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1: Agarwal N, Dutta Satyarthee G. Symptomatic Diffuse Vasospasm After Resection of Temporal Ganglioglioma: Review of the Literature with Case Illustration. *World Neurosurg.* 2019 Dec;132:230-235. doi: 10.1016/j.wneu.2019.08.239. Epub 2019 Sep 7. Review. PubMed PMID: 31505290.

**BACKGROUND:** Symptomatic cerebral vasospasm may occur in the setting of aneurysmal subarachnoid hemorrhage, traumatic brain injury, or after anterior skull base surgery, but its occurrence is extremely rare in the background of glioma surgical resection.

**CASE DESCRIPTION:** We present a rare case of symptomatic diffuse vasospasm, which is the fourth reported case of symptomatic vasospasm after temporal lobectomy and the third in the setting of a glial tumor. This patient, a 10-year-old boy, developed bilateral, progressive cerebral infarcts because of diffuse vasospasm after anteromesial temporal lobectomy for a left temporal ganglioglioma leading to significant morbidity.

**CONCLUSIONS:** The risk factors, likely pathogenesis and the importance of early diagnosis and timely institution of treatment, in such cases are discussed in the background of relevant literature. The current case represents the first report of symptomatic diffuse vasospasm occurring after surgical resection of intracranial ganglioglioma in the Western literature.

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PMID: 31505290 [Indexed for MEDLINE]

2: Agarwal R, Gagrani M, Mahajan A, Sharma N. Fulminant *Sphingomonas paucimobilis* keratitis: case study and review of literature. *BMJ Case Rep.* 2019 Dec 3;12(12). pii: e231642. doi: 10.1136/bcr-2019-231642. PubMed PMID: 31801779.

*Sphingomonas paucimobilis* is a low-virulence gram-negative bacillus known to cause various ocular infections such as endophthalmitis, panophthalmitis and keratitis that are usually associated with an underlying risk factor such as peri-partum or postpartum phase, cataract surgery, contact lens use, neurotrophic keratopathy or ocular trauma. We report a case of spontaneously occurring perforated corneal ulcer caused by the organism in a young man managed by penetrating keratoplasty. The course was followed by endophthalmitis with graft infection culminating in phthisis bulbi despite aggressive medical and surgical management. Along with reporting this case, we also present a review of literature on ocular infections caused by the same organism.

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PMID: 31801779

3: Aggarwal S, Jena S, Panda S, Sharma S, Dhawan B, Nath G, Singh NP, Nayak KC, Singh DV. Antibiotic Susceptibility, Virulence Pattern, and Typing of *Staphylococcus aureus* Strains Isolated From Variety of Infections in India. *Front Microbiol.* 2019 Dec 4;10:2763. doi: 10.3389/fmicb.2019.02763. eCollection 2019. PubMed PMID: 31866962; PubMed Central PMCID: PMC6904308.

*Staphylococcus aureus* is one of the major causes of nosocomial infections. This organism produces powerful toxins and cause superficial lesions, systemic infections, and several toxemic syndromes. A total of 109 *S. aureus* strains isolated from a variety of infections like ocular diseases, wound infection, and sputum were included in the study. Minimum inhibitory concentration (MIC) was

determined against 8 antimicrobials. PCR determined the presence of 16S rRNA, nuc, mecA, czrC, qacA/B, pvl, and toxin genes in *S. aureus* isolates. Pulse-field gel electrophoresis (PFGE), multi-locus sequence typing (MLST), SCCmec, spa-, and agr-typing and serotyping determined the diversity among them. All isolates of *S. aureus* were resistant to two or more than two antibiotics and generated 32 resistance patterns. These isolates were positive for 16S rRNA and *S. aureus*-specific nuc gene, but showed variable results for mecA, czrC, and qacA/B and pvl genes. Of the 32 methicillin-resistant *S. aureus* (MRSA), 13 strains carried SCCmec type V, seven type IV, two type III, and nine carried unreported type UT6. Of the 109 strains, 98.2% were positive for hlg, 94.5% for hla, 86.2% for sei, 73.3% for efb, 70.6% for cna, 30.2% for sea, and 12.8% for sec genes. Serotypes VII and VI were prevalent among *S. aureus* strains. PFGE analysis grouped the 109 strains into 77 clusters. MLST classified the strains into 33 sequence types (ST) and eight clonal complexes (CCs) of which 12 were singletons, and two belong to new allelic profiles. Isolates showed 46 spa-types that included two new spa-types designated as t14911 and t14912. MRSA and methicillin-susceptible *S. aureus* (MSSA) isolates were diverse in terms of antibiotic resistance pattern, toxin genotypes, SCCmec types, serotypes and PFGE, MLST, and spa-types. However, few isolates from eye infection and wound infection belong to CC239, ST239, and spa-type t037/t657. The study thus suggests that *S. aureus* strains are multidrug resistant, virulent, and diverse irrespective of sources and place of isolation. These findings necessitate the continuous surveillance of multidrug-resistant and virulent *S. aureus* and monitoring of the transmission of infection.

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4: Agrawal K, Garg R, Bhatnagar S. Knowledge and Awareness of End-of-life Care among Doctors Working in Intensive Care Units at a Tertiary Care Center: A Questionnaire-based Study. *Indian J Crit Care Med.* 2019 Dec;23(12):568-573. doi: 10.5005/jp-journals-10071-23293. PubMed PMID: 31988547; PubMed Central PMCID: PMC6970212.

**Introduction:** End-of-life care (EOLC) is an increasingly important concern in the management of terminally ill patients. Effective EOLC depends significantly on the physicians working in the critical care units. Thus, adequate knowledge of critical care professionals regarding EOLC is important. We conducted this study to evaluate the awareness and knowledge of doctors working in critical care units toward EOLC.

**Materials and methods:** Doctors working in critical care units were invited to fill paper-based questionnaire. The validated questionnaire was constructed based on the existing literature on EOLC and expert opinion. The questionnaire comprised four sections: demographic details, experience with EOLC situations, general awareness of EOLC, and specific awareness of EOLC in clinical practice. The collected data were analyzed by descriptive analysis.

**Results:** Most respondents had not counseled more than five families regarding EOLC over 1 month. Majority of the respondents (81.7%) had heard of EOLC; the major source of information being their work in the concerned specialty. Only 29.2% of the respondents applied EOLC principles in their clinical practice. Main barriers were lack of information and training. Only 20.3% of the respondents were aware of Indian guidelines about EOLC. Majority of the respondents disagree regarding the usage of critical care units and resuscitation of terminally ill patients and were in favor of home care. One-third respondents felt uncomfortable

in discussing EOLC issues with the families. Half of the respondents felt that they were only somewhat competent in managing EOLC issues. Most respondents opined that training and education in medical curriculum for terminally ill patients are lacking and were in strong favor of inclusion of specific training for the same.

Conclusion: The EOLC needs to be an integral part of critical care management and teaching curriculum. An integral referral system may also be an option for various advance disease patients getting treatment from critical care specialists for EOLC decision.

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5: Agrawal R, Agarwal A, Jabs DA, Kee A, Testi I, Mahajan S, McCluskey PJ, Gupta A, Palestine A, Denniston A, Banker A, Invernizzi A, Fonollosa A, Sharma A, Kumar A, Curi A, Okada A, Schlaen A, Heiligenhaus A, Kumar A, Gurbaxani A, Bodaghi B, Islam Shah B, Lowder C, Tappeiner C, Muccioli C, Vasconcelos-Santos DV, Goldstein D, Behra D, Das D, Makhoul D, Baglivo E, Denisova E, Miserocchi E, Carreno E, Asyari F, Pichi F, Sen HN, Uy H, Nascimento H, Tugal-Tutkun I, Arevalo JF, Davis J, Thorne J, Hisae Yamamoto J, Smith J, Garweg JG, Biswas J, Babu K, Aggarwal K, Cimino L, Kuffova L, Agarwal M, Zierhut M, Agarwal M, De Smet M, Tognon MS, Errera MH, Munk M, Westcott M, Soheilian M, Accorinti M, Khairallah M, Nguyen M, Kon OM, Mahendradas P, Yang P, Neri P, Ozdal P, Amer R, Lee R, Distia Nora R, Chhabra R, Belfort R, Mehta S, Shoughy S, Luthra S, Mohamed SO, Chee SP, Basu S, Teoh S, Ganesh S, Barisani-Asenbauer T, Guex-Crosier Y, Ozyazgan Y, Akova Y, Habot-Wilner Z, Kempen J, Nguyen QD, Pavesio C, Gupta V; Collaborative Ocular Tuberculosis Study (COTS) Group. Standardization of Nomenclature for Ocular Tuberculosis - Results of Collaborative Ocular Tuberculosis Study (COTS) Workshop. *Ocul Immunol Inflamm*. 2019 Dec 10:1-11. doi: 10.1080/09273948.2019.1653933. [Epub ahead of print] PubMed PMID: 31821096.

Purpose: To standardize a nomenclature system for defining clinical phenotypes, and outcome measures for reporting clinical and research data in patients with ocular tuberculosis (OTB). Methods: Uveitis experts initially administered and further deliberated the survey in an open meeting to determine and propose the preferred nomenclature for terms related to the OTB, terms describing the clinical phenotypes and treatment and reporting outcomes. Results: The group of experts reached a consensus on terming uveitis attributable to tuberculosis (TB) as tubercular uveitis. The working group introduced a SUN-compatible nomenclature that also defines disease "remission" and "cure", both of which are relevant for reporting treatment outcomes. Conclusion: A consensus nomenclature system has been adopted by a large group of international uveitis experts for OTB. The working group recommends the use of standardized nomenclature to prevent ambiguity in communication and to achieve the goal of spreading awareness of this blinding uveitis entity.

DOI: 10.1080/09273948.2019.1653933

PMID: 31821096

6: Ahmad J, Khubaib M, Sheikh JA, Panca R, Kumar S, Srinivasan A, Babu MM, Hasnain SE, Ehtesham NZ. Disorder-to-order transition in PE-PPE proteins of

*Mycobacterium* tuberculosis augments the pro-pathogen immune response. FEBS Open Bio. 2020 Jan;10(1):70-85. doi: 10.1002/2211-5463.12749. Epub 2019 Dec 17. PubMed PMID: 31643141; PubMed Central PMCID: PMC6943233.

A growing body of evidence supports the hypothesis that intrinsically disordered proteins often mediate host-pathogen interactions and modulate host functions for pathogen survival and virulence. *Mycobacterium tuberculosis* (M.tb) has evolved largely through reductive evolution, with a few exceptions such as the glycine-alanine-rich PE-PPE/PGRS protein family, which has been expanding in pathogenic mycobacteria. Here, our analyses of the M.tb proteome and secretome revealed that the PE-PGRS subfamily is enriched for disordered regions and disordered binding sites, pointing to their importance in host-pathogen interactions. As a case study, the secondary structure of PE35-PPE68 and PE32-PPE65 of the pathogenesis-related RD1 and RD8 regions was analyzed through Fourier-transform infrared spectroscopy. These disordered proteins displayed a considerable structural shift from disordered to ordered while engaged in the formation of complexes. While these proteins are immunogenic individually and enhance the pro-pathogen response, their corresponding complexes enhanced the responses manifold as displayed here by PE35 and PPE68. It is likely that M.tb exploits such disorder-order structural dynamics as a strategy to mount a pro-pathogen response and subvert host defense for productive infection. This functional gain also serves as a means to compensate genomic content loss due to reductive evolution.

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7: Angmo D, Dhiman R, Chaurasia S, Sihota R, Tandon R. Pigment dispersion syndrome presenting as endothelial dystrophy: An atypical presentation. J Curr Ophthalmol. 2018 Dec 2;31(4):446-449. doi: 10.1016/j.joco.2018.11.004. eCollection 2019 Dec. PubMed PMID: 31844799; PubMed Central PMCID: PMC6896454.

**Purpose:** To describe an atypical presentation of pigment dispersion syndrome (PDS) with diffuse, homogeneous pigment deposition on the corneal endothelium and its management.

**Methods:** A 44-year-old female was referred to a cornea clinic as a case of endothelial dystrophy. Slit-lamp examination revealed bilateral, diffuse, and homogeneous pigment deposition on entire corneal endothelium without any iris transillumination defects. Intraocular pressure (IOP) at presentation were 18 mmHg OD and 16 mmHg OS. Gonioscopy showed dense, homogeneous pigment deposition in the angles. The optic nerve head examination revealed a cup disc ratio of 0.6:1-0.7:1 in both eyes with neuroretinal rim thinning.

**Results:** Peripheral Nd:YAG laser peripheral iridotomy (PI) was performed. On follow-up, a localized clear pigment free endothelial area was noted over the iridotomy sites bilaterally. IOP was well controlled within 12-14 mmHg with prostaglandin analogue at last follow-up of 24 months.

**Conclusions:** Diffuse homogeneous pigment dispersion on the endothelium may occur in atypical cases of PDS which may clear in the areas overlying the PI site and, therefore, should not be confused with endothelial disease. This case demonstrates the significance of a thorough clinical evaluation in cases with unusual presentation.

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DOI: 10.1016/j.joco.2018.11.004  
PMCID: PMC6896454  
PMID: 31844799

8: Anupa G, Sharma JB, Roy KK, Sengupta J, Ghosh D. An assessment of the multifactorial profile of steroid-metabolizing enzymes and steroid receptors in the eutopic endometrium during moderate to severe ovarian endometriosis. *Reprod Biol Endocrinol*. 2019 Dec 26;17(1):111. doi: 10.1186/s12958-019-0553-0. PubMed PMID: 31878927; PubMed Central PMCID: PMC6933937.

**BACKGROUND:** Previous studies of expression profiles of major endometrial effectors of steroid physiology in endometriosis have yielded markedly conflicting conclusions, presumably because the relative effects of type of endometriosis, fertility history and menstrual cycle phases on the measured variables were not considered. In the present study, endometrial mRNA and protein levels of several effectors of steroid biosynthesis and action in patients with stage III-IV ovarian endometriosis (OE) with known fertility and menstrual cycle histories were compared with the levels in control endometrium to test this concept.

**METHODS:** Endometrial samples were collected from patients without endometriosis (n=32) or OE stages III-IV (n=52) with known fertility and cycle histories. qRT-PCR and immunoblotting experiments were performed to measure levels of NR5A1, STAR, CYP19A1, HSD17Bs, ESRs and PGR transcripts and proteins, respectively. Tissue concentrations of steroids (P4, T, E1 and E2) were measured using ELISAs.

**RESULTS:** The levels of expression of aromatase and ER $\beta$  were lower (P<0.0001) and 17 $\beta$ -HSD1 (P<0.0001) and PRA (P<0.01) were higher in OE endometrium. Lower aromatase levels and higher 17 $\beta$ -HSD1 levels were detected in fertile (aromatase: P<0.05; 17 $\beta$ -HSD1: P<0.0001) and infertile (aromatase: P<0.0001; 17 $\beta$ -HSD1: P<0.0001) OE endometrium than in the matched control tissues. Both proliferative (PP) and secretory (SP) phase OE samples expressed aromatase (P<0.0001) and ER $\beta$  (PP: P<0.001; SP: P<0.01) at lower levels and 17 $\beta$ -HSD1 (P<0.0001) and PRA (PP: P<0.01; SP: P<0.0001) at higher levels than matched controls. Higher 17 $\beta$ -HSD1 (P<0.01) and E2 (P<0.05) levels and a lower (P<0.01) PRB/PRA ratio was observed in infertile secretory phase OE endometrium than in control.

**CONCLUSIONS:** We report that dysregulated expression of 17 $\beta$ -HSD1 and PGR resulting in hyperestrogenism and progesterone resistance during the secretory phase of the menstrual cycle, rather than an anomaly in aromatase expression, was the hallmark of eutopic endometrium from infertile OE patients. Furthermore, the results provide proof of concept that the fertility and menstrual cycle histories exerted relatively different effects on steroid physiology in the endometrium from OE patients compared with the control subjects.

DOI: 10.1186/s12958-019-0553-0  
PMCID: PMC6933937  
PMID: 31878927

9: Anuragi RP, Lakshmy R, Bhardwaj DN, Bharti DR, Sikary AK, Behera C. Association of lipid profile with completed suicides: A hospital-based case-control study. *Asian J Psychiatr*. 2019 Dec;46:19-20. doi: 10.1016/j.ajp.2019.09.028. Epub 2019 Sep 27. PubMed PMID: 31586796.

10: Arora S, Passah A, Nalli H, Goyal H, Tripathi M, Shamim SA, Das CJ, Kumar R. Posterior Reversible Encephalopathy Syndrome: Pattern on (18)F-Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography Correlated with Magnetic Resonance Imaging in Pediatric Hypertensive Encephalopathy. *Indian J Nucl Med*.

2020 Jan-Mar;35(1):72-73. doi: 10.4103/ijnm.IJNM\_149\_19. Epub 2019 Dec 31. PubMed PMID: 31949377; PubMed Central PMCID: PMC6958944.

Posterior reversible encephalopathy syndrome (PRES) is characterized clinically by headache, seizures, vomiting, altered mental status, and blurred vision. However, with overlapping and atypical clinical symptoms, PRES becomes a diagnostic challenge. We describe the imaging findings of PRES in magnetic resonance imaging and 18F-fluorodeoxyglucose positron emission tomography-computed tomography in an 11-year-old child who presented with features of hypertensive encephalopathy.

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PMID: 31949377

11: Arora S, Damle NA, Meel R, Sharma S, Sen S, Bal C, Lata K, Prakash S, Yadav D, Angamuthu M. Orbital IgG4 Disease: Imaging Findings on 68Ga-DOTANOC PET/CT. Nucl Med Mol Imaging. 2019 Dec;53(6):432-435. doi: 10.1007/s13139-019-00611-z. Epub 2019 Oct 25. PubMed PMID: 31867079; PubMed Central PMCID: PMC6898689.

Immunoglobulin G4 (IgG4)-related diseases are a spectrum of systemic inflammatory conditions of unknown etiology, which are characterized by infiltration of tissues by IgG4 plasma cells and sclerosing inflammation (Cheuk and Chan Adv Anat Pathol 17:303-32, 2010). Although this condition was initially described in relation to autoimmune pancreatitis, now it has been reported in almost every organ system of body (Zen and Nakanuma Am J Surg Pathol 34:1812-9, 2010, Masaki et al. Ann Rheum Dis 68:1310-5, 2009). Orbital involvement by IgG4 disease can involve extraocular muscles (EOM), lacrimal glands, conjunctiva, eyelids, infraorbital nerve, orbital fat, and nasolacrimal system (McNab and McKelvie. Ophthal Plast Reconstr Surg 31:167-78, 2015, Katsura et al. Neuroradiology 54:873-82, 2012). The basis of using 68Ga-DOTANOC PET/CT in IgG4 orbital disease is the known expression of somatostatin receptors in chronic inflammatory cells (Cuccurullo et al. Indian J Radiol Imaging 27:509-16, 2017) and also avidity shown previously in other IgG4-related diseases (Cheng et al. Clin Nucl Med 43:773-6, 2018).

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DOI: 10.1007/s13139-019-00611-z  
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PMID: 31867079

12: Arora S, Kumar R, Passah A, Tripathi M, Agarwala S, Khadgawat R, Bal C. Prospective evaluation of 68Ga-DOTANOC positron emission tomography/computed tomography and 131I-meta-iodobenzylguanidine single-photon emission computed tomography/computed tomography in extra-adrenal paragangliomas, including uncommon primary sites and to define their diagnostic roles in current scenario. Nucl Med Commun. 2019 Dec;40(12):1230-1242. doi: 10.1097/MNM.0000000000001096. PubMed PMID: 31633647.

AIM: To evaluate Ga-DOTANOC positron emission tomography/computed tomography (PET/CT) and I-meta-iodobenzylguanidine single-photon emission computed tomography/computed tomography (131I-MIBG SPECT/CT) in patients with paragangliomas, including uncommon primaries.  
METHODS: Ninety patients were prospectively enrolled, and both scans were done within 2 weeks of each other. Lesions were grouped as Head/neck, abdominal,

uncommon primary paraganglioma, and metastatic lesions. In most histopathology was used as reference standard.

RESULTS: PET/CT had sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 97%, 94%, 99%, 88%, 97% respectively on patient wise analysis (90) and 98%, 94%, 99%, 85% and 97% respectively on lesion wise analysis (149). Comparison with MIBG SPECT/CT: Significant difference in sensitivities noted (PET/CT-98%, I-131 MIBG -39%) ( $P < 0.001$ ), however, no significant difference in specificities (94% and 100%, respectively). Group-wise analysis: Head/Neck: Significant difference noted between PET/CT (sensitivity 100%) and I-131 MIBG SPECT/CT (sensitivity 22%) ( $P = 0.001$ ). Abdominal: No significant difference noted in sensitivities and specificities of PET/CT and I-131 MIBG SPECT/CT. Uncommon paraganglioma: PET/CT detected 10 of 11, while I-131 MIBG detected only 2 of 11 uncommon paraganglioma. Metastatic sites: Significant difference noted between PET/CT (sensitivity 97%) and I-131 MIBG SPECT/CT (sensitivity 33%) ( $P < 0.0001$ ).

CONCLUSION: The study demonstrates high diagnostic accuracy of Ga-DOTANOC PET/CT and superiority over I MIBG SPECT/CT for evaluation of extra-adrenal paraganglioma. The current diagnostic role of I-131 MIBG seems limited to abdominal paragangliomas and for theranostic purpose.

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PMID: 31633647

13: Arya DS, Chowdhury S, Chawla R, Das AK, Ganie MA, Kumar KMP, Nadkar MY, Rajput R. Clinical Benefits of Fixed Dose Combinations Translated to Improved Patient Compliance. *J Assoc Physicians India*. 2019 Dec;67(12):58-64. PubMed PMID: 31801333.

Pharmacotherapy with fixed dose combination (FDC) drugs is becoming popular as evidence-based clinical guidelines recommend using multiple therapeutic agents in complex regimens for many chronic diseases including type 2 diabetes mellitus (T2DM). FDC formulations have unique advantages such as complementary mechanism of action, synergistic effects, better tolerability, elongated product life-cycle management, and cost savings. Polypharmacy is a frequent problem in T2DM patients having hypertension, dyslipidemia, and other comorbidities. Use of FDCs is a rational approach for achieving optimal therapeutic benefits while minimizing pill-burden. Greater convenience with decreased pill-burden leads to improved adherence, resulting in superior clinical outcomes and greater cost-effectiveness. However, the general guidance for the clinical development and approval of FDC drugs in India is not much standardized. For rationale approval, the central and state regulators must harmonize their procedures for licensing FDCs. Because regulatory approval of FDCs is based on bioavailability data, similar to the way generic medications are approved, the lack of prospective, randomized controlled trials directly comparing FDCs with their component drugs administered as separate pills should not be considered a limitation to their use. Nevertheless, all new and existing FDC products should be subjected to submission of longterm safety surveillance through closely monitored national level postmarketing studies.

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14: Baa AK, Naik RD, Vanidassane I, Arora S, Shamim SA, Mallick S, Batra A. Unusual Gastric Metastasis in Triple-Negative (Estrogen Receptor/Progesterone Receptor/HER2neu Negative) GATA-Binding Protein 3-Positive Breast Cancer. *Indian J Nucl Med*. 2020 Jan-Mar;35(1):82-83. doi: 10.4103/ijnm.IJNM\_156\_19. Epub 2019

Dec 31. PubMed PMID: 31949382; PubMed Central PMCID: PMC6958957.

Triple-negative breast cancer (TNBC) accounts for 20%-25% of breast cancer cases. Around 10%-15% of patients with breast cancer present with upfront metastasis. Lymph node, bone, and liver are common sites of metastasis in hormone-positive breast cancer while brain, lungs, and liver in TNBC. Although visceral metastasis is common in TNBC, metastasis to stomach is unusual. Morphological similarity of primary gastric carcinoma and lobular invasive breast carcinoma often leads to misdiagnosis. Meticulous review of histopathology and immunohistochemistry is essential for diagnosis. We present a case of carcinoma breast with unusual gastric nodular metastasis detected on 18F-fluorodeoxyglucose positron emission tomography-computed tomography.

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15: Baby A, Kesav P, Kumar P, Madhusudhan KS. CT-guided percutaneous nephrostomy in an obstructed pelvic pancake kidney: a report of a novel transiliopsoas approach. *BMJ Case Rep.* 2019 Dec 4;12(12). pii: e232665. doi: 10.1136/bcr-2019-232665. PubMed PMID: 31806635.

Pancake kidney is a rare renal fusion anomaly with increased risk of complications, such as stone disease and infections, due to altered urodynamics. Image-guided (ultrasonography and fluoroscopy) percutaneous nephrostomy (PCN) is performed to decompress an obstructed pancake kidney. However, routine image guidance may be unable to provide a suitable access in complex clinical scenarios. The approach for PCN in a low-lying fused kidney is difficult due to a limited safe posterior retroperitoneal paraspinal route, and anterior transperitoneal approach poses risks of urine leak and peritonitis. We report a case of an obstructed pancake kidney managed by CT-guided PCN through a transiliopsoas approach.

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16: Bagri N, Jana M, Sundaram DD. Pseudorheumatoid Arthropathy of Childhood: A Mimicker of Juvenile Idiopathic Arthritis. *Indian J Pediatr.* 2019 Dec;86(12):1158-1159. doi: 10.1007/s12098-019-02983-8. Epub 2019 May 27. PubMed PMID: 31134535.

17: Bansal VK, Krishna A, Prajapati OP, Baksi A, Kumar S, Garg P, Misra MC. Outcomes following laparoscopic internal drainage of walled off necrosis of pancreas: experience of 134 cases from a tertiary care centre. *Surg Endosc.* 2019 Dec 6. doi: 10.1007/s00464-019-07282-z. [Epub ahead of print] PubMed PMID: 31811455.

**INTRODUCTION:** Internal drainage of walled off necrosis of pancreas has been considered as the standard of care. For symptomatic walled off necrosis (WON) of pancreas with the advent of laparoscopy and refinement of techniques and instrumentation, laparoscopic internal drainage is becoming the standard surgical drainage procedure for these patients. However, there is a dearth of literature

regarding outcomes following laparoscopic drainage. Most of the studies have small number of patients with limited follow-up. We in this study describe our experience of laparoscopic internal drainage of walled off necrosis over the last 13 years.

**MATERIALS AND METHODS:** This is a retrospective analysis of a prospectively maintained database. All patients with WON undergoing laparoscopic internal drainage between January 2005 and December 2018 were included. Primary outcome measure was successful drainage. Secondary outcome measures included morbidity, hospital stay, re-intervention rate and mortality. Patients were followed up post-operatively at 1 week, 4 weeks, 3 months and then annually thereafter. Ultrasonography was done periodically for the assessment of cyst resolution.

**RESULTS:** Between 2005 and 2018, 154 surgical drainage procedures were performed for symptomatic pseudocyst/walled off necrosis. Out of these, 134 underwent laparoscopic drainage; 129 patients (96.3%) underwent laparoscopic cystogastrostomy and 5 (3.7%) underwent laparoscopic cystojejunostomy. Majority of the patients were male (male:female=6:1) with a mean age of 36±12.9 years (range 15-58 years). The mean operative time was 94 min (range 64-144 min). There were three conversions because of intra-operative bleeding. The overall post-operative morbidity was 8.9%. The average hospital stay was 4.4 days (2-19 days). The mean duration of follow-up was 5.5 years (range 6 months-13 years). Complete cyst resolution was achieved in 95.5% (n=128) patients. There has been no mortality till date.

**CONCLUSION:** In conclusion, laparoscopic internal drainage is a very effective technique for drainage of WON with an excellent success rate.

DOI: 10.1007/s00464-019-07282-z

PMID: 31811455

18: Barwal I, Kumar R, Dada T, Yadav SC. Effect of Ultra-Small Chitosan Nanoparticles Doped with Brimonidine on the Ultra-Structure of the Trabecular Meshwork of Glaucoma Patients. *Microsc Microanal*. 2019 Dec;25(6):1352-1366. doi: 10.1017/S1431927619000448. PubMed PMID: 31018876.

Brimonidine, an anti-glaucoma medicine, acts as an adrenergic agonist which decreases the synthesis of aqueous humour and increases the amount of drainage through Schlemm's canal and trabecular meshwork, but shows dose-dependent (0.2% solution thrice daily) toxicity. To reduce the side effects and improve the efficacy, brimonidine was nanoencapsulated on ultra-small-sized chitosan nanoparticles (nanobrimonidine) (28 ± 4 nm) with 39% encapsulation efficiency, monodispersity, freeze-thawing capability, storage stability, and 2% drug loading capacity. This nanocomplex showed burst, half, and complete release at 0.5, 45, and 100 h, respectively. Nanobrimonidine did not show any in vitro toxicity and was taken up by caveolae-mediated endocytosis. The nanobrimonidine-treated trabeculectomy tissue of glaucoma patients showed better dilation of the trabecular meshwork under the electron microscope. This is direct evidence for better bioavailability of nanobrimonidine after topical administration. Thus, the developed nanobrimonidine has the potential to improve the efficacy, reduce dosage and frequency, and improve delivery to the anterior chamber of the eye.

DOI: 10.1017/S1431927619000448

PMID: 31018876

19: Behera C, Sikary AK, Mridha AR, Pandey RM, Satapathy S, Lalwani S, Gupta S. Association of menstruation cycle with completed suicide: a hospital-based case-control study. *Arch Womens Ment Health*. 2019 Dec;22(6):771-777. doi: 10.1007/s00737-019-00964-6. Epub 2019 Apr 26. PubMed PMID: 31028472.

The purpose of the study was to determine the phases of the menstrual cycle in

the reproductive age group of females who committed suicide as compared with a control group of females who died from causes other than suicide. The study included 86 cases in the suicidal group and 80 cases in the non-suicidal group. The menstrual phase was decided by the gross and histological examination of the uterus and ovary at autopsy. Deaths were more common during the secretory phase (56.9%) in the suicidal group, while in the non-suicidal group, death occurred more commonly in the proliferative phase (66.3%). In reference to proliferative phase, deaths were more in the secretory phase and menstrual phase in the suicidal group, adjusted odd's ratio (OR) being 3.7 ( $p=0.042$ ) and 4.7 ( $p=0.032$ ), respectively. Corpus luteum was present in the right ovary of 43 and 14 victims of suicidal and non-suicidal deaths, respectively, while it was in the left ovary of 3 and 11 victims of suicidal and non-suicidal death, respectively. Odd's ratio was 10.3 for corpus luteum to be in the right ovary in comparison with the left ovary for the suicidal group ( $p=0.001$ ). This study revealed that suicidal chances in a woman are significantly more in the menstrual phase and the secretory phase of the menstrual cycle. The presence of corpus luteum in the right ovary is associated with an increased risk of suicide, but the reason is not known.

DOI: 10.1007/s00737-019-00964-6

PMID: 31028472

20: Bhagwat SR, Hajela K, Bhutada S, Choudhary K, Saxena M, Sharma S, Kumar A. Identification of unexplored substrates of the serine protease, thrombin, using N-terminomics strategy. *Int J Biol Macromol*. 2020 Feb 1;144:449-459. doi: 10.1016/j.ijbiomac.2019.12.137. Epub 2019 Dec 17. PubMed PMID: 31862363.

The function and regulation of thrombin is a complex as well as an intriguing aspect of evolution and has captured the interest of many investigators over the years. The reported substrates of thrombin are coagulation factors V, VIII, XI, XIII, protein C and fibrinogen. However, these may not be all the substrate of thrombin and therefore its functional role(s), may not have been completely comprehended. The purpose of our study was to identify hitherto unreported substrates of thrombin from human plasma using a N-terminomics protease substrate identification method. We identified 54 putative substrates of thrombin of which 12 are already known and 42 are being reported for the first time. Amongst the proteins identified, recombinant siglec-6 and purified serum alpha-1-acid glycoprotein were validated by cleavage with thrombin. We have discussed the probable relevance of siglec-6 cleavage by thrombin in human placenta mostly because an upregulation in the expression of siglec-6 and thrombin has been reported in the placenta of preeclampsia patients. We also speculate the role of alpha-1-acid glycoprotein cleavage by thrombin in the acute phase as alpha-1-acid glycoprotein is known to be an inhibitor of platelet aggregation whereas thrombin is known to trigger platelet aggregation.

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PMID: 31862363

21: Bhari N, Sharma VK, Singh S, Parihar A, Arava S. Effect of Q-switched Nd-YAG laser on the clinical, pigmentary, and immunological markers in patients with lichen planus pigmentosus: A pilot study. *Dermatol Ther*. 2019 Dec 29:e13208. doi: 10.1111/dth.13208. [Epub ahead of print] PubMed PMID: 31885158.

The persistent discoloration in lichen planus pigmentosus (LPP) is secondary to persistent melanophages in the superficial dermis in these patients. We evaluated

the effect of Q-switched Nd-YAG laser on the clinical, pigmentary, and immunological markers in patients with LPP. Nine females with a clinical diagnosis of LPP were included in the study. After six sessions of laser with toning protocol, performed over a representative area of 5×5cm<sup>2</sup> at 2-weekly intervals, the mean clinical improvement as per the physician assessment was 25.7% (10-40%). There was no significant reduction in melanin and erythema index. On expression analysis using quantitative-polymerase chain reaction, the reduction in tyrosinase (p = 0.03) was statistically significant, though, the reduction in other pigment and immunological markers was not significant. The immunohistochemistry quantification data of corresponding proteins also did not show any significant difference. Post inflammatory hypopigmentation was noted in one patient. Q-switched Nd-YAG laser toning protocol resulted in modest clinical and histological improvement in patients of LPP.

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DOI: 10.1111/dth.13208

PMID: 31885158

22: Bharti P, Mahajan S, Mahajan S, Ramam M, Gupta V. Yellowish periumbilical plaque with keratotic papules. *Indian J Dermatol Venereol Leprol*. 2019 Dec 12. doi: 10.4103/ijdv.IJDVL\_828\_18. [Epub ahead of print] PubMed PMID: 31857518.

23: Bhat I, Bellapukonda S. A novel Technique for Arterial Cannulation in Neonates: Angulation of Arterial Cannula. *Asian J Anesthesiol*. 2019 Dec 1;57(4):132-134. doi: 10.6859/aja.201912\_57(4).0006. Epub 2019 Nov 6. PubMed PMID: 31726802.

24: Bhatia R, Sharma G, Patel C, Garg A, Roy A, Bali P, Singh N, Sisodia P, Sreenivas V, Srivastava MVP, Prasad K. Coronary Artery Disease in Patients with Ischemic Stroke and TIA. *J Stroke Cerebrovasc Dis*. 2019 Dec;28(12):104400. doi: 10.1016/j.jstrokecerebrovasdis.2019.104400. Epub 2019 Oct 9. PubMed PMID: 31606321.

**BACKGROUND AND OBJECTIVES:** Ischemic stroke (IS) and coronary artery disease (CAD) share common risk factors and one may be the harbinger of the other. We aimed to study prevalence of symptomatic and asymptomatic CAD in a cohort of consecutive patients with IS and assess its relationship with intracranial and extracranial large artery cerebrovascular disease (LAD).

**METHODS:** All consecutive eligible IS and Transient Ischemic Attack (TIA) patients were recruited into the study. Both clinically suspected and asymptomatic patients (N=259) underwent myocardial Stress-rest Gated Technetium-99m (Tc99m) MIBI Myocardial Perfusion SPECT scan performed on a dual head SPECT-CT to estimate evidence of myocardial ischemia.

**RESULTS:** Three hundred patients completed the study. Forty one patients were previously diagnosed cases of definitive CAD. Twelve patients were clinically suspected to have CAD and 247 patients were asymptomatic. Among these, 12 patients (4.81%) had a positive SPECT. The overall prevalence of CAD was 17.67% (n=53). Presence of diabetes was an independent predictor of CAD (OR 1.98, 95% CI 1.07-3.67. P .02). No significant association was found between the presence of LAD and CAD in all subgroup comparisons. However, there was a suggestion of higher LAD among patients with known CAD compared with others.

**CONCLUSIONS:** CAD is prevalent in patients with ischemic stroke. No definitive relationship was found between CAD and intracranial or extracranial LAD. Population based stratification tools are needed to further assess the need to

detect subclinical CAD in patients with stroke.

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DOI: 10.1016/j.jstrokecerebrovasdis.2019.104400

PMID: 31606321

25: Bhatia SJ, Makharia GK, Abraham P, Bhat N, Kumar A, Reddy DN, Ghoshal UC, Ahuja V, Rao GV, Devadas K, Dutta AK, Jain A, Kedia S, Dama R, Kalapala R, Alvares JF, Dadhich S, Dixit VK, Goenka MK, Goswami BD, Issar SK, Leelakrishnan V, Mallath MK, Mathew P, Mathew P, Nandwani S, Pai CG, Peter L, Prasad AVS, Singh D, Sodhi JS, Sud R, Venkataraman J, Midha V, Bapaye A, Dutta U, Jain AK, Kochhar R, Puri AS, Singh SP, Shimpi L, Sood A, Wadhwa RT. Indian consensus on gastroesophageal reflux disease in adults: A position statement of the Indian Society of Gastroenterology. *Indian J Gastroenterol*. 2019 Oct;38(5):411-440. doi: 10.1007/s12664-019-00979-y. Epub 2019 Dec 5. PubMed PMID: 31802441.

The Indian Society of Gastroenterology developed this evidence-based practice guideline for management of gastroesophageal reflux disease (GERD) in adults. A modified Delphi process was used to develop this consensus containing 58 statements, which were generated by electronic voting iteration as well as face-to-face meeting and review of the supporting literature primarily from India. These statements include 10 on epidemiology, 8 on clinical presentation, 10 on investigations, 23 on treatment (including medical, endoscopic, and surgical modalities), and 7 on complications of GERD. When the proportion of those who voted either to accept completely or with minor reservation was 80% or higher, the statement was regarded as accepted. The prevalence of GERD in India ranges from 7.6% to 30%, being <10% in most population studies, and higher in cohort studies. The dietary factors associated with GERD include use of spices and non-vegetarian food. *Helicobacter pylori* is thought to have a negative relation with GERD; *H. pylori* negative patients have higher grade of symptoms of GERD and esophagitis. Less than 10% of GERD patients in India have erosive esophagitis. In patients with occasional or mild symptoms, antacids and histamine H<sub>2</sub> receptor blockers (H<sub>2</sub>RAs) may be used, and proton pump inhibitors (PPI) should be used in patients with frequent or severe symptoms. Prokinetics have limited proven role in management of GERD.

DOI: 10.1007/s12664-019-00979-y

PMID: 31802441

26: Bhatla N, Singhal S, Saraiya U, Srivastava S, Bhalerao S, Shamsunder S, Chavan N, Basu P, Purandare CN; (on behalf of FOGSI Expert group). Screening and management of preinvasive lesions of the cervix: Good clinical practice recommendations from the Federation of Obstetrics and Gynaecologic Societies of India (FOGSI). *J Obstet Gynaecol Res*. 2019 Dec 9. doi: 10.1111/jog.14168. [Epub ahead of print] Review. PubMed PMID: 31814222.

In India, there are marked variations in resources for cervical cancer screening. For the first time, resource-stratified screening guidelines have been developed that will be suitable for low middle-income countries with similar diversities. The current article describes the process and outcomes of these resource stratified guidelines for screening and treatment of preinvasive lesions of cervix. Evidence from literature was collated and various guidelines were reviewed by an expert panel. Based on the level of evidence, guidelines were developed for screening by human papillomavirus (HPV) testing, cytology and visual inspection after application of acetic acid (VIA), and management of screen positive lesions in different resource settings. Expert opinion was used for certain country-specific situations. The healthcare system was stratified

into two resource settings - good or limited. The mode of screening and treatment for each was described. HPV testing is the preferred method for cervical cancer screening. VIA by trained providers is especially suitable for low resource settings until an affordable HPV test becomes available. Healthcare providers can choose the most appropriate screening and treatment modality. A single visit approach is encouraged and treatment may be offered based on colposcopy diagnosis ('see and treat') or even on the basis of HPV test or VIA results ('screen and treat'), if compliance cannot be ensured. The Federation of Obstetrician and Gynaecologists of India Good Clinical Practice Recommendations (FOGSI) GCPR are appropriately designed for countries with varied resource situations to ensure an acceptable cervical cancer prevention strategy.

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DOI: 10.1111/jog.14168

PMID: 31814222

27: Bhawal UK, Li X, Suzuki M, Taguchi C, Oka S, Arikawa K, Tewari N, Liu Y. Treatment with low-level sodium fluoride on wound healing and the osteogenic differentiation of bone marrow mesenchymal stem cells. *Dent Traumatol*. 2019 Dec 3. doi: 10.1111/edt.12532. [Epub ahead of print] PubMed PMID: 31797525.

**BACKGROUND/AIMS:** Lacerations of the oral mucosa and fractures of alveolar processes commonly occur in traumatic dental injuries (TDIs). Impaired wound healing and tissue regeneration have severe consequences on the quality of life. Bone marrow mesenchymal stem cells (BMMSCs) possess the ability of self-renewal and multipotential differentiation. Treatment with low-level sodium fluoride (NaF) has emerged as a promising approach to enhance wound repair. The aim of this study was to assess the effects of low-level NaF on soft tissue healing and on the proliferation, migration and extracellular matrix synthesis of BMMSCs. **MATERIAL AND METHODS:** BMMSCs derived from mice were treated with 50  $\mu$ M, 500  $\mu$ M, or 5 mM NaF for 12, 24, and 48 hours, and cell proliferation was assessed by the MTS assay. Cell motility was detected at 12 and 24 hours by a wound healing assay, and osteoblastic differentiation for 21 days by 1% Alizarin Red S staining in 50  $\mu$ M NaF-treated BMMSCs. Gene expression of Runx2 and Osteocalcin was evaluated by quantitative real-time PCR. An experimental rat skin wound model was employed, and levels of c-Myc, Ki67, fibronectin, and vimentin were assessed by immunohistochemistry. **RESULTS:** There was a significant induction in the proliferation and migration of BMMSCs treated with 50  $\mu$ M NaF. The expression of Ki67 and c-Myc protein was increased in tissues treated with 50  $\mu$ M NaF, and the expression of fibronectin and vimentin in the 50  $\mu$ M NaF-treated tissues was stimulated. Alizarin Red staining revealed enhanced mineralization in 50  $\mu$ M NaF-treated BMMSCs with increased expression of Runx2 and Osteocalcin, indicating their upregulated osteogenic differentiation. **CONCLUSION:** Low-level NaF could promote soft tissue healing and hard tissue regeneration.

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PMID: 31797525

28: Chakraborty S, Vellarikkal SK, Sivasubbu S, Roy SS, Tandon N, Bharadwaj D. Role of Tmem163 in zinc-regulated insulin storage of MIN6 cells: Functional exploration of an Indian type 2 diabetes GWAS associated gene. *Biochem Biophys Res Commun*. 2020 Feb 19;522(4):1022-1029. doi: 10.1016/j.bbrc.2019.11.117. Epub 2019 Dec 6. PubMed PMID: 31813547.

Genome wide association study for type 2 diabetes discovered TMEM163 as a risk locus. Perturbations in TMEM163 expression was reported to be associated with impaired intracellular zinc homeostasis. Physiological concentration of zinc is instrumental to maintain insulin storage and functionality in pancreatic  $\beta$  cells. We found abundant TMEM163 expression in human pancreas, both at transcriptional and translational levels. Knockdown of endogenous Tmem163 in MIN6 cells resulted in increased intracellular zinc and total insulin content, coupled with compromised insulin secretion at high glucose stimuli. Furthermore, Tmem163 knockdown led to enhanced cellular glucose uptake. Upon next generation sequencing, one-third of the studied T2D patients were found to have a novel missense variant in TMEM163 gene. Study participants harboring this missense variant displayed a trend of higher glycemic indices. This is the first report on exploring the biological role of TMEM163 in relation to T2D pathophysiology.

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DOI: 10.1016/j.bbrc.2019.11.117

PMID: 31813547

29: Chakraborty S, Dakle P, Sinha A, Vishweswaraiah S, Nagori A, Salimath S, Prakash YS, Lodha R, Kabra SK, Ghosh B, Faruq M, Mahesh PA, Agrawal A. Genetic variations in olfactory receptor gene OR2AG2 in a large multigenerational family with asthma. *Sci Rep.* 2019 Dec 13;9(1):19029. doi: 10.1038/s41598-019-54718-6. PubMed PMID: 31836740; PubMed Central PMCID: PMC6911056.

It is estimated from twin studies that heritable factors account for at-least half of asthma-risk, of which genetic variants identified through population studies explain only a small fraction. Multi-generation large families with high asthma prevalence can serve as a model to identify highly penetrant genetic variants in closely related individuals that are missed by population studies. To achieve this, a four-generation Indian family with asthma was identified and recruited for examination and genetic testing. Twenty subjects representing all generations were selected for whole genome genotyping, of which eight were subjected to exome sequencing. Non-synonymous and deleterious variants, segregating with the affected individuals, were identified by exome sequencing. A prioritized deleterious missense common variant in the olfactory receptor gene OR2AG2 that segregated with a risk haplotype in asthma, was validated in an asthma cohort of different ethnicity. Phenotypic tests were conducted to verify expected deficits in terms of reduced ability to sense odors. Pathway-level relevance to asthma biology was tested in model systems and unrelated human lung samples. Our study suggests that OR2AG2 and other olfactory receptors may contribute to asthma pathophysiology. Genetic studies on large families of interest can lead to efficient discovery.

DOI: 10.1038/s41598-019-54718-6

PMCID: PMC6911056

PMID: 31836740

30: Chaudhari VA, Pradeep R, Ramesh H, Bhandare MS, Dhar P, Pal S, Palaniswamy S, Jeswanth S, Menon RN, Singh AN, Sabnis S, Rao GV, Shrikhande SV. Surgery for cystic tumors of pancreas: Report of high-volume, multicenter Indian experience over a decade. *Surgery.* 2019 Dec;166(6):1011-1016. doi: 10.1016/j.surg.2019.07.013. Epub 2019 Sep 19. PubMed PMID: 31543321.

BACKGROUND: Pancreatic cystic neoplasms remain uncommon. Although data are accumulating on the incidence of pancreatic cystic neoplasms in the published literature, Indian data on these tumors are sparse.

**MATERIAL AND METHODS:** We collated data from prospectively maintained databases of patients operated for cystic tumors of the pancreas from 2007 to 2016 at 7 academic centers across India to gain insights into clinical presentation and outcome of the operative treatment of these tumors. Data were compared with large series across the world to understand the regional differences in this pathology.

**RESULTS:** Of the 423 patients, there were 98 (23.2%) serous cystic neoplasms, 128 (30.2%) mucinous neoplasms, 34(8%) intraductal papillary mucinous neoplasms, and 121 (28.6%) solid pseudopapillary epithelial neoplasms managed in these 7 academic centers. Malignancy (adenocarcinoma, malignant intraductal papillary mucinous neoplasms, and mucinous cystadenocarcinoma) was reported in 39 (9.2%) patients. Median age at presentation was 41 years, and the female-to-male ratio was 3.4:1. At presentation, 81% of patients were symptomatic. A total of 66.7% of lesions were located in body and tail region of the pancreas. Median tumor size was 6 cm. Operative resection with curative intent was performed in 405 of these 423 patients. Major morbidity occurred in 12%, and 30-day perioperative mortality was 0.9%. Laparoscopic resections were performed in 18% and spleen-preserving resections were performed in 3% of patients.

**CONCLUSION:** Female preponderance, young age, and a benign nature of most pancreatic cystic neoplasms were observed. Large size of tumors on presentation, fewer intraductal papillary mucinous neoplasm resections, and a much greater incidence of solid pseudopapillary epithelial neoplasms were distinctive of this study. Although the proportion of laparoscopic resections and splenic preservation was less compared with Western centers, the perioperative morbidity and mortality was on par with established standards.

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PMID: 31543321

31: Chaudhary RS, Gupta A, Sharma A, Gupta S, Sofi RA, Sundar D, Sihota R, Somarajan BI, Singh A, Sangwan R, Gupta V. Long-term functional outcomes of different subtypes of primary congenital glaucoma. *Br J Ophthalmol*. 2019 Dec 23. pii: bjophthalmol-2019-315131. doi: 10.1136/bjophthalmol-2019-315131. [Epub ahead of print] PubMed PMID: 31871047.

**AIM:** To analyse long-term visual outcomes across different subtypes of primary congenital glaucoma (PCG).

**METHODS:** Patients with PCG with a minimum of 5-year follow-up post surgery were included in the study. Snellen visual acuity recordings taken at their last follow-up were analysed. We evaluated the results using Kaplan-Meier curves to predict the probability of maintaining good vision (as defined by a visual acuity of 6/18 or better) in our patients after 30-year follow-up. The results were also analysed to determine whether there were any differences in the long-term visual acuities with time between the neonatal and infantile PCG. We also analysed the reasons for poor visual outcomes.

**RESULTS:** We assessed a cohort of 140 patients with PCG (235 eyes) with an average follow-up of 127±62.8 months (range 60-400 months). Overall, the proportion of eyes with good visual acuity was 89 (37.9%), those with fair visual acuity between 6/60 and 6/18 was 41 (17.4%), and those with poor visual acuity ( $\leq 6/60$ ) was 105 (44.7%). We found a significant difference ( $p=0.047$ ) between neonatal and infantile patients with PCG whereby the neonatal cohort fared worse off in terms of visual morbidity. On Kaplan-Meier analysis, the cumulative probability of survival of a visual acuity of 6/18 or better was more among the infantile PCG in comparison to the neonatal PCG ( $p=0.039$ ) eyes, and more among the bilateral than the unilateral affected eyes ( $p=0.029$ ). Amblyopia was the most important cause for poor visual acuity as shown on a Cox proportional-hazards regression model.

**CONCLUSIONS:** Long-term visual outcomes of infantile are better than neonatal PCG.

Eyes with unilateral have worse visual outcomes compared with those with bilateral PCG because of the development of dense amblyopia.

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PMID: 31871047

32: Chauhan S, Sen S, Singh N, Sharma A, Pushker N, Kashyap S, Chawla B. Human papillomavirus in ocular malignant tumours: a study from a tertiary eye care centre in North India. *Can J Ophthalmol*. 2019 Dec;54(6):688-693. doi: 10.1016/j.jcjo.2019.03.001. Epub 2019 Apr 16. PubMed PMID: 31836101.

**OBJECTIVE:** The present study aims to detect the presence of human papillomavirus (HPV) in ocular malignant tumours, including retinoblastoma, eyelid squamous cell carcinoma (SCC), and sebaceous gland carcinoma (SGC), in the North Indian population.

**DESIGN:** Prospective observational non randomized study.

**PARTICIPANTS:** In this study, 142 prospective cases of ocular malignant tumours (retinoblastoma, SGC, and SCC) were included.

**METHODS:** HPV was detected by multiplex PCR using PGMY09/11 primers in 142 patients with ocular malignancies. This was followed by genotyping using linear array (reverse hybridization).

**RESULTS:** Of the 142 tumours studied, 72 were retinoblastoma, 30 SGC, and 40 SCC. The HPV genome was detected in 2.8% (4 of 142) of cases by multiplex PCR; all positive cases (4 of 40) were SCC. Genotyping revealed that all positives belonged to the high-risk HPV16 genotype. HPV-positive SCC patients had better disease-free survival. Retinoblastoma and SGC cases were negative for HPV.

**CONCLUSIONS:** Low prevalence of HPV in ocular malignancies was observed in this study. The HPV genome was detected only in ocular squamous cell carcinoma cases and these patients were associated with better prognosis. HPV may not have a role in retinoblastoma and SGC in the North Indian population.

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DOI: 10.1016/j.jcjo.2019.03.001  
PMID: 31836101

33: Chawla D, Kaur T, Joshi A, Singh N. 3D bioprinted alginate-gelatin based scaffolds for soft tissue engineering. *Int J Biol Macromol*. 2020 Feb 1;144:560-567. doi: 10.1016/j.ijbiomac.2019.12.127. Epub 2019 Dec 16. PubMed PMID: 31857163.

Increase in the number of patients suffering from Osteoarthritis is prevalent nowadays and hence, there is need for tissue regeneration. Fabricating a 3D structure giving a better control mimicking the actual tissue properties, especially for osteo-chondral applications is a challenge due to several constraints (like suitable biomaterial for cell encapsulation, mimicking mechanical properties). Here, we mimic the natural process of tissue formation by encapsulating cells in an optimized 3D construct which improves mechanical properties by matrix secretion. We investigated different concentrations of Alginate-Gelatin ink and further characterized the optimized concentration. Behaviour of different infill percentage on the bioactivity and morphology of the scaffold was also investigated. For observing the behaviour of cells on different infill percentages within the scaffolds of same concentration, we used osteoblasts (MG63) cells. The optimized material concentration with the adequate

infill showed printability, adequate viscosity, and increased swelling. Both, 20 and 25% infill within the Alginate-Gelatin scaffolds (2.5% w/v Alginate and 5% w/v Gelatin) resulted in higher viability and proliferation of osteoblast cells. Additionally, to control the shape retention ability of the scaffolds dual crosslinking was applied. Thus, the developed Alginate-Gelatin based 3D scaffold maintains the required balance between biomechanics and soft tissue regeneration.

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PMID: 31857163

34: Damodaran S, Bajaj MS, Sharma P, Kumar A, Chawla R, Pujari A, Garg G, Temkar S. Swept-source optical coherence tomography features of regressed macular retinoblastoma. *Indian J Ophthalmol*. 2019 Dec;67(12):2013-2018. doi: 10.4103/ijo.IJO\_533\_19. PubMed PMID: 31755441; PubMed Central PMCID: PMC6896562.

**Purpose:** To describe the swept-source optical coherence tomography (SS-OCT) features of regressed macular retinoblastoma (RB).

**Methods:** A cross-sectional observational study was carried out in 13 patients with regressed macular RB with good fixation in at least one eye. Fundus photography and SS-OCT were documented. High-resolution scans with good signal strength were selected. The types of clinical regression and SS-OCT characteristics of the regressed lesions (presence of vitreous detachment, intratumor schisis/cavitation, calcification, foveal dip, and OCT pattern) were noted.

**Results:** Of the 13 eyes, 7 (53%) were group B, 4 (30%) were group C, and 2 (17%) were group D. Lesion involving fovea was seen in seven eyes (53%). On SS-OCT, the lesion was isodense to hyperdense in all cases. Three patterns of regressed RB were noted on OCT. Intralesion calcification was noted in eight cases. Subretinal fluid was not detected in any of the cases.

**Conclusion:** SS-OCT is a useful technology to image and analyze cases of regressed macular RB including large lesions. SS-OCT system helps in successful imaging even in smaller children.

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PMCID: PMC6896562

PMID: 31755441

35: Davis AA. Unindicated hysterectomies in India: the aftermath. *BMJ Case Rep*. 2019 Dec 17;12(12). pii: e230129. doi: 10.1136/bcr-2019-230129. PubMed PMID: 31852688.

Unindicated hysterectomy is a disturbing problem in India. Women are counselled into the procedure by the fear of cancer, and by reinforcing their notion that unrelated somatic problems are solved by the removal of the uterus. This is a case of a woman from the state of Bihar, India, who was referred to us after an unindicated hysterectomy at the age of 24, performed as a first-line treatment for lower abdominal pain. This highlights the problem of rising hysterectomy in India and the lack of integrated treatment for women with the debilitating condition of chronic pelvic pain. Pelvic pain and vaginal discharge are often not indicative of pelvic inflammatory disease, and need a more considerate and broad-minded approach. Public health initiatives should take more account of women's lack of knowledge of reproductive health and make efforts to disseminate such information by the use of television, radio and newspapers in local languages.

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36: Dawar R, Nangia S, Thukral A, Chopra S, Khanna R. Factors Impacting Practice of Home Kangaroo Mother Care with Low Birth Weight Infants Following Hospital Discharge. *J Trop Pediatr*. 2019 Dec 1;65(6):561-568. doi: 10.1093/tropej/fmz007. PubMed PMID: 30768199.

**OBJECTIVE:** To identify enablers and barriers related to home Kangaroo Mother Care (KMC) adoption after hospital discharge.

**STUDY DESIGN:** An exploratory study, using a mixed methods evaluation, followed 60 mother-infant dyads from the hospital ward to 4 weeks post-hospital discharge.

**RESULTS:** Fifty-three of the mothers (88.3%) completed all study visits. The majority of mothers were breastfeeding and practicing skin-to-skin contact 4 weeks post-discharge. Seven mothers (13.2%) discontinued skin-to-skin contact at 4 weeks. KMC was practiced on average 3.3h/day and 5.1days/week. The top two enablers reported were significantly related to the amount of time skin-to-skin was practiced, with support for household responsibilities being most significant ( $U=195$ ,  $p=0.008$ ). Lack of privacy ( $p=0.002$ ) and lack of motivation ( $p=0.034$ ) were negatively correlated to duration of skin-to-skin contact.

**CONCLUSION:** Future programs may increase dissemination and adoption of home KMC by specifically addressing enablers and barriers correlated to duration of skin-to-skin contact.

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37: Dema T, Tripathy JP, Thinley S, Rani M, Dhendup T, Laxmeshwar C, Tenzin K, Gurung MS, Tshering T, Subba DK, Penjore T, Lhazeen K. Suicidal ideation and attempt among school going adolescents in Bhutan - a secondary analysis of a global school-based student health survey in Bhutan 2016. *BMC Public Health*. 2019 Dec 2;19(1):1605. doi: 10.1186/s12889-019-7791-0. PubMed PMID: 31791280; PubMed Central PMCID: PMC6889681.

**BACKGROUND:** Suicide is one of the leading causes of death and Disability Adjusted Life Years (DALYs) worldwide. The economic, emotional and human cost of suicidal behaviour to individuals, families, communities and society makes it a serious public health issue. We aim to determine the prevalence and factors associated with self-reported suicidal behaviour (suicidal ideation and attempt) among school going adolescents (13-17 years).

**METHODS:** This is a secondary analysis of a nationally representative data for Bhutan namely Global School Based Student Health Survey in 2016 which reports on various dimensions of adolescent health including suicidal behaviour. The survey employed a multistage sampling method to recruit participants aged 13-17 years ( $n=5809$ ) from 50 schools (25 each in rural and urban area). The survey used an anonymous self-administered pre-tested 84-item questionnaire. Weighted analysis was done. Adjusted prevalence ratios (aPRs) and adjusted Odds Ratios (aORs) have been presented with 95% confidence intervals (95% CI).

**RESULTS:** A total of 667 (11.6%) adolescents reported considering a suicide attempt whereas 656 (11.3%) reported attempting suicide in the past 12 months. Among those reporting suicidal ideation, 388 (58.6%) reported attempting a suicide and 274 (41.4%) had ideation alone, whereas, 247 (38.9%) reported

attempting a suicide without previous ideation. Female sex, food insecurity, physical attack, sexual violence, bullying, feeling of loneliness, low parental engagement, reported worry about lack of sleep, urge to use drugs/alcohol, smokeless tobacco use, drug abuse and parental smoking were the factors associated with suicidal attempt. All these factors except smokeless tobacco use and parental smoking were associated with suicidal ideation. Having helpful/close friends was found to be protective against suicide ideation.

CONCLUSION: Suicidal behaviour among school going adolescents in Bhutan is high and alarming, especially among girls. Bullying, sexual violence, feeling of loneliness and drug abuse were some of the key risk factors identified. It is important to identify these risk factors early and effectively tackle them in order to prevent suicides. It requires a multi-faceted intervention with the support of the children, community, teachers and parents.

DOI: 10.1186/s12889-019-7791-0

PMCID: PMC6889681

PMID: 31791280

38: Deshpande A, S H C, Kumar S, Shaw M, Khurana R. Diagnostic dilemma in a case of diffuse pulmonary arteriovenous malformation with vascular stenosis! *Ann Thorac Surg.* 2019 Dec 23. pii: S0003-4975(19)31911-3. doi: 10.1016/j.athoracsur.2019.10.088. [Epub ahead of print] PubMed PMID: 31877288.

Diffuse pulmonary arterio-venous malformation (PAVM) is a rare entity, exact incidence of which is unknown. It can be limited to a single lobe, or diffusely involve one or both the lungs. The early diagnosis and treatment is crucial, as it is associated with increased frequency of thoracic and neurological complications. Different diagnostic modalities offer some advantage over the other. None of the reported cases in literature has associated stenosis of any major artery. Here, we describe a rare case of diffuse PAVM limited to a lobe associated with descending pulmonary artery stenosis.

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DOI: 10.1016/j.athoracsur.2019.10.088

PMID: 31877288

39: Dhar R, Pethusamy K, Singh S, Mukherjee I, Seethy A, Sengupta B, Srivastava T, Sarkar S, Mandal V, Karmakar M, Gupta S, Ghosh A, Karmakar S. Draft genome of *Ompok bimaculatus* (Pabda fish). *BMC Res Notes.* 2019 Dec 26;12(1):825. doi: 10.1186/s13104-019-4867-y. PubMed PMID: 31878964; PubMed Central PMCID: PMC6933649.

OBJECTIVE: Pabda (*Ompok bimaculatus*) is a freshwater catfish, largely available in Asian countries, especially in Bangladesh, India, Pakistan and Nepal. This fish is highly valued for its fabulous taste and high nutritional value and is very popular as a rich source of proteins, omega-3 and omega-6 fatty acids, vitamins and mineral for growing children, pregnant females and elders. We performed de-novo sequencing of *Ompok bimaculatus* using a hybrid approach and present here a draft assembly for this species for the first time.

DATA DESCRIPTION: The genome of *Ompok bimaculatus* (Fig. 1: Table 1, Data file 3) from Ganges river, has been sequenced by hybrid approach using Illumina short reads and PacBio long reads followed by structural annotations. The draft genome assembly was found to be 718 Mb with N50 size of 81 kb. MAKER gene annotation tool predicted 21,371 genes.

DOI: 10.1186/s13104-019-4867-y

PMCID: PMC6933649

PMID: 31878964

40: Dhawan A, Mishra AK, Ambekar A, Chatterjee B, Agrawal A, Bhargava R. Estimating the size of substance using street children in Delhi using Respondent-Driven Sampling (RDS). *Asian J Psychiatr*. 2019 Dec 5;48:101890. doi: 10.1016/j.ajp.2019.101890. [Epub ahead of print] PubMed PMID: 31841817.

Street children as a population sub-group exist in significant numbers in the developing world and have been reported to be vulnerable to adverse health and risk behaviours that include physical and sexual risk behaviour. However, the estimation of prevalence for various psychoactive substances among the street children in a representative sample has not been attempted in the developing country like India. This is challenging due to the absence of an appropriate sampling frame, the population living in isolation, hiding their identity and concealing their behaviour. Use of psychoactive substances in street children is riddled with these challenges. The present investigation describes the findings from size estimation study on a representative sample of street child (n = 766) in Delhi, by implementing the Respondent Driven Sampling Methodology (RDS). The weighted prevalence for three commonest substances was found as Tobacco (31.1 %), alcohol (13.5 %) and inhalants (11.3 %) used during the last one year with the estimated number as -Tobacco (21,770), Alcohol (9450) and Inhalants (5600). Almost one third of street children were using some substance. Also, a large majority of ever users were also using substances currently. The study demonstrates successfully the implementation of RDS for the estimation of the prevalence of psychoactive substances in a representative manner. A large majority of street children use psychoactive substances, and there is a need for more of such studies in other metropolitan cities so that local level interventions and planning can be done for treatment and prevention of psychoactive substances among the street children. The important public health implications had been discussed.

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PMID: 31841817

41: Dhiman A, Kumar C, Mishra SK, Sikri K, Datta I, Sharma P, Singh TP, Haldar S, Sharma N, Bansal A, Ahmad Y, Kumar A, Sharma TK, Tyagi JS. Theranostic Application of a Novel G-Quadruplex-Forming DNA Aptamer Targeting Malate Synthase of *Mycobacterium tuberculosis*. *Mol Ther Nucleic Acids*. 2019 Dec 6;18:661-672. doi: 10.1016/j.omtn.2019.09.026. Epub 2019 Oct 4. PubMed PMID: 31704587; PubMed Central PMCID: PMC6849348.

The successful management of tuberculosis (TB) requires efficient diagnosis and treatment. Further, the increasing prevalence of drug-resistant TB highlights the urgent need to develop novel inhibitors against both drug-susceptible and drug-resistant forms of disease. Malate synthase (MS), an enzyme of the glyoxylate pathway, plays a vital role in mycobacterial persistence, and therefore it is considered as an attractive target for novel anti-TB drug development. Recent studies have also ascribed an adhesin function to MS and established it as a potent diagnostic biomarker. In this study, a panel of *Mycobacterium tuberculosis* (Mtb) MS-specific single-stranded DNA aptamers was identified by Systematic Evolution of Ligands by EXponential enrichment (SELEX). The best-performing G-quadruplex-forming 44-mer aptamer, MS10, was optimized post-SELEX to generate an 11-mer aptamer, MS10-Trunc. This aptamer was characterized by various biochemical, biophysical, and in silico techniques. Its theranostic activity toward Mtb was established using enzyme inhibition, host cell binding, and invasion assays. MS10-Trunc aptamer exhibited high affinity for

MS (equilibrium dissociation constant [KD] ~19 pM) and displayed robust inhibition of MS enzyme activity with IC50 of 251.1 nM and inhibitor constant (Ki) of 230 nM. This aptamer blocked mycobacterial entry into host cells by binding to surface-associated MS. In addition, we have also demonstrated its application in the detection of tuberculous meningitis (TBM) in patients with sensitivity and specificity each of >97%.

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DOI: 10.1016/j.omtn.2019.09.026

PMCID: PMC6849348

PMID: 31704587

42: Fatima S, Kamble SS, Dwivedi VP, Bhattacharya D, Kumar S, Ranganathan A, Van Kaer L, Mohanty S, Das G. Mycobacterium tuberculosis programs mesenchymal stem cells to establish dormancy and persistence. *J Clin Invest*. 2019 Dec 17. pii: 128043. doi: 10.1172/JCI128043. [Epub ahead of print] PubMed PMID: 31647784.

Tuberculosis (TB) remains a major infectious disease worldwide. TB treatment displays a biphasic bacterial clearance, in which the majority of bacteria clear within the first month of treatment, but residual bacteria remain nonresponsive to treatment and eventually may become resistant. Here, we have shown that Mycobacterium tuberculosis was taken up by mesenchymal stem cells (MSCs), where it established dormancy and became highly nonresponsive to isoniazid, a major constituent of directly observed treatment short course (DOTS). Dormant M. tuberculosis induced quiescence in MSCs and promoted their long-term survival. Unlike macrophages, where M. tuberculosis resides in early-phagosomal compartments, in MSCs the majority of bacilli were found in the cytosol, where they promoted rapid lipid synthesis, hiding within lipid droplets. Inhibition of lipid synthesis prevented dormancy and sensitized the organisms to isoniazid. Thus, we have established that M. tuberculosis gains dormancy in MSCs, which thus serve as a long-term natural reservoir of dormant M. tuberculosis. Interestingly, in the murine model of TB, induction of autophagy eliminated M. tuberculosis from MSCs and consequently, the addition of rapamycin to an isoniazid treatment regimen successfully attained sterile clearance and prevented disease reactivation.

DOI: 10.1172/JCI128043

PMID: 31647784

43: Fulpagare PH, Saraswat A, Dinachandra K, Surani N, Parhi RN, Bhattacharjee S, S S, Purty A, Mohapatra B, Kejrewal N, Agrawal N, Bhatia V, Ruikar M, Gope RK, Murira Z, De Wagt A, Sethi V. Antenatal Care Service Utilization Among Adolescent Pregnant Women—Evidence From Swabhimaan Programme in India. *Front Public Health*. 2019 Dec 12;7:369. doi: 10.3389/fpubh.2019.00369. eCollection 2019. PubMed PMID: 31921737; PubMed Central PMCID: PMC6927275.

**Purpose:** Pregnant adolescent girls (15-19 years) are more vulnerable to poor health and nutrition than adult pregnant women because of marginalization and lack of knowledge about the antenatal care (ANC) services. The present study aims to test this hypothesis and assess determinants of ANC service utilization among currently adolescent pregnant women. **Methods:** Data were drawn from the baseline survey of SWABHIMAAN project, which had been conducted in three states of India: Bihar, Chhattisgarh, and Odisha. Out of a total 2,573 pregnant women (15-49 years) included in the sample, about 10% (N = 278) were adolescent girls (15-19 years) at the time of the survey, and the rest were adults. Sample was selected from the population using simple random sampling, and information was collected using pretested questionnaires. **Results:** For all indicators of ANC service

utilization, performance of adolescent pregnant women was better than adult pregnant women. However, significant variations were reported in the level of services received by adult pregnant women for different indicators. Religion, wealth, food insecurity, Village Health Sanitation and Nutrition Day meeting, Public Distribution System and Integrated Child Development Services entitlements, and knowledge of family planning methods had a significant effect on the ANC service utilization. Conclusion: Adolescent pregnant women have shown better utilization of selected indicators than their adult counterparts. Utilization of full ANC services starting from first trimester itself for adolescent pregnant women is an urgent need in present context. Intervention program must pay attention to such adolescent married girls who are entering into the motherhood phase of their lives.

Copyright © 2019 Fulpagare, Saraswat, Dinachandra, Surani, Parhi, Bhattacharjee, S, Purty, Mohapatra, Kejrewal, Agrawal, Bhatia, Ruikar, Gope, Murira, De Wagt and Sethi.

DOI: 10.3389/fpubh.2019.00369

PMCID: PMC6927275

PMID: 31921737

44: Gandhi JS, Smith SC, Paner GP, McKenney JK, Sekhri R, Osunkoya AO, Baras AS, DeMarzo AM, Chevillie JC, Rafael JE, Trpkov K, Colecchia M, Ro JY, Montironi R, Menon S, Hes O, Williamson SR, Hirsch MS, Netto GJ, Fine SW, Sirohi D, Kaushal S, Sangoi A, Robinson BD, Kweldam CF, Humphrey PA, Hansel DE, Schultz L, Magi-Galluzzi C, Przybycin CG, Shah RB, Mehra R, Kunju LP, Aron M, Kryvenko ON, Kench JG, Kuroda N, Tavora F, van der Kwast T, Grignon DJ, Epstein JI, Reuter VE, Amin MB. Reporting Practices and Resource Utilization in the Era of Intraductal Carcinoma of the Prostate: A Survey of Genitourinary Subspecialists. *Am J Surg Pathol.* 2019 Dec 23. doi: 10.1097/PAS.0000000000001417. [Epub ahead of print] PubMed PMID: 31876580.

Intraductal carcinoma of the prostate (IDC-P) has been recently recognized by the World Health Organization classification of prostatic tumors as a distinct entity, most often occurring concurrently with invasive prostatic adenocarcinoma (PCa). Whether documented admixed with PCa or in its rare pure form, numerous studies associate this entity with clinical aggressiveness. Despite increasing clinical experience and requirement of IDC-P documentation in protocols for synoptic reporting, the specifics of its potential contribution to assessment of grade group (GG) and cancer quantitation of PCa in both needle biopsies (NBx) and radical prostatectomy (RP) specimens remain unclear. Moreover, there are no standard guidelines for incorporating basal cell marker immunohistochemistry (IHC) in the diagnosis of IDC-P, either alone or as part of a cocktail with AMACR/racemase. An online survey containing 26 questions regarding diagnosis, reporting practices, and IHC resource utilization, focusing on IDC-P, was undertaken by 42 genitourinary subspecialists from 9 countries. The degree of agreement or disagreement regarding approaches to individual questions was classified as significant majority (>75%), majority (51% to 75%), minority (26% to 50%) and significant minority (≤25%). IDC-P with or without invasive cancer is considered a contraindication for active surveillance by the significant majority (95%) of respondents, although a majority (66%) also agreed that the clinical significance/behavior of IDC-P on NBx or RP with PCa required further study. The majority do not upgrade PCa based on comedonecrosis seen only in the intraductal component in NBx (62%) or RP (69%) specimens. Similarly, recognizable IDC-P with GG1 PCa was not a factor in upgrading in NBx (78%) or RP (71%) specimens. The majority (60%) of respondents include readily recognizable IDC-P in assessment of linear extent of PCa at NBx. A significant majority (78%) would use IHC to confirm or exclude intraductal carcinoma if other biopsies showed no PCa, while

60% would use it to confirm IDC-P with invasive PCa in NBx if it would change the overall GG assignment. Nearly half (48%, a minority) would use IHC to confirm IDC-P for accurate Gleason pattern 4 quantitation. A majority (57%) report the percentage of IDC-P when present, in RP specimens. When obvious Gleason pattern 4 or 5 PCa is present in RP or NBx, IHC is rarely to almost never used to confirm the presence of IDC-P by the significant majority (88% and 90%, respectively). Most genitourinary pathologists consider IDC-P to be an adverse prognostic feature independent of the PCa grade, although recommendations for standardization are needed to guide reporting of IDC-P vis a vis tumor quantitation and final GG assessment. The use of IHC varies widely and is performed for a multitude of indications, although it is used most frequently in scenarios where confirmation of IDC-P would impact the GG assigned. Further study and best practices recommendations are needed to provide guidance with regards to the most appropriate indications for IHC use in scenarios regarding IDC-P.

DOI: 10.1097/PAS.0000000000001417

PMID: 31876580

45: Ghose S, Ghosh S, Tanwar VS, Tolani P, Kutum R, Sharma A, Bhardwaj N, Shamsudheen KV, Verma A, Jayarajan R, Dash D, Sivasubbu S, Scaria V, Seth S, Sengupta S. Investigating Coronary Artery Disease methylome through targeted bisulfite sequencing. *Gene*. 2019 Dec 30;721:144107. doi: 10.1016/j.gene.2019.144107. Epub 2019 Sep 6. PubMed PMID: 31499127.

**BACKGROUND:** Gene environment interactions leading to epigenetic alterations play pivotal role in the pathogenesis of Coronary Artery Disease (CAD). Altered DNA methylation is one such epigenetic factor that could lead to altered disease etiology. In this study, we comprehensively identified methylation sites in several genes that have been previously associated with young CAD patients.

**METHODS:** The study population consisted of 42 healthy controls and 33 young CAD patients (age group <50 years). We performed targeted bisulfite sequencing of promoter as well as gene body regions of several genes in various pathways like cholesterol synthesis and metabolism, endothelial dysfunction, apoptosis, which are implicated in the development of CAD.

**RESULTS:** We observed that the genes like GALNT2, HMGCR were hypermethylated in the promoter whereas LDLR gene promoter was hypomethylated indicating that intracellular LDL uptake was higher in CAD patients. Although APOA1 did not show significant change in methylation but APOC3 and APOA5 showed variation in methylation in promoter and exonic regions. Glucokinase (GCK) and endothelial nitric oxide synthase 3 (NOS3) were hyper methylated in the promoter. Genes involved in apoptosis (BAX/BCL2/AKT2) and inflammation (PHACTR1/LCK) also showed differential methylation between controls and CAD patients. A combined analysis of the methylated CpG sites using machine learning tool revealed 14 CpGs in 11 genes that could discriminate CAD cases from controls with over 93% accuracy.

**CONCLUSIONS:** This study is unique because it highlights important gene methylation alterations which might predict the risk of young CAD in Indian population. Large scale studies in different populations would be important for validating our findings and understanding the epigenetic events associated with CAD.

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DOI: 10.1016/j.gene.2019.144107

PMID: 31499127 [Indexed for MEDLINE]

46: Giridhar P, Kashyap L, Mallick S, Dutt Upadhyay A, Rath GK. Impact of surgery and adjuvant treatment on the outcome of extraocular sebaceous carcinoma: a systematic review and individual patient's data analysis of 206 cases. *Int J*

Dermatol. 2019 Dec 18. doi: 10.1111/ijd.14739. [Epub ahead of print] PubMed PMID: 31850516.

**BACKGROUND:** Extraocular sebaceous carcinoma (EOSC) is an aggressive malignancy of the sebaceous gland. Surgery is considered the cornerstone of treatment, but there is lack of clarity about extent and adjuvant treatment.

**METHODS:** We conducted a systematic review and analysis of individual patient data of all published cases of EOSC to look into demography, pattern of care, importance of type of surgery, and other adjuvant treatment and survival outcome. A search of PubMed and Google Scholar was done with the key words sebaceous carcinoma, extraocular sebaceous carcinoma, and Muir-Torre syndrome till December 2017. The data were compiled in an Excel chart and analyzed using SPSS IBM software.

**RESULTS:** Data of 206 patients were retrieved. Median age at presentation was 65 years (range: 11-96 years). Surgery was performed in all except 13 patients. Of these 13, eight were deemed inoperable for extensive disease, and five had metastatic disease. Median PFS and OS for the entire cohort were 84 months (95% CI: 10-158 months) and 92 months (95% CI: 59-126 months). Univariate analysis revealed significantly poor survival for patients with a metastatic disease, regional nodal metastasis, and those with Mohs micrographic or incomplete surgery.

**CONCLUSION:** EOSC is a disease of elderly patients with good prognosis. Complete surgery with regional lymph node dissection is standard treatment. The role of adjuvant radiotherapy is debatable but can be considered in patients with incomplete surgery or high-risk factors.

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PMID: 31850516

47: Govindaswamy A, Trikha V, Gupta A, Mathur P, Mittal S. An unusual case of post-trauma polymicrobial cutaneous diphtheria. *Infection*. 2019 Dec;47(6):1055-1057. doi: 10.1007/s15010-019-01300-x. Epub 2019 Apr 5. PubMed PMID: 30953325.

We report a rare case of post-traumatic cutaneous diphtheria in a patient referred from a hospital in rural India. The diagnosis of cutaneous diphtheria was confirmed by the isolation of *Corynebacterium diphtheriae* cultured from the ulcer of the leg, along with *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Arcanobacterium haemolyticum*. The patient was kept on isolation and treated with erythromycin for 14 days without antitoxin. He was discharged when his subsequent cultures turned out to be negative. Chemoprophylaxis was also given to his family members. Such a case highlights the revisiting of vaccination strategies and the role of cutaneous carriers in transmission of this deadly disease.

DOI: 10.1007/s15010-019-01300-x  
PMID: 30953325

48: Goyal A, Malhotra R, Kulshrestha V, Kachhawa G. Severe hyperandrogenism due to ovarian hyperthecosis in a young woman. *BMJ Case Rep*. 2019 Dec 17;12(12). pii: e232783. doi: 10.1136/bcr-2019-232783. PubMed PMID: 31852694.

Hyperandrogenism is a relatively common clinical problem. However, severe hyperandrogenism causing virilisation is rare. A 27-year-old woman presented with generalised hirsutism, clitoromegaly, breast atrophy and secondary amenorrhoea. She had serum testosterone levels elevated to the adult male range.

Administration of gonadotropin-releasing hormone (GnRH) analogue resulted in >50% suppression of serum testosterone which was suggestive of luteinising hormone-dependent ovarian hyperandrogenism. Imaging studies of abdomen and pelvis were normal, and ovarian venous sampling failed to show a gradient between the two sides. A presumptive diagnosis of ovarian hyperthecosis was, therefore, considered. Medical treatment with GnRH analogue and combined oral contraceptive pills was initiated to which an excellent clinical and biochemical response was noted. This case highlights a rare presentation of ovarian hyperthecosis in a young woman with severe hyperandrogenism mimicking a virilising neoplasm.

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DOI: 10.1136/bcr-2019-232783

PMID: 31852694

49: Goyal A, Gupta Y. Pre-analytical factors in blood glucose measurement. *Diabetes Res Clin Pract*. 2019 Dec;158:107802. doi: 10.1016/j.diabres.2019.107802. Epub 2019 Jul 26. PubMed PMID: 31356833.

50: Grace AG, Mittal A, Jain S, Tripathy JP, Satyanarayana S, Tharyan P, Kirubakaran R. Shortened treatment regimens versus the standard regimen for drug-sensitive pulmonary tuberculosis. *Cochrane Database Syst Rev*. 2019 Dec 12;12:CD012918. doi: 10.1002/14651858.CD012918.pub2. Review. PubMed PMID: 31828771; PubMed Central PMCID: PMC6953336.

**BACKGROUND:** Tuberculosis causes more deaths than any other infectious disease worldwide, with pulmonary tuberculosis being the most common form. Standard first-line treatment for drug-sensitive pulmonary tuberculosis for six months comprises isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE) for two months, followed by HRE (in areas of high TB drug resistance) or HR, given over a four-month continuation phase. Many people do not complete this full course. Shortened treatment regimens that are equally effective and safe could improve treatment success.

**OBJECTIVES:** To evaluate the efficacy and safety of shortened treatment regimens versus the standard six-month treatment regimen for individuals with drug-sensitive pulmonary tuberculosis.

**SEARCH METHODS:** We searched the following databases up to 10 July 2019: the Cochrane Infectious Diseases Group Specialized Register; the Central Register of Controlled Trials (CENTRAL), in the Cochrane Library; MEDLINE (PubMed); Embase; the Latin American Caribbean Health Sciences Literature (LILACS); Science Citation Index-Expanded; Indian Medlars Center; and the South Asian Database of Controlled Clinical Trials. We also searched the World Health Organization (WHO) International Clinical Trials Registry Platform, ClinicalTrials.gov, the Clinical Trials Unit of the International Union Against Tuberculosis and Lung Disease, the UK Medical Research Council Clinical Trials Unit, and the Clinical Trials Registry India for ongoing trials. We checked the reference lists of identified articles to find additional relevant studies.

**SELECTION CRITERIA:** We searched for randomized controlled trials (RCTs) or quasi-RCTs that compared shorter-duration regimens (less than six months) versus the standard six-month regimen for people of all ages, irrespective of HIV status, who were newly diagnosed with pulmonary tuberculosis by positive sputum culture or GeneXpert, and with presumed or proven drug-sensitive tuberculosis. The primary outcome of interest was relapse within two years of completion of anti-tuberculosis treatment (ATT).

**DATA COLLECTION AND ANALYSIS:** Two review authors independently selected trials, extracted data, and assessed risk of bias for the included trials. For

dichotomous outcomes, we used risk ratios (RRs) with 95% confidence intervals (CIs). When appropriate, we pooled data from the included trials in meta-analyses. We assessed the certainty of evidence using the GRADE approach.

**MAIN RESULTS:** We included five randomized trials that compared fluoroquinolone-containing four-month ATT regimens versus standard six-month ATT regimens and recruited 5825 adults with newly diagnosed drug-sensitive pulmonary tuberculosis from 14 countries with high tuberculosis transmission in Asia, Africa, and Latin America. Three were multi-country trials that included a total of 572 HIV-positive people. These trials excluded children, pregnant or lactating women, people with serious comorbid conditions, and those with diabetes mellitus. Four trials had multiple treatment arms. Moxifloxacin replaced ethambutol in standard four-month, daily or thrice-weekly ATT regimens in two trials; moxifloxacin replaced isoniazid in four-month ATT regimens in two trials, was given daily in one trial, and was given with rifapentine instead of rifampicin daily for two months and twice weekly for two months in one trial. Moxifloxacin was added to standard ATT drugs for three to four months in one ongoing trial that reported interim results. Gatifloxacin replaced ethambutol in standard ATT regimens given daily or thrice weekly for four months in two trials. Follow-up ranged from 12 months to 24 months after treatment completion for the majority of participants. Moxifloxacin-containing four-month ATT regimens

Moxifloxacin-containing four-month ATT regimens that replaced ethambutol or isoniazid probably increased the proportions who experienced relapse after successful treatment compared to standard ATT regimens (RR 3.56, 95% CI 2.37 to 5.37; 2265 participants, 3 trials; moderate-certainty evidence). For death from any cause, there was probably little or no difference between the two regimens (2760 participants, 3 trials; moderate-certainty evidence). Treatment failure was rare, and there was probably little or no difference in proportions with treatment failure between ATT regimens (2282 participants, 3 trials; moderate-certainty evidence). None of the participants given moxifloxacin-containing regimens developed resistance to rifampicin, and these regimens may not increase the risk of acquired resistance (2282 participants, 3 trials; low-certainty evidence). Severe adverse events were probably little or no different with moxifloxacin-containing four-month regimens that replaced ethambutol or isoniazid, and with three- to four-month regimens that augmented standard ATT with moxifloxacin, when compared to standard six-month ATT regimens (3548 participants, 4 trials; moderate-certainty evidence).

Gatifloxacin-containing four-month ATT regimens Gatifloxacin-containing four-month ATT regimens that replaced ethambutol probably increased relapse compared to standard six-month ATT regimens in adults with drug-sensitive pulmonary tuberculosis (RR 2.11, 95% CI 1.56 to 2.84; 1633 participants, 2 trials; moderate-certainty evidence). The four-month regimen probably made little or no difference in death compared to the six-month regimen (1886 participants, 2 trials; moderate-certainty evidence). Treatment failure was uncommon and was probably little or no different between the four-month and six-month regimens (1657 participants, 2 trials; moderate-certainty evidence). Acquired resistance to isoniazid or rifampicin was not detected in those given the gatifloxacin-containing shortened ATT regimen, but we are uncertain whether acquired drug resistance is any different in the four- and six-month regimens (429 participants, 1 trial; very low-certainty evidence). Serious adverse events were probably no different with either regimen (1993 participants, 2 trials; moderate-certainty evidence).

**AUTHORS' CONCLUSIONS:** Evidence to date does not support the use of shortened ATT regimens in adults with newly diagnosed drug-sensitive pulmonary tuberculosis. Four-month ATT regimens that replace ethambutol with moxifloxacin or gatifloxacin, or isoniazid with moxifloxacin, increase relapse substantially compared to standard six-month ATT regimens, although treatment success and serious adverse events are little or no different. The results of six large ongoing trials will help inform decisions on whether shortened ATT regimens can

replace standard six-month ATT regimens. 9 December 2019 Up to date All studies incorporated from most recent search All eligible published studies found in the last search (10 Jul, 2019) were included.

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PMCID: PMC6953336 [Available on 2020-12-12]

PMID: 31828771

51: Gunathilaka PKG, Jat KR, Sankar J, Lodha R, Kabra SK. Propofol versus Fentanyl for Sedation in Pediatric Bronchoscopy: A Randomized Controlled Trial. *Indian Pediatr.* 2019 Dec 15;56(12):1011-1016. PubMed PMID: 31884429.

OBJECTIVE: To compare propofol and fentanyl to induce conscious sedation in children undergoing flexible bronchoscopy.

STUDY DESIGN: Randomized controlled trial.

SETTING: Pediatric Pulmonology division at a tertiary care center in Delhi, India.

PARTICIPANTS: Children aged 3-15 years who underwent flexible bronchoscopy.

INTERVENTION: Children received either intravenous propofol 1 mg/kg administered as a slow bolus over 1 minute followed by 2 mg/kg/hour infusion, or intravenous Fentanyl 2 µg/kg administered as a slow bolus over one minute.

OUTCOMES: Primary outcome was time to achieve conscious sedation (Ramsay score 3). Secondary outcomes were need for adjuvant midazolam, physician satisfaction, level of cough, recovery features, and side-effects in the groups.

RESULTS: 53 children (propofol 27, fentanyl 26) were enrolled in the study. The mean (SD) time taken to achieve Ramsay score 03 was lower in propofol than fentanyl [15.7 (4.4) s vs 206 (55) s,  $P < 0.001$ ]. Propofol arm had significantly higher physician satisfaction, less requirement of adjuvant midazolam, less coughing and faster regain of full consciousness. There was no difference in drug side-effects between the groups.

CONCLUSIONS: Propofol has a shorter sedation induction time, less coughing during procedure, less recovery time, and better physician satisfaction compared to fentanyl for flexible bronchoscopy in children.

PMID: 31884429

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Cryopyrin-associated periodic fever syndrome (CAPS) represents an increasingly recognized disease group entity, with varied presentations. CAPS includes 3 clinical entities, namely, familial cold-induced autoinflammatory syndrome (FCAS; MIM #120100), Muckle-Wells syndrome (MWS; MIM #191900) and chronic inflammatory neurologic cutaneous and articular syndrome (CINCA; MIM #607115); which share several overlapping clinical features. These patients often present with early-onset episodes of fever and rash, and variable systemic signs and symptoms, making it a great mimicker of other systemic autoimmune diseases. The episodes are transient and related to exposure to cold temperature and worsen in the winter season. We hereby present a case presenting with recurrent seasonal fever and rash, diagnosed as FCAS/ MWS overlap based on clinical signs and symptoms and positive testing for NLRP3 gene mutation. We also discuss the clinical presentation and complications of CAPS, chiefly FCAS and MWS, along with the

previously described pediatric cases of CAPS. We tried to review the complexities of management of such patients, including the genetic diagnosis and the role of biological therapy. Based on the review of the literature, given the evident broad spectrum of symptoms and signs, use of next-generation sequencing can help in prompt diagnosis and early initiation of biological agents, which may play a great role in reducing the complications that these patients may experience in the long run.

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PMID: 31858722

53: Gupta N, Sharma A, Sharma A. Emerging biomarkers in Multiple Myeloma: A review. *Clin Chim Acta*. 2019 Dec 31;503:45-53. doi: 10.1016/j.cca.2019.12.026. [Epub ahead of print] Review. PubMed PMID: 31901479.

Multiple Myeloma (MM) is the second most common hematological malignancy after non-Hodgkin lymphoma and is manifested by uncontrolled proliferation and accumulation of abnormal plasma cells in the bone marrow (BM). The incidence along with deaths associated with MM is on rise due to lack of an effective diagnosis at an early stage. The identification of MM decades ago marks the adoption of certain conventional markers such as plasma cell percentage in BM, serum protein electrophoresis for M-band and urinary Bence-Jones protein. This was then followed by utilization of  $\beta_2$  microglobulin and serum albumin for determining the staging of MM. The need for a better diagnostic or prognostic marker prompts researchers and hence, certain novel markers have been tested which includes extracellular matrix proteins, angiogenic factors, telomeres and telomerase along with the immune markers. Nowadays, proteomic and genomic studies are being performed to identify novel diagnostic and/or prognostic markers for MM. Followed by this, comes the emerging concept of liquid biopsy which allows easy and non-invasive detection of the disease. The liquid biopsy comprises of circulatory tumor cells along with the nucleic acids (microRNAs and cell-free DNA) released from the tumor cells in peripheral circulation which could be a true representation of BM. This review, hence, summarizes the emerging biomarkers involved in the diagnosis and prognosis of MM.

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DOI: 10.1016/j.cca.2019.12.026  
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**BACKGROUND AND OBJECTIVES:** Diagnosis of Parkinson's with higher accuracy is always desirable to slow down the progression of the disease and improved quality of life. There are evidences of inherent neurological differences between male and females as well as between elderly and adults. However, the potential of such gender and age information have not been exploited yet for Parkinson's identification.

**METHODS:** In this paper, we develop a sex-specific and age-dependent classification method to diagnose the Parkinson's disease using the online handwriting recorded from individuals with Parkinson's (n = 37; m/f-19/18; age-69.3 ± 10.9yrs) and healthy controls (n = 38; m/f-20/18; age-62.4 ± 11.3yrs). A support vector machine ranking method is used to present the features specific to their dominance in sex and age group for Parkinson's diagnosis.

**RESULTS:** The sex-specific and age-dependent classifier was observed significantly outperforming the generalized classifier. An improved accuracy of 83.75% (SD = 1.63) with the female-specific classifier, and 79.55% (SD = 1.58) with the old-age dependent classifier was observed in comparison to 75.76% (SD = 1.17) accuracy with the generalized classifier.

**CONCLUSIONS:** Combining the age and sex information proved to be encouraging in classification. A distinct set of features were observed to be dominating for higher classification accuracy in a different category of classification.

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**INTRODUCTION:** Strong association exists between celiac disease and autoimmune endocrinopathies such as type I diabetes and hypothyroidism; there is a lack of data on the involvement of other endocrine organs such as pituitary-gonadal axis. Furthermore, there is lack of data on the spectrum of involvement of endocrine organs varying from organ autoimmunity to subclinical and clinical disease. We evaluated consecutive treatment-naïve patients with celiac disease (CeD) for clinical and subclinical endocrinopathies.

**METHODS:** Of 154 screened, 74 treatment-naïve patients with CeD were recruited. They underwent hormonal and/or functional assessment of beta cell of pancreas, thyroid gland, pituitary-gonadal axis, and parathyroid glands.

**RESULTS:** Of the 74 patients with CeD, 31 (41.9%) had at least one clinical or subclinical endocrinopathy and 9 (12.2%) had multiple endocrinopathies. Most common of them were clinical or subclinical type I diabetes and autoimmune thyroid disease. Interestingly, 8 (10.8%) patients also were found to have functional hypopituitarism and 7/54 (12.9%) having isolated hypogonadotropic hypogonadism.

**CONCLUSIONS:** Patients with CeD have high percentages of not only clinical endocrinopathy including pituitary-gonadal axis dysfunction but also subclinical endocrinopathy. Whether commencement of gluten-free diet will lead to reversal of

subclinical endocrinopathies requires further follow up studies.

DOI: 10.1007/s12664-019-01006-w  
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**PURPOSE OF STUDY:** Ultrasound (US) for lumbar puncture has seen the most success in obese patients and in patients with difficult to palpate landmarks. We aimed to elucidate the advantage of the use of routine US for performing lumbar punctures over the traditional landmark method.

**STUDY DESIGN:** This was a prospective study with consecutive sampling with a sample size of convenience. Three residents were chosen to perform the lumbar punctures after a training session. Patients were assigned to either the US group or the landmark group. The outcomes studied were number of attempts at needle insertion, patient and physician anxiety, pain experienced, time to procedure, number of traumatic attempts and the difficulties faced during the procedure.

**RESULTS:** A total of 77 patients were included in this study, of which 36 patients (46.8%) underwent landmark-based lumbar puncture and 41 (53.2%) underwent US-guided lumbar puncture. There was no statistically significant difference between the two groups among the following characteristics: number of attempts to a successful procedure, number of traumatic punctures, procedure time, preprocedure anxiety of the participants and physicians and pain score rating of the procedure.

**CONCLUSION:** There was no significant difference between the landmark method and US-guided method for performing lumbar puncture in the number of successful attempts, number of traumatic punctures, procedure time and pain during the procedure. Further studies are required to elucidate the advantage of the use of ultrasonography in subsets of the population such as the low body mass index population.

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PMID: 31806733

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**OBJECTIVES:** While the burden of dementia is increasing in low- and middle-income countries, there is a low rate of diagnosis and paucity of research in these

regions. A major challenge to study dementia is the limited availability of standardised diagnostic tools for use in populations with linguistic and educational diversity. The objectives of the study were to develop a standardised and comprehensive neurocognitive test battery to diagnose dementia and mild cognitive impairment (MCI) due to varied etiologies, across different languages and educational levels in India, to facilitate research efforts in diverse settings.

**METHODS:** A multidisciplinary expert group formed by Indian Council of Medical Research (ICMR) collaborated towards adapting and validating a neurocognitive test battery, that is, the ICMR Neurocognitive Tool Box (ICMR-NCTB) in five Indian languages (Hindi, Bengali, Telugu, Kannada, and Malayalam), for illiterates and literates, to standardise diagnosis of dementia and MCI in India.

**RESULTS:** Following a review of existing international and national efforts at standardising dementia diagnosis, the ICMR-NCTB was developed and adapted to the Indian setting of sociolinguistic diversity. The battery consisted of tests of cognition, behaviour, and functional activities. A uniform protocol for diagnosis of normal cognition, MCI, and dementia due to neurodegenerative diseases and stroke was followed in six centres. A systematic plan for validating the ICMR-NCTB and establishing cut-off values in a diverse multicentric cohort was developed.

**CONCLUSIONS:** A key outcome was the development of a comprehensive diagnostic tool for diagnosis of dementia and MCI due to varied etiologies, in the diverse socio-demographic setting of India.

DOI: 10.1017/S1355617719001127

PMID: 31826780

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**Introduction:** Acute pancreatitis is an inflammatory condition of the pancreas, which runs a severe course in 20% of patients, wherein it is associated with high mortality. It is associated with several pleuro-pulmonary complications with variable severity that may occur either in isolation but are frequently present in combination. Clinicians need to be aware of these complications for early and appropriate management. **Areas covered:** We performed a systematic search of the PUBMED database (1970-2019) to identify relevant articles focusing on pleuro-pulmonary complications that may occur in patients with acute pancreatitis. We also retrieved articles describing the pathophysiological mechanisms and treatment approach of the various complications. **Expert opinion:** Acute pancreatitis is usually a self-limiting disease, but the development of organ failure during the course worsens the clinical outcome. Pulmonary complications usually occur early in the course of acute pancreatitis. Clinicians need to recognize the various pulmonary complications of acute pancreatitis, early during the disease, and manage them appropriately and aggressively to improve outcomes.

DOI: 10.1080/17476348.2020.1698951

PMID: 31779502

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**BACKGROUND:** Previous epidemiological studies, largely conducted in high-income

countries and cross-sectional, have suggested a relatively strong association between exposure to dichlorodiphenyldichloroethylene (DDE), a metabolite of the pesticide dichlorodiphenyltrichloroethane (DDT), and type 2 diabetes. DDT is widely used in India and the prevalence of type 2 diabetes there is increasing, but the association between these factors has not been explored to date.

**OBJECTIVE:** The objective was to estimate the association of the p,p' isomer of DDE with incident type 2 diabetes in India.

**METHODS:** A nested case-control study was conducted in a representative prospective cohort of adults from two cities in India. Participants were enrolled in 2010-11 (n=12,271) and followed for annual assessment of chronic diseases including type 2 diabetes. Baseline plasma samples from incident cases of diabetes (n=193) and sex-city-matched controls (n=323) were selected for analysis of p,p-DDE. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using conditional logistic regression.

**RESULTS:** At baseline, cases had higher p,p-DDE concentrations: geometric mean (95% CI) 330 (273-399) ng/g lipid compared to 223 (189-262) ng/g lipid among controls. Delhi participants had higher p,p-DDE concentrations: 579 (521-643) ng/g lipid compared to 122 (102-145) ng/g lipid in Chennai. In unadjusted models, being in the highest versus lowest quartile of p,p-DDE was associated with a more than doubling of the odds of diabetes: unadjusted OR (95% CI), 2.30 (1.19, 4.43). However, this effect was no longer significant after adjustment for age: adjusted (95% CI), 0.97 (0.46, 2.06).

**DISCUSSION:** Results suggest that levels of p,p'-DDE in Delhi are exceptionally high, but we did not observe a significant association between p,p-DDE and incident type 2 diabetes. As this is the first study to evaluate this association in India, more studies are needed to inform our understanding of the association in this context, including potential routes of exposure.

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PMCID: PMC6860016 [Available on 2020-12-01]

PMID: 31654984

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With advances in therapeutic methods, there is a high survival rate among leukemia patients, of an extent more than 80%. However, chemotherapeutic drugs used to treat these patients have adverse effects on their overall health profile including fertility. The primary aim of this study was to identify differentially expressed proteins in seminal plasma of acute lymphoblastic leukemia (ALL) survivors compared to age-matched healthy controls, which can provide molecular basis of idiopathic infertility in such survivors. Differential proteome profiling was performed by 2D-differential in-gel electrophoresis, protein spots were identified by mass spectrometry and selective differentially expressed proteins (DEPs) were validated by western blotting and ELISA method. Out of eight DEPs identified, five proteins (isocitrate dehydrogenase 1, semenogelin 1, lactoferrin, prolactin-inducible protein, and human serum albumin) were upregulated and three (pepsinogen, prostate specific antigen and prostatic acid

phosphatase) were downregulated. Expression profiles of these proteins are suggestive of reduction in semen quality in ALL survivors and can further be explored to determine their fertility status.

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DOI: 10.1016/j.repbio.2019.11.002

PMID: 31711845

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**BACKGROUND:** Genomic studies have delineated distinct molecular subgroups of urothelial carcinomas whose prognostic impact extends beyond traditional stage and grade groupings. The 'basal' subgroup shows increased gene expression levels of KRT5, KRT6, and KRT14 and low expression levels of GATA binding protein 3, and is associated with an extremely poor outcome. Identification of this subset is necessary for improved patient management and research on targeted therapies. We aimed to assess the prognostic utility of immunohistochemistry (IHC) for basal markers: cytokeratin 5/6 (CK5/6) and 14 (CK14), and luminal markers: cytokeratin 20 (CK20) and Gata3 in muscle invasive urothelial carcinomas (MIBC).

**MATERIALS AND METHODS:** Study was of retrospective design (2014-2017). All chemotherapy naïve patients of MIBC undergoing radical cystectomy were included. IHC was performed on formalin fixed paraffin-embedded whole tumor sections.

**RESULTS:** Among 40 cases of MIBC included, 45% (18/40) were positive for one or both basal markers, 37.5% (15/40) were positive for one or both luminal markers, while 15% (6/40) were positive for both basal and luminal markers. One case did not express any of the four markers. MIBCs expressing only basal markers presented at an advanced stage with frequent squamous differentiation and showed a trend towards shorter overall survival. Gata3+ MIBCs showed the best outcome irrespective of expression of other markers, while CK14+/Gata3- MIBCs were associated with worst outcomes. Gata3-/CK14- MIBCs showed intermediate survival outcomes. CK5/6, CK20 and p53 expression did not significantly correlate with outcome.

**CONCLUSION:** IHC for Gata-3 and CK14 stratified MIBC into distinct prognostic subsets.

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DOI: 10.1016/j.anndiagpath.2019.08.001

PMID: 31494492

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Context: Noncompliance with thyroxine therapy is the most common cause of poor control of hypothyroidism. An open-label prospective study to compare once-weekly thyroxine (OWT) with standard daily thyroxine (SDT) was undertaken.

Design: Patients taking thyroxine doses of  $>3 \mu\text{g}/\text{kg}/\text{d}$ , with or without normalization of TSH, were included and administered directly observed OWT or nonobserved SDT according to patient preference based on their weight for 6 weeks. Furthermore, patients on OWT were advised to continue the same at home without supervision.

Results: Twenty six of 34 patients on OWT and 7 of 18 patients on SDT achieved a TSH  $<10 \mu\text{IU}/\text{mL}$  ( $P < 0.05$ ), and 2 patients from the SDT arm were lost to follow-up. During home treatment, 15 of 25 at 12 weeks and 19 of 23 contactable patients at a median follow-up of 25 months maintained TSH below target.

Thyroxine absorption test was unable to predict normalization of TSH at 6 weeks of OWT therapy. No adverse events were seen with OWT-treated patients over the 12-week follow-up period. OWT has significantly higher efficacy ( $\text{OR} = 5.1$ ) than SDT for patients with thyroxine-resistant hypothyroidism and is not associated with side effects.

Conclusion: OWT benefits a majority of patients in the long-term treatment of thyroxine-resistant hypothyroidism, in the real-world setting.

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PMCID: PMC6834071

PMID: 31723717

69: Jayaraj P, Sen S. Evaluation of PD-L1 and PD-1 expression in aggressive eyelid sebaceous gland carcinoma and its clinical significance. *Indian J Ophthalmol.* 2019 Dec;67(12):1983-1987. doi: 10.4103/ijo.IJO\_2056\_18. PubMed PMID: 31755433; PubMed Central PMCID: PMC6896547.

Purpose: Eyelid sebaceous gland carcinoma (SGC) is an aggressive but rare malignancy of ocular region. Over-expression of PD-L1 and PD-1 has been demonstrated in a variety of solid tumors including conjunctival melanoma. PD-L1 is an immunoinhibitory molecule that suppresses the effective T cells response against tumor antigen leading to the progression of tumors. Inhibitors of the interaction of PD-L1 and PD-1 are associated with good clinical response various carcinomas. The prognostic value of the PD-1/PD-L1 axis in SGC remains unexplored. The purpose of this study was to evaluate expressions of PD-1 and its ligand PD-L1 in SGC and correlate its expression with clinicopathological features and patients survival.

Methods: The immunohistochemical expression of PD-L1 and PD-1 was evaluated in 30 SGC cases.

Results: PD-L1 immunopositivity was detected in 41.9% of the SGC cases. PD-1 expression in tumor infiltrative lymphocytes (TILs) was observed in 53.3% samples. Tumor PD-L1 positivity, PD-1 expression in TILs and tumor size ( $>10 \text{ mm}$ ) was associated with reduced disease-free survival. On multivariate analysis only tumor size ( $>10 \text{ mm}$ ) and a combined positivity of PD-L1 in tumor cells and PD-1 in TILs with an odds ratio of 5.212 (95% confidence interval 1.449-18.737) continued to be significantly associated with SGC recurrence.

Conclusion: PD-L1 is overexpressed in 50% of SGC cases. The combined tumor PD-L1 positivity and TILs showing PD-1 expression within the same SGC patient's samples predict high-risk SGC, suggesting that the up-regulation of PD-L1 in tumor cells and PD-1 positivity within the same SGC patient may aggravate tumor recurrence.

DOI: 10.4103/ijo.IJO\_2056\_18

PMCID: PMC6896547

PMID: 31755433

70: Jha J, Singh MK, Singh L, Pushker N, Bajaj MS, Sen S, Kashyap S. Prognostic relevance of ATM protein in uveal melanoma and its association with clinicopathological factors. *Int J Clin Oncol*. 2019 Dec;24(12):1526-1535. doi: 10.1007/s10147-019-01519-6. Epub 2019 Aug 3. PubMed PMID: 31377937.

**PURPOSE:** Uveal melanoma (UM) is an intraocular malignancy commonly arising from choroid which can cause visual loss or metastasis. Ataxia-telangiectasia mutated (ATM) protein is an activator of DNA damage response and its role in uveal melanoma (UM) is still unexplored. Therefore, the study aims to detect the expression and localization of ATM protein and its association with clinicopathological parameters **METHODS:** Expression of nuclear ATM (nATM) was investigated on 69 formalin fixed paraffin embedded choroidal melanoma samples by immunohistochemistry and validated by western blotting. Results were then correlated with clinical and histopathological parameters. Prognostic significance was determined by the Kaplan-Meier analysis and the multivariate analysis by Cox's hazard proportional method.

**RESULTS:** Loss of nATM was observed in 65% of cases, which was statistically significant with the reduced disease-free survival ( $p=0.042$ ). This loss was more frequently found in cases with high-risk histopathological factors like epithelioid cell type, tumor infiltrating lymphocytes and high pigmentation which might help in the progression of melanoma. On multivariate analysis, extraocular spread and loss of nATM were found to be independent prognostic factors ( $p<0.05$ ).

**CONCLUSION:** Our data suggest that loss of nATM protein might serve as a poor prognostic marker in the pathogenesis of uveal melanoma which may lead to increased risk of metastasis.

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PMID: 31377937

71: Jha P, Manjunath N, Singh J, Mani K, Garg A, Kaur K, Sharma MC, Raheja A, Suri A, Sarkar C, Suri V. Analysis of PD-L1 expression and T cell infiltration in different molecular subgroups of diffuse midline gliomas. *Neuropathology*. 2019 Dec;39(6):413-424. doi: 10.1111/neup.12594. Epub 2019 Oct 17. PubMed PMID: 31625205.

Diffuse midline gliomas (DMGs) are rare and devastating tumors with limited therapeutic options. Programmed death-ligand 1 (PD-L1) expression represents a potential predictive biomarker for immunotherapy. One hundred and twenty-six DMGs (89 adult and 37 pediatric) were assessed for immune profile (PD-L1, cluster of differentiation (CD3, CD8) and genetic markers (mutation in 27th amino acid of histone H3 (H3K27M), alpha thalassemia/mental retardation syndrome X-linked (ATRX), isocitrate dehydrogenase 1 (IDH1), p53) by immunohistochemistry. Sanger sequencing was done for IDH1 and H3K27M. The thalamus was the commonest site. Four molecular subgroups of DMGs were identified. H3K27M mutation was more frequent in children ( $P = 0.0001$ ). The difference in median overall survival (OS) was not significant in any of the four molecular subgroups ( $P > 0.05$ ). PD-L1 expression was significantly higher in H3K27M/IDH1 double-negative adult glioblastomas (GBMs) ( $P = 0.002$ ). Strong PD-L1 expression was more frequent in grade IV tumors and thalamic location, although the difference was not significant ( $P = 0.14$  and  $P = 0.19$  respectively). Positive PD-L1 expression was significantly associated with high tumor-infiltrating lymphocytes count ( $P < 0.05$ ). There was no significant difference in median OS in PD-L1-positive versus negative cases among four genetic subgroups ( $P > 0.05$ ). On univariate analysis, there was no direct correlation of PD-L1 with any genetic alteration, except H3K27M mutation ( $P = 0.01$ ). CD3 infiltration was similar in both adults

and pediatric ages (84.3% and 78.4%, respectively) while CD8 expression was significantly greater in adults compared to children (74.1% vs 37.8%,  $P = 0.0001$ ). This is the first comprehensive analysis highlighting molecular and immune profiles of DMGs. Despite molecular and clinicopathological diversity, overall survival in DMGs remains dismal. Multicentric studies with larger numbers of cases should be undertaken for stratifying DMGs according to their age, immune and molecular profiles, to develop effective immunotherapies.

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PMID: 31625205

72: Jobin SP, Maitra S, Baidya DK, Subramaniam R, Prasad G, Seenu V. Role of serial lactate measurement to predict 28-day mortality in patients undergoing emergency laparotomy for perforation peritonitis: prospective observational study. *J Intensive Care*. 2019 Dec 11;7:58. doi: 10.1186/s40560-019-0418-9. eCollection 2019. PubMed PMID: 31890220; PubMed Central PMCID: PMC6907168.

**Background:** Serial lactate measurement is found to predict mortality in septic shock. Majority of patients with perforation peritonitis for emergency laparotomy are in sepsis and mortality rate is substantial. However, lactate dynamics has not been studied in this patient population.

**Methods:** After institutional ethics clearance and informed written consent, 113 patients with suspected or proven perforation peritonitis presenting for emergency laparotomy were recruited in this prospective observational trial.

Baseline Mannheim peritonitis index (MPI), SOFA and APACHE II score were calculated. Lactate values were obtained at baseline, immediate and 24-h postoperative period. Primary outcome was 28-day mortality.

**Results:** Mortality was 15.04% at 28 days. Age, SOFA, qSOFA, APACHE, preoperative lactate, MPI and site of perforation were significantly different between survivors and non-survivors. Arterial lactate values at preoperative (cut off 2.75 mmol/L), immediate postoperative (cut off 2.8 mmol/L) and 24-h-postoperative period (cut off 2.45 mmol/L) independently predicted mortality at day 28.

Combination of MPI and 24-h lactate value was best predictor of mortality with AUC 0.99.

**Conclusion:** Preoperative, immediate postoperative and 24-h postoperative lactate value independently predict 28-day mortality in perforation peritonitis patients undergoing emergency laparotomy. Combination of MPI and 24-h lactate value is the most accurate predictor of mortality.

**Trial registration:** Clinical Trial Registry of India - CTRI/2018/01/011103.

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PMID: 31890220

73: Kakkar A, Sakthivel P, Mahajan S, Thakar A. Nasopharyngeal Papillary Adenocarcinoma as a Second Head and Neck Malignancy. *Head Neck Pathol*. 2019 Dec;13(4):699-704. doi: 10.1007/s12105-018-0944-0. Epub 2018 Jun 19. PubMed PMID: 29923095; PubMed Central PMCID: PMC6854352.

Nasopharyngeal adenocarcinomas are rare tumours, and include neoplasms arising from the nasopharyngeal surface epithelium as well as those of minor salivary gland origin, each of which is distinct from the other. The former encompasses nasopharyngeal papillary adenocarcinoma (NPAC), also known as low grade NPAC and

thyroid-like NPAC, an extremely unusual malignancy bearing histomorphological similarity to papillary thyroid carcinoma, and displaying indolent clinical behaviour. We report the case of a 41-year-old lady who developed NPAC as a second malignancy five-and-a-half years after being diagnosed and treated for a diffuse astrocytoma in the frontal lobe. In addition, we discuss the differential diagnosis, as well as raise certain pathogenetic considerations with regard to this unique neoplasm.

DOI: 10.1007/s12105-018-0944-0

PMCID: PMC6854352

PMID: 29923095

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**Background:** Calcium requirement increases during pregnancy, thereby increasing the chances of developing hypocalcaemia. Hypocalcaemia may be associated with pregnancy-related complications. Therefore, we planned this study to estimate the prevalence of hypocalcaemia among pregnant women attending secondary care hospital, and to study the association between hypocalcaemia and pregnancy outcomes.

**Materials and Methods:** This study was conducted in a secondary level hospital at Ballabgarh, district Faridabad, Haryana, India. Consecutive pregnant women with gestation period more than 28 weeks were enrolled. Dietary calcium intake was ascertained using 24-hour dietary recall method. Serum calcium estimation was done by Biolis 24i auto analyser. Outcome of pregnancy (preterm delivery, low birth weight (LBW) babies, and neonatal mortality) was assessed telephonically 3 months after the enrolment.

**Results:** A total of 696 pregnant women were enrolled in the study. Mean (SD) dietary calcium intake and serum calcium level was 796.4 (360.4) mg/day and 9.56 (0.94) mg/dl respectively. Prevalence (95% CI) of hypocalcaemia was 23.9% (20.8 - 27.2%). Serum total calcium level was not associated with dietary calcium intake (p-value = 0.36). Mean serum calcium level was significantly lower in mothers who had LBW babies. Pre-eclampsia, preterm delivery, and neonatal mortality were not associated with serum calcium level.

**Conclusion:** Serum calcium level may not be related to dietary calcium level. Hence, the current recommendation of calcium supplementation during antenatal period appears to be inconclusive among our study population.

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Conjoined twins are a rare outcome of conception associated with numerous anomalies involving multiple organ systems. Musculoskeletal abnormalities like vertebral anomalies, sacral agenesis, foot deformities and hip dysplasia have been described in literature. We describe two cases of pyopagus twins with congenital talipes equinovarus and congenital vertical talus deformity which have not been described previously in this type of conjoined twins. The orthopaedist

should look actively for such deformities in this patient population and be wary of the difficulties associated with their management.

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AIMS: Recently, strategies of cancer treatment using combination of agents with distinct molecular mechanism(s) of action are considered more promising due to its high efficacy and reduced systemic toxicity. The study is aimed to improve the efficacy of selective estrogen receptor modulator, Centchroman (CC) by combination with the phytoestrogen Genistein (GN).

METHODS: Cytotoxicity was evaluated by Sulforhodamine B assay. Cell cycle analysis was done through flow cytometry. Further, Apoptosis was analyzed using Annexin V/PI staining, tunel assay and electron microscopic examination and verified using western blot analysis. In order to validate the in vitro results, in vivo analysis was performed using 4T1-syngeneic mouse model.

KEY FINDINGS: In this study, we report that the dietary isoflavone genistein (GN) synergistically improved antineoplasticity of CC in breast cancer by arresting cells at G2/M phase culminating in ROS dependent apoptosis. The combination of CC plus GN caused dysregulation of Bax and Bcl-2 ratio inducing mitochondrial dysfunction, activation of Caspase-3/7, -9 and PARP cleavage. Further, combination significantly suppresses phosphorylation of PI3K/Akt/NF- $\kappa$ B, enhancing apoptosis. Additionally, combination markedly reduced tumor growth compared to CC and GN alone in mouse 4T1 breast tumor model.

SIGNIFICANCE: Together, these studies suggest that GN represents a potential adjunct molecule whose role in CC induced apoptosis deserves attention.

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Oral diseases, including dental caries, periodontitis, and edentulism (toothlessness), affect about 3.5 billion people worldwide. A cross-sectional study was conducted to assess the oral health status and treatment needs of government employees employed at an organization in New Delhi. Oral health information was recorded using the standard World Health Organization's (WHO) Oral Health Assessment Tool. A total of 476 employees at various levels of administration were screened at their worksite. Dental caries and periodontal disease were present in more than half of the participants. Around 56% had decayed teeth, 20% had missing teeth, and 16% had filled teeth. Bleeding from gums was seen in 71% and periodontitis in 59% of participants. Preventive treatment and oral health promotion was required in at least 41% of the screened individuals. Annual workplace oral examinations may help in decreasing the oral disease burden and create awareness on the oral health among employees.

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**BACKGROUND:** The pancreatobiliary carcinomas are characterized by presence of desmoplastic stroma. Overexpression of secreted protein acid and rich in cysteine (SPARC), a matrix producing agent has been documented in pancreatic ductal adenocarcinomas, with survival benefits. This study was targeted to see if SPARC expression in pancreatobiliary carcinomas is responsible for stromal desmoplasia and its prognostic significance.

**METHODS:** In this retrospective study 48 cases of pancreatic cancer and 27 cases of cholangiocarcinoma were analyzed. The expression pattern of SPARC and vascular endothelial growth factor (VEGF) (angiogenic factors) was evaluated by immunohistochemistry on formalin fixed paraffin embedded tissues.

Immunoreactivity was scored semi quantitatively based on stain intensity and stain distribution. SPARC expression was correlated with tumor histology, stromal desmoplasia, VEGF expression, various histological parameters and overall survival in patients. Real time polymerase chain reaction was performed in few cases to validate the immunohistochemistry expression pattern.

**RESULTS:** SPARC expression was high in peritumoral stroma in pancreatic carcinoma than in pancreatic controls; however, SPARC expression pattern was not grossly different in desmoplastic and non-desmoplastic pancreatobiliary carcinomas and in cholangiocarcinomas. No definite correlation was noted between SPARC expression and histological markers of severity and overall survival data.

**CONCLUSIONS:** The relevance of SPARC expression in pancreato-biliary carcinomas though may still be important for therapeutic decision making, it is not responsible for peritumoral stromal desmoplasia in these tumors and it does not have any significant prognostic implication.

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Bisphenols are widely used in the synthesis of polycarbonate plastics, epoxy resins, and thermal paper, which are used in manufacturing items of daily use. Packaged foods and drinks are the main sources of exposure to bisphenols. These chemicals affect humans and animals by disrupting the estrogen, androgen, progesterone, thyroid, and aryl hydrocarbon receptor functions. Bisphenols exert numerous harmful effects because of their interaction with receptors, reactive oxygen species (ROS) formation, lipid peroxidation, mitochondrial dysfunction, and cell signal alterations. Both cohort and case-control studies have determined an association between bisphenol exposure and increased risk of cardiovascular diseases, neurological disorders, reproductive abnormalities, obesity, and diabetes. Prenatal exposure to bisphenols results in developmental disorders in animals. These chemicals also affect the immune cells and play a significant role in initiating the inflammatory response. Exposure to bisphenols exhibit age, gender, and dose-dependent effects. Even at low concentrations, bisphenols exert toxicity, and hence deserve a critical assessment of their uses. Since bisphenols have a global influence on human health, the need to discover the underlying pathways involved in all disease conditions is essential. Furthermore, it is important to promote the use of alternatives for bisphenols, thereby restricting their uses.

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**BACKGROUND:** Whether online resources can facilitate spread of palliative care knowledge and skills in India is an urgent question given few providers and a large, ageing population.

**OBJECTIVES:** We surveyed needs and feasibility regarding e-learning.

**METHODS:** Indian, Australian and North American palliative care experts developed an electronic survey using Qualtrics, emailed to all registrants of the 2017 Indian Association of Palliative Care (IAPC) conference and distributed during the conference.

**RESULTS:** Of 60 respondents (66% men, 60% doctors), most worked in hospitals and had oncology backgrounds, and 35% were from Kerala and Tamil Nadu. Most (90.9%) received palliative care training in India or overseas with 41% trained in a Trivandrum Institute of Palliative Sciences residential course (4-6 weeks). 17% completed the IAPC essential certificate and 22% had undertaken various distance learning courses. Interest in online training was substantial for most aspects of palliative care.

CONCLUSION: There was a high level of interest and reported feasibility in taking a case-based online course. This pilot survey provides support for online case-based education in India, particularly among physicians.

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Apart from their established role in embryonic development, neurotrophins (NTs) have diverse functions in the nervous system. Their role in the integration of physiological and biochemical aspects of the nervous system is currently attracting much attention. Based on a systematic analysis of the literature, we here propose a new paradigm that, by exploiting a novel role of NTs, may help explain the genesis of stress-related psychiatric disorders, opening new avenues for better management of the same. We hypothesize that NTs as an integrated network play a crucial role in maintaining an individual's psychological wellbeing. Given the evidence that stress can induce chronic disruption of the hypothalamic-pituitary-adrenal (HPA) axis which, in turn, is causally linked to several psychiatric disorders, this function may be mediated through the homeostatic mechanisms governing regulation of this axis. In fact, NTs, such as nerve growth factor (NGF) and brain derived neurotrophic factor (BDNF) are known to participate in neuroendocrine regulation. Recent studies suggest epigenetic modification of NT-HPA axis interplay in the precipitation of psychiatric disorders. Our article highlights why this new knowledge regarding NTs should be considered in the etiogenesis and treatment of stress-induced psychopathology.

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Background: The etiology of schizophrenia is extensively debated, and multiple

factors have been contended to be involved. A panoramic view of the contributing factors in a genome-wide study can be an effective strategy to provide a comprehensive understanding of its causality. Materials and Methods: GSE53987 dataset downloaded from GEO-database, which comprised mRNA expression data of post-mortem brain tissue across three regions from control (C) and age-matched subjects (T) of schizophrenia (N = Hippocampus [HIP]: C-15, T-18, Prefrontal cortex [PFC]: C-15, T-19, Associative striatum [STR]: C-18, T-18). Bio-conductor-*affy*-package used to compute mRNA expression, and further t-test applied to investigate differential gene expression. The analysis of the derived genes performed using the PANTHER Classification System and NCBI database. Further, a protein interactome analysis of the derived gene set was performed using STRING v10 database (<https://string-db.org/>) Results: A set of 40 genes showed significantly altered ( $p < 0.01$ ) expression across all three brain regions. The analyses unraveled genes implicated in biological processes and events, and molecular pathways relating basic neuronal functions. Conclusions: The aberrant expression of genes maintaining basic cell machinery explains compromised neuronal processing in SCZ.

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Aqueous extract of the bark of *Terminalia arjuna* (TA) is used by a large population in the Indian subcontinent for treating various cardiovascular conditions. Animal experiments have shown its anti-atherogenic, anti-hypertensive, and anti-inflammatory effects. It has several bioactive ingredients with hemodynamic, ROS scavenging, and anti-inflammatory properties. Earlier we have done limited proteomic and transcriptomic analysis to show its efficacy in ameliorating cardiac hypertrophy induced by isoproterenol (ISO) in rats. In the present study we have used high-throughput sequencing of the mRNA from control and treated rat heart to further establish its efficacy. ISO (5 mg/kg/day s.c.) was administered in male adult rats for 14 days to induce cardiac hypertrophy. Standardized aqueous extract TA bark extract was administered orally. Total RNA were isolated from control, ISO, ISO + TA, and TA treated rat hearts and subjected to high throughput sequence analysis. The modulations of the transcript levels were then subjected to bio-informatics analyses using established software. Treatment with ISO downregulated 1,129 genes and upregulated 204 others. Pre-treatment with the TA bark extracts markedly restored that expression pattern with only 97 genes upregulated and 85 genes downregulated. The TA alone group had only 88 upregulated and 26 downregulated

genes. The overall profile of expression in ISO + TA and TA alone groups closely matched with the control group. The genes that were modulated included those involved in metabolism, activation of receptors and cell signaling, and cardiovascular and other diseases. Networks associated with those genes included those involved in angiogenesis, extracellular matrix organization, integrin binding, inflammation, drug metabolism, redox metabolism, oxidative phosphorylation, and organization of myofibril. Overlaying of the networks in ISO and ISO\_TA group showed that those activated in ISO group were mostly absent in ISO\_TA and TA group, suggesting a global effect of the TA extracts. This study for the first time reveals that TA partially or completely restores the gene regulatory network perturbed by ISO treatment in rat heart; signifying its efficacy in checking ISO-induced cardiac hypertrophy.

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Taxol® (generic name Paclitaxel) is a chemotherapeutic drug, effective against head, neck, breast, lung, bladder, ovary, and cervix cancers. Rising demands in chemotherapy and limited supply of natural taxol have ultimately increased the cost of the drug. Semi synthesis using taxol precursors is not able to meet the global supply and has intensified the need to find alternative ways of taxol production. In the present study, 34 different endophytes were isolated from *Taxus* sp. collected from Shimla, Himachal Pradesh (India). Primary screening of taxol-producing fungi was carried out based on the presence of *dbat* gene, essential for the taxol biosynthetic pathway. A fungal isolate TPF-06 was screened to be a taxol-producing strain based on the PCR amplification results. It was characterized and identified as *Aspergillus fumigatus* by 18S rRNA (Accession No. KU-837249). Multiple sequence alignment (MSA) of nuclear ribosomal internal transcribed spacer (ITS) region and phylogenetic analysis confirmed that strain belonged to *A. fumigatus* clade (Accession No. MF-374798) and is endophytic in nature. Presence of taxol was detected and quantified by High-Performance Liquid Chromatography (HPLC) and characterized by using Thin Layer Chromatography (TLC), Ultraviolet (UV) spectroscopy, Mass spectrometry (MS), Fourier-Transform Infrared Spectroscopy (FTIR) and Nuclear Magnetic Resonance (NMR) spectroscopy. Microbial fermentation in the S7 medium yielded 1.60 g/L of taxol, which to the best of our knowledge is the highest taxol production from an endophytic fungus. Findings of the present study suggest that the *A. fumigatus* is an excellent alternate source for taxol supply, and it may become a highly potent strain on a commercial scale. The involvement of *dbat* gene in *A. fumigatus* KU-837249 strain further suggested a way of increasing taxol yield in fungi by medium engineering and recombinant DNA technology in the future.

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**Purpose:** Retinal hemangioblastomas (RHs) are characteristic of von Hippel-Lindau (VHL) disease. Early diagnosis of retinal lesions may aid in systemic diagnosis. Early identification of VHL is life-saving and also prevents vision loss. Fundus fluorescein angiography (FFA) is a useful tool in the diagnosis and management of RHs. The aim of this study is to report FFA features of RH using ultra-widefield (UWF) imaging.

**Methods:** A retrospective cross-sectional study of consecutive patients of RH who underwent UWF FFA at a tertiary eye care center. Images were analyzed and assessed by authors. The main outcome measures were (a) the number and size of RH in each eye and (b) vascular characteristics of the retina. UWF-FFA characteristics in each eye were tabulated. The number of clock hours involved by these characteristics and their correlation with the number and size of RH were analyzed.

**Results:** The study evaluated 24 eyes of 13 patients. The mean age was 28.4 years. The median number of RHs in an eye was 3.5 (range 1-16), and the size of RHs varied from 0.1 to 4 disc diameters. Novel UWF-FFA findings noted in this study were the presence of abnormal capillary network in 22 of 24 eyes (91.7%), capillary leakage in 15 of 24 eyes (62.5%), and capillary telangiectasia in 7 of 24 eyes (29.2%). In addition, feeder arterioles and venules showed bulbous projections in 8 of 24 eyes (33.3%).

**Conclusion:** The UWF-FFA characteristics of RH, which have not been described before, were identified. These add to our understanding of the pathogenesis of the disease and may pave the way for future therapeutic targets.

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**AIM:** To study the role of internal limiting membrane (ILM) peeling in the prevention of macular epiretinal membrane (ERM) formation following pars plana vitrectomy (PPV) for rhegmatogenous retinal detachment (RRD).

**METHODS:** In a randomised trial, patients with macula-off RRD (duration  $\leq$ 3 months) with proliferative vitreoretinopathy grade  $\leq$ 1 and absence of pre-existing maculopathy were recruited from June 2016 to May 2018. Patients were randomised into two groups: group 1 (conventional treatment) underwent PPV alone, while group 2 underwent PPV with macular ILM peeling. The main outcome measures were macular ERM formation (detected on optical coherence tomography), corrected distance visual acuity (CDVA), retinal attachment and central macular thickness (CMT) at last follow-up (minimum 6 months).

**RESULTS:** Sixty patients (30 in each group) completed the required follow-up. The two groups were comparable in sex distribution, age, duration of RRD, baseline CDVA and duration of follow-up (median 15.5 vs 14 months). Macular ERM developed in 20% (n=6) and 0% of eyes in groups 1 and 2, respectively (p=0.002). Retinal

reattachment was attained in all eyes. There was no statistical difference in final CDVA between the groups ( $p=0.43$ ). Dissociated optic nerve fibre layer (DONFL) was found in 0% and 40% ( $n=12$ ) of eyes in groups 1 and 2, respectively ( $p=0.0001$ ). However, DONFL did not significantly affect the final CDVA ( $p=0.84$ ). The final CMT was  $266.0\pm 37.5\mu\text{m}$  and  $270.0\pm 73.7\mu\text{m}$  in groups 1 and 2, respectively, with no statistical difference ( $p=0.62$ ).

CONCLUSIONS: ILM peeling prevents macular ERM formation following PPV for RRD but provides similar visual outcomes as compared with conventional treatment.

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Anti-inflammatory drugs are well known to reduce the risk of colon cancer and prophylactic use of such agents is gaining acceptance as a cancer prevention therapy. As artesunate, an antimalarial drug, has been shown to exhibit chemopreventive properties, the present study was carried out to evaluate its inhibitory effect on oxidative stress and inflammation in a rat model of colon carcinogenesis. A chemical carcinogen, 1,2-dimethylhydrazine was injected twice at an interval of 1 week to induce preneoplastic lesions in the colon and the parameters indicating oxidative stress and inflammation were evaluated after 8 weeks. Artesunate (50 and 150 mg/kg) and aspirin (60 mg/kg) were administered orally throughout the study. Analysis of colon tissue revealed that both the drugs preserved histoarchitecture, inhibited cellular influx, decreased the levels of oxidative stress and inflammatory markers, downregulated cyclooxygenase-2, inducible nitric oxide synthase, nuclear factor  $\kappa\text{B}$ , and interleukin  $1\beta$  in comparison to the experimental control. Suppression of oxidative stress and pro-inflammatory signaling by both the drugs were found to contribute to inhibition of colon carcinogenesis. The protection afforded by these drugs was found to be comparable. Our study shows that like aspirin, use of artesunate could also reduce the risk of colon cancer and it has a potential for further evaluation for the treatment purpose.

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A large section of cellular proteins in both prokaryotic and eukaryotic systems have oligomeric property. Intently, oligomerization of protein is an invaluable phenomenon from the point of view of protein evolution. This review comprises an

overview on modulation of protein oligomerization. The comprehensive modulation of protein oligomerization can be supportive for effective drug designing in the future. The common mechanisms of protein oligomerization are domain swapping and ligand induced dimerization. Infrequent mechanism of protein oligomerization involves point mutations at the dimer interface, post-translational modification and insertion/deletion at the interface. Predominantly, ligand induced oligomerization is the most useful method to regulate the protein oligomerization that can act as a modulator. Thus, functional modulation of oligomeric proteins can be done, both in-vitro and in-vivo, using various artificial and natural modulators, respectively. Though, the biophysical methods, like microscopy and spectroscopy, have strong potential to characterize the oligomeric proteins. Oligomeric proteins can be characterized biochemically too. Hence, this review illustrates the regulation of protein oligomerization using several modulators, in the future, these can be used for effective drug designing to cure several diseases associated with oligomeric proteins.

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**PURPOSE:** To determine the effect of intravitreal silicone oil (SO) on multifocal electroretinogram (mfERG) and the changes in mfERG following SO removal.

**METHODS:** Twelve eyes of 12 patients with SO in vitreous cavity with corrected distance visual acuity (CDVA) >20/200 were prospectively enrolled as cases over a period from July 2016 to June 2018. The fellow normal eyes served as control. The eyes were evaluated with P1 and N1 wave amplitude and implicit time on mfERG at baseline, 1 and 4 weeks after SO removal.

**RESULTS:** The mean age was 44.9±18.9 (range 18-74) years. The indication for SO injection was retinal detachment (n=9, three macula-on eyes, six macula-off eyes) and endophthalmitis (n=3). The median (range) LogMAR CDVA at baseline was 0.54 (0.18-0.78) in cases and did not change post-SO removal (p=0.29). There was a significant decrease in average P1 and N1 wave amplitude (p=0.0001 and 0.0001, respectively) and delay in average P1 and N1 wave implicit time (p=0.0002 and 0.021, respectively) in cases as compared to controls. The macular status and duration of SO tamponade did not have a significant correlation with mfERG parameters. There was a significant increase in average P1 and N1 wave amplitude (p=0.009 and 0.003, respectively) at 1 week following SO removal but no change in average P1 and N1 wave implicit time (p=0.41 and 0.37, respectively).

**CONCLUSION:** mfERG may be reliably performed for the assessment of macular function in SO-filled eyes. Intravitreal SO exerts an insulating effect on the density of the electric potentials.

DOI: 10.1007/s10633-019-09710-w

PMID: 31327119 [Indexed for MEDLINE]

100: Lahariya C, Bhardwaj P. Adult vaccination in India: status and the way forward. *Hum Vaccin Immunother.* 2019 Dec 6:1-3. doi: 10.1080/21645515.2019.1692564. [Epub ahead of print] PubMed PMID: 31743073.

In the last two decades, the childhood vaccination coverage in most low and

middle-income countries including India has increased. Additional vaccines are being offered through national immunization programs as well as through private sector and the benefits of vaccination are reaching to more children than ever. This has resulted in major decrease in vaccine preventable diseases and contributed to decline in the morbidity and mortality rates. This development is expected to result in epidemiological transition (which is already happening) and mandates for policies and strategies to extend the benefit of available vaccines and vaccination beyond traditionally target age groups to include the adults, elderly and the at-risk populations. This article reviews the present status of adult vaccination in India and proposes a few approaches to move towards life course vaccination.

DOI: 10.1080/21645515.2019.1692564

PMID: 31743073

101: Lamsal R, Mahajan C, Chauhan V, Gupta N, Mishra N, Rath GP. Effect of Pregabalin on Postcraniotomy Pain in Patients Undergoing Supratentorial Tumor Surgery: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Neurosci Rural Pract.* 2019 Oct;10(4):641-645. doi: 10.1055/s-0039-3399490. Epub 2019 Dec 11. PubMed PMID: 31831983; PubMed Central PMCID: PMC6906094.

**Background and Objectives** Suboptimal management of postcraniotomy pain causes sympathetic and hemodynamic perturbations, leading to deleterious effects on the neurological system and overall patient outcome. Opioids are the mainstay of postoperative pain management but have various problems when given in high doses, or for prolonged durations in neurosurgical patients. The ideal method of pain control following craniotomy generally relies on a combination of various drugs. Oral pregabalin may be an attractive alternative in these patients. **Materials and Methods** Sixty, American Society of Anesthesiologists class I and II patients posted for elective supratentorial craniotomy, aged 18 and 60 years, were randomly assigned into three groups of 20 each to receive oral placebo (Group A), pregabalin 75 mg (Group B), or pregabalin 150 mg (Group C) before the induction of anesthesia. At the end of the surgery, patient-controlled analgesia was started with intravenous fentanyl. Visual analog scale (VAS) score was recorded every 2 hours for 24 hours, along with total postoperative fentanyl requirement. **Results** There were no differences in sex, duration of surgery or anesthesia and total intraoperative fentanyl administered among the three groups. The median postoperative VAS score (Group A-18.0, Group B-20, and Group C-22.0;  $p = 0.63$ ) was similar in all the groups. However, postoperative fentanyl requirement over 24 hours was least in the group that received 150 mg pregabalin (Group A-190  $\mu\text{g}$ , Group B-240  $\mu\text{g}$ , and Group C-100  $\mu\text{g}$ ;  $p = 0.03$ ). **Conclusions** Even though pain scores were not significantly different, patients receiving 150 mg oral pregabalin required the least amount of postoperative opioids.

DOI: 10.1055/s-0039-3399490

PMCID: PMC6906094

PMID: 31831983

102: Lantuejoul S, Tsao MS, Cooper WA, Girard N, Hirsch FR, Roden AC, Lopez-Rios F, Jain D, Chou TY, Motoi N, Kerr KM, Yatabe Y, Brambilla E, Longshore J, Papotti M, Sholl LM, Thunnissen E, Rekhtman N, Borczuk A, Bubendorf L, Minami Y, Beasley MB, Botling J, Chen G, Chung JH, Dacic S, Hwang D, Lin D, Moreira A, Nicholson AG, Noguchi M, Pelosi G, Poleri C, Travis W, Yoshida A, Daigneault JB, Wistuba II, Mino-Kenudson M. PD-L1 Testing for Lung Cancer in 2019: Perspective from the IASLC Pathology Committee. *J Thorac Oncol.* 2019 Dec 20. pii: S1556-0864(19)33847-X. doi: 10.1016/j.jtho.2019.12.107. [Epub ahead of print] Review. PubMed PMID: 31870882.

The recent development of immune checkpoint inhibitors (ICI) has led to promising advances in the treatment of non-small cell and small cell lung cancer patients with advanced or metastatic disease. Most of ICI target the PD-1/PD-L1 axis with the aim of restoring anti-tumor immunity. Multiple clinical trials for ICI have examined a predictive value of PD-L1 protein expression in tumor cells and/or tumor-infiltrating immune cells by immunohistochemistry (IHC), for which different assays with specific IHC platforms were applied. Of those, some PD-L1 IHC assays have been validated for the prescription of the corresponding agent for first- or second-line treatment. However, not all laboratories are equipped with the dedicated platforms and many laboratories have set up in-house or laboratory developed tests, which are more affordable than generally expensive clinical trial-validated assays. Although PD-L1 IHC test is now deployed in the most pathology laboratories, its appropriate implementation and interpretation are critical as a predictive biomarker and can be challenging due to the multiple antibody clones and platforms or assays available and given the typically small size of samples provided. As many articles have been published since the issue of the IASLC Atlas of PD-L1 immunohistochemistry testing in lung cancer, this review by the IASLC pathology committee provides updates on the indications of ICI for lung cancer in 2019, and discusses important considerations on pre-analytical, analytical and post-analytical aspects of PD-L1 IHC testing, including specimen type, validation of assays, external quality assurance and training.

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DOI: 10.1016/j.jtho.2019.12.107  
PMID: 31870882

103: Law TJ, Lipnick M, Joshi M, Rath GP, Gelb AW. The path to safe and accessible anaesthesia care. *Indian J Anaesth.* 2019 Dec;63(12):965-971. doi: 10.4103/ija.IJA\_756\_19. Epub 2019 Dec 11. PubMed PMID: 31879420; PubMed Central PMCID: PMC6921309.

The increasing focus on and importance of surgical care in achieving universal health coverage requires the development of safe and accessible anaesthesia services. Increasing access to care by supporting the necessary inputs to the anaesthesia system, including medications, equipment and personnel, must be accompanied by processes that support high-quality care, including support for education, and guidelines for standards, and training. As safe, high-quality care requires an integrated approach, each element must be supported together, i.e., in an integrated manner to ensure that anaesthesia care reaches those who need it, and in the safest possible manner. Several important efforts have been undertaken globally to address and foster these elements, and resources to guide these processes exist for low- and middle-income countries to improve them. This review highlights both the needs and resources for safe and high-quality care that patients deserve.

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DOI: 10.4103/ija.IJA\_756\_19  
PMCID: PMC6921309  
PMID: 31879420

104: Lepe M, Oltulu P, Canepa M, Wu RI, Deeken A, Alex D, Dinares C, Doxtader EE, Fitzhugh VA, Gibier JB, Jain D, Janaki N, Jelinek A, Labiano T, L'Imperio V, Michael C, Mukhopadhyay S, Pagni F, Panizo A, Pijuan L, Quintana LM, Roy-Chowdhuri S, Sanchez-Font A, Sansano I, Sauter J, Skipper D, Spruill LS,

Torous V, Gardner JM, Jiang XS. #EBUSTwitter: Novel Use of Social Media for Conception, Coordination, and Completion of an International, Multicenter Pathology Study. Arch Pathol Lab Med. 2019 Dec 17. doi: 10.5858/arpa.2019-0297-OA. [Epub ahead of print] PubMed PMID: 31846366.

Author information:

(1)From the Department of Pathology, Hospital of the University of Pennsylvania, Philadelphia (Dr Lepe); the Department of Pathology, Meram Faculty of Medicine, Necmettin Erbakan University, Konya, Turkey (Dr Oltulu); the Department of Pathology, Rhode Island Hospital, Providence (Dr Canepa); the Department of Clinical Pathology & Laboratory Medicine, University of Pennsylvania Health System, Philadelphia (Dr Wu); the Department of Pathology, Summa Health Systems, Akron, Ohio (Drs Deeken and Jelinek); the Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, New York (Drs Alex and Sauter); Patologia, Vall d'Hebron Hospital, Barcelona, Spain (Drs Dinares and Sansano); the Department of Pathology, Cleveland Clinic, Cleveland, Ohio (Drs Doxtader and Mukhopadhyay); the Department of Pathology and Laboratory Medicine, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark (Dr Fitzhugh); Centre de Biologie, University of Lille, Lille, France (Dr Gibier); the Department of Pathology, All India Institute of Medical Sciences, New Delhi, India (Dr Jain); the Department of Pathology, Case Western Reserve University, Cleveland, Ohio (Drs Janaki and Michael); Patologia, Complejo Hospitalario de Navarra, Navarra, Spain (Drs Labiano and Panizo); the Department of Pathology, University of Milano Bicocca, Monza, Italy (Dr L'Imperio and Pagni); Patologia, Hospital del Mar, Barcelona, Spain (Drs Pijuan and Sanchez-Font); the Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Massachusetts (Dr Quintana); the Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston (Dr Roy-Chowdhuri); the Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston (Drs Skipper and Spruill); the Department of Pathology, Massachusetts General Hospital, Boston (Dr Torous); the Department of Pathