1), Mani S(1), Varghese AM(2).
IgG4-related disease with sinonasal involvement: A case series. Indian J Radiol Imaging. 2014 Apr;24(2):117-20. doi: 10.4103/0971-3026.134384. Author information:

(1)Department of Radiology, Christian Medical College, Vellore, Tamil Nadu, India.

(2)Department of Oto-Rhino-Laryngology, Christian Medical College, Vellore, Tamil Nadu, India.

We present the imaging findings in two cases of IgG4-related disease involving the sinonasal region in the
pediatric age group. Imaging findings in IgG4-related disease affecting the nasal cavity and paranasal sinuses have been rarely reported in literature. The diagnosis is made by a combination of clinical, imaging, and histopathologic findings. Radiologists should be aware of the imaging findings of this condition to ensure early diagnosis and treatment.

**RESULTS:** Seventy-nine students (86.8%) were multimodal in their learning preference, and 12 students (13.8%) were unimodal. The highest unimodal preference was K-7.7%. Surprisingly, there were no visual unimodal learners. The commonest learning preference was the bimodal category, of which the highest percentage was seen in the AR (33%) and AR (16.5%) category. The most common unimodal preference was ARK (8.9%). The total individual scores in each category were V-371, A-588, R/W-432, and K-581; auditory and kinesthetic being the highest preference. Visual mode had the lowest overall score. There was no significant difference in preference between the sexes.

**CONCLUSION:** Students possess a wide diversity in learning preferences. This necessitates teachers to effectively deliver according to the needs of the student. Multiple modalities of information presentation are necessary to keep the attention and motivation of our students requiring a shift from the traditional large-group teacher-centric lecture method to an interactive, student-centric multimodal approach.

Author information:
Department of Anesthesia, Christian Medical College, Vellore, Tamil Nadu, India.

PMID: 25024500 [PubMed]

Rid A(1), Saxena A(2), Baqui AH(3), Bhan A(4), Bines J(5), Bouesseau MC(6), Caplan A(7), Colgrove J(8), Dhai A(9), Gomez-Diaz R(10), Green SK(11), Kang G(12), Lagos R(13), Loh P(14), London AJ(15), Mulholland K(16), Neels P(17), Pitisuttithum P(18), Sarr SC(19), Selgelid M(20), Sheehan M(21), Smith PG(22).


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(5)Murdoch Childrens Research Institute, University of Melbourne, Parkville, VIC, Australia.
(6)Service Delivery and Safety, World Health Organization, Geneva, Switzerland.
(7)Division of Medical Ethics, NYU School of Medicine, New York, NY, United States.
(8)Mailman School of Public Health, Columbia University, New York, NY, United States.
(9)Steve Biko Centre for Bioethics, University of Witwatersrand, Johannesburg, South Africa.
(10)Instituto Mexicano del Seguro Social, Centro Médico Nacional Siglo XXI, Ciudad de Mexico, D.F., Mexico.
(11)Ethical, Social and Cultural Program for Global Health, St. Michael's Hospital and University of Toronto, Toronto, ON, Canada.
(12)Christian Medical College, Vellore, Tamil Nadu, India.
(13)Hospital de Niños Roberto del Río, Santiago de Chile, Chile.
(14)Melbourne Law School, University of Melbourne, Carlton, VIC, Australia.
(15)Department of Philosophy, Carnegie Mellon University, Pittsburgh, PA, United States.
(16)London School of Hygiene and Tropical Medicine, London, United Kingdom.
(17)Vaccine Advice BVBA, Zoersel, Belgium.
(18)Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.
(19)Ministry of Health and Social Action 1, Dakar-Fann, Senegal.
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(22)Medical Research Council (MRC) Tropical Epidemiology Group, London School of Hygiene and Tropical Medicine, London, United Kingdom.

Vaccines are among the most cost-effective interventions against infectious diseases. Many candidate vaccines targeting neglected diseases in low- and middle-income countries are now progressing to large-scale clinical testing. However, controversy surrounds the appropriate design of vaccine trials and, in particular, the use of unvaccinated controls (with or without placebo) when an efficacious vaccine already exists. This paper specifies four situations in which placebo use may be acceptable, provided that the study question cannot be answered in an active-controlled trial design; the risks of delaying or foregoing an efficacious vaccine are mitigated; the risks of using a placebo control are justified by the social and public health value of the research; and the research is responsive to local health needs. The four situations are: (1) developing a locally affordable vaccine, (2) evaluating the local safety and efficacy of an existing vaccine, (3) testing a new vaccine when an existing vaccine is considered inappropriate for local use (e.g. based on epidemiologic or demographic factors), and (4) determining the local burden of disease.

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Sabharwal S(1), Macaden AR(2), Abrol N(1), Mukha RP(1), Kekre NS(1).
A novel computer based stent registry to prevent retained stents: Will patient directed automated short message service and letter generator help?
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OBJECTIVE: The objective of this study was to evaluate the feasibility of a computer based stent registry with patient directed automated information system to prevent retained double J stents.

MATERIALS AND METHODS: A stent registry system was developed in collaboration with our Computerized Hospital Information Processing Service Department. This computer based stent registry with patient directed automated information system was integrated with the existing clinical work station. We reviewed the records retrospectively and assessed the feasibility of the system in reminding clinicians and patients regarding the stent and its date of removal.

RESULTS: In a short run at our department, this new system appeared feasible, with patients promptly responding to the short message service and letter alerts.

CONCLUSIONS: Computer based stent registry with patient directed automated information system is feasible in a clinical setting. A prospective study is needed for evaluation of its efficacy in preventing retained stents.

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Osteochondromas are the most common benign tumors of the bone. They mostly arise from the appendicular skeleton and present clinically in the second or third decade of life. Osteochondromas arising from the subaxial cervical spine and presenting after the 5th decade of life are extremely rare. We report a 52-year-old male patient who presented with numbness and subjective weakness of left upper and lower limbs and neck pain, and had lobulated bony hard fixed swelling in the right lower cervical paraspinal region. Radiological images revealed a bony swelling arising from C4 and C5 lamina with a cartilaginous cap and intraspinal extension. Excision biopsy with stabilisation of the spine was performed. Histopathological examination of the specimen confirmed the diagnosis of osteochondroma. We conclude surgical excision of such rare tumors, including the cartilaginous cap as well as the intraspinal component can reliably produce a good clinical outcome.

INTL
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Selot RS, Hareendran S, Jayandharan GR(1).
Developing immunologically inert adeno-associated virus (AAV) vectors for gene therapy: possibilities and limitations.

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Gene therapy has become a clinical reality as demonstrated by remarkable benefits seen in Phase I/II clinical trials for hemophilia B, lipoprotein lipase deficiency and Leber’s congenital amarousis. The choice of, and the improved understanding in vector characteristics have contributed significantly to this success. The adeno-associated virus (AAV) vectors used in these trials have been long known to be relivel safe and efficacious. However, certain factors, most notably host immunity to the vector, prevent their widespread use. In patients who have pre-existing antibodies to AAV, these vectors will be rapidly cleared. Administration of a relatively high initial dose of vector to achieve and sustain a higher margin of therapeutic benefit is limited by concerns of vector dose-dependent T cell response. Frequent vector administration necessitated by the non-integrating nature of the virus is difficult due to the variable, yet significant host immunological memory. Thus generation of AAV vectors that are immunologically inert is pivotal for the long-term success with this promising vector system. Several strategies, that aim targeted disruption of antigenic sites or those that chemically modify the vectors have been proposed for host immune evasion. While these approaches have been successful in the pre-clinical model systems, this continues to be a field of intense experimentation and constant improvisation due to limited information available on vector immunology or data from human studies. This review forms a comprehensive report on current strategies available to generate immunologically inert AAV vectors and their potential in mediating long term gene transfer.

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PURPOSE: The aim of this study was to describe a case series of Papulaspora equi keratomycosis, with clinical and laboratory characteristics of an organism that has not been reported from scrapings of corneal ulcers from humans.

METHODS: This is a retrospective chart review of 5 patients whose diagnostic corneal scrapings had grown P. equi on culture between 2008 and 2013. The clinical presentation, diagnostic tests, management, and the outcome of the ulcers are described.

RESULTS: All patients showed characteristic features of fungal corneal ulcers on clinical examination. Only
2 of the 5 patients reported having a history of injury to their eyes. One patient showed surface pigmentation that could mimic a dematiaceous ulcer. All the patients responded to topical antifungal treatment with 5% natamycin or prepared 2% ketoconazole drops.

CONCLUSIONS: Corneal ulcers may be caused by rare organisms, as in our series of patients who had P. equi keratomycosis, a hitherto unreported human pathogen. All the patients responded to treatment with conventional topical antifungal medications.


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In inflammatory carotid pseudotumor is a rare differential of a unilateral neck swelling in the carotid triangle. A 48-year-old man presented with a firm nontender gradually progressive left neck swelling for five months. Computed tomography angiogram revealed a mass encasing the common carotid. Patient underwent excision; histopathology was reported as inflammatory pseudotumor. Patient had a recurrence after eight months. Steroids were prescribed with which the swelling resolved, patient remained recurrence free at two-year follow-up.


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Vascular complications in closed clavicular fractures are uncommon, with an incidence of only 0.4%. Subclavian artery injury can present acutely or can have a delayed presentation with arm ischemia. We report the case of an undetected subclavian pseudoaneurysm in a patient with a nonunion fracture clavicle who was referred with persistent ischemia following attempted brachial embolectomy at another center, along with a review of literature to support the hypothesis that in addition to repair of the aneurysm, treatment of the psuedarthrosis by fixation of the clavicle is essential.
Shetty S(1), Kapoor N, Prabhu AJ, Paul TV.
Paget's disease: a unique case snippet.
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Shetty S(1), Varghese RT(2), Shanthy N(3), Paul TV(1).
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Focal osteosclerosis of the skull in primary hyperparathyroidism.
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Sreekanth R(1), Pallapati SC(1), Thomas BP(2).
Tuberculous Botryomycosis of the Hand: Case Report.
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We report a case of a 17-year-old boy who presented with botryoid lesions of both hands. These lesions resembled those of cutaneous botryomycosis. We treated him with surgical debridement and were unable to isolate infective agents initially. However, 3 months later Mycobacterium tuberculosis grew in the culture. One year of antituberculous drug therapy resulted in healing of the lesions.

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Haemophilia care - beyond the treatment guidelines.
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Care for people with haemophilia (PWH) has improved much over the last two decades leading to near normal lives for those receiving early regular prophylaxis with clotting factor concentrates (CFC). Yet, there are significant limitations of those practices. In the absence of a well-defined optimal prophylaxis protocol, there are wide variations in practices with a two to threefold difference in doses. In those parts of the world where there are constraints on the availability of CFC, episodic replacement remains the norm for most patients even though it is evident that this does not change the natural history of the disease over a wide range of doses. Suitable prophylactic protocols therefore need to be developed wherever possible at these doses. Finally, there are only limited data on long-term outcomes in haemophilia from anywhere in the world. The practice of documenting specific outcomes as part of the regular evaluation of PWH needs to be established and the appropriate instruments used to assess them. Definitions of
clinical events and endpoints of interventions in clinical studies are being developed to help such data collection. The correlations between different replacement therapy protocols and specific outcomes will help define what is best at different dose levels. Such data will allow better health planning and treatment choices throughout the world.

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**Syed KA(1), Paul RR(2), Varghese AM(2), Joseph NA(2).**

Emergency ventilation with a Chevalier Jackson’s metal tracheostomy tube.


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Chevalier Jackson’s metal tracheostomy tube is the oldest tracheostomy tube and has survived to the present day. This is probably because it is easy to use and cost-effective. However its biggest limitation is that it lacks provision to connect to a ventilating circuit in an emergency. Here we describe a simple and effective technique for ventilation with Chevalier Jackson’s metal tracheostomy tube. Ventilation can be achieved by connecting the tracheostomy tube to an appropriate size universal 15mm endotracheal tube connector. We have also worked out a formula for selection of appropriate connector for various sizes of tracheostomy tube.

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**Post traumatic nasolacrimal drainage obstruction is an uncommon presentation of naso-orbito-ethmoid fracture. Dacryocystorhinostomy (DCR) with or without silicon intubation is the universally accepted treatment modality. Here we report a case of recurrent lacrimal sac abscess due to post traumatic nasolacrimal drainage obstruction following naso-orbito-ethmoid fracture. The patient had previously undergone incision and drainage thrice and twice failed DCR. In the background of extensive nasal synechiae and twice failed DCR, dacryocystectomy was performed. Post operatively patient has improved and is symptom free for past 14 months. This is the first report of a successful dacryocystectomy for a post traumatic dacryocystitis.**

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Varghese MJ(1), Hussain T, George PV, Pati PK, Jose JV.

The shadow within: a colossal left atrium.


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Dacryocystectomy: an uncommon indication—a case report.


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Varghese MJ, Patel TV, George PV, Pati PK, Jose VJ. Mammoth right atrium.
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An unusually long survival of a patient with glioblastoma of spinal cord: a case report.
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Primary glioblastoma of spinal cord are rare and are associated with poor survival especially in adults. We report a case of glioblastoma of thoracic spinal cord (D3 to D6) in an adult treated with partial resection surgery and radiation therapy with a survival of six years with good quality of life. The patient had paraplegia at presentation but improved after surgery and radiation therapy to grade 4 in both lower limbs. After 5 years, he developed new lesion in a different location of the spine (L1, L2 & L5) along with multiple lesions over entire spine and was treated with radiation therapy and a year later developed a new lesion intracranially in the posterior fossa involving cerebellopontine angle region infiltrating brainstem. He was treated with palliative radiotherapy and is on chemotherapy with Temozolomide and is still alive with ability to do activities of daily living at the time of this report. Radiation therapy provided prolonged local control with effective palliation of symptoms and good quality of life in this patient enabling to do activities of daily living.

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Vyas R(1), Zacharah A(2), Swamidasan I(3), Doris P(4), Harris I(5).
Blended distance education program for junior doctors working in rural hospitals in India.
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CONTEXT: Distance learning, supported with supervised clinical work, has been successful in helping doctors located in remote rural areas to practice effectively. Graduates of Christian Medical College (CMC), Vellore, India, have a 2-year service obligation to work in small hospitals mainly located in rural areas. The Fellowship in Secondary Hospital Medicine (FSHM) program is a year-long blended on-site and distance learning program, designed by CMC to support and provide education opportunities for its recent graduates working in small hospitals in rural areas. The FSHM program was designed to help junior doctors develop the knowledge and skills to practice effectively in rural hospitals.

ISSUES: The FSHM program consists of 15 paper-based distance learning modules focused on helping to develop knowledge to practice in rural hospitals; three contact sessions at CMC, which focused on developing the necessary skills; project work focused on improving local health services; and networking between peers and with faculty. Two years after implementation of the FSHM program in 2007, the vast majority of students (81%) and faculty (80%) rated the distance learning modules as very good or excellent in helping students develop the knowledge to practice in secondary hospitals. Also, most of the students (88%) and faculty (87%) rated the contact sessions as good or very good in helping students to apply what they had learned in secondary hospitals. Focus group discussions revealed that all of the program participants recognized that the distance learning modules and contact sessions helped them in providing patient care in rural hospitals.
LESSONS LEARNED: Well-designed distance learning modules, supported with contact sessions by medical school faculty members, help junior doctors to practice effectively in rural hospitals and reduce their isolation.

INTERNATIONAL PUBLICATIONS = 164
NATIONAL PUBLICATIONS = 73

TOTAL PUBLICATIONS FROM JAN 2014 – JUN 2014 = 237

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Senapati J(1), Devasia AJ(1), Ganapule A(1), George L(2), Viswabandya A(1).
Sorafenib Induced Hand Foot Skin Rash in FLT3 ITD Mutated Acute Myeloid Leukemia-A Case Report and Review of Literature.
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Sorafenib is a novel small molecule multiple kinase inhibitor which has been used for metastatic renal cancer, hepatocellular cancer. Sorafenib induced skin rash has been discussed as a side effect in trials in both, FLT3 wild type and mutated acute myeloid leukemia (AML), as monotherapy or as combination with other chemotherapeutic agents. We describe a patient with FLT 3 ITD mutated AML, who was started on adjunctive Sorafenib therapy. Skin reactions manifested as NCI Grade III palmoplantar erythrodysesthesia (PPE), requiring drug discontinuation. Several pathogenic mechanisms have been implicated in Sorafenib induced skin reactions, but none has been conclusively proven. While treatment options are varied for early stage skin reactions, drug discontinuation remains the only possible therapy presently for severe grade skin reaction.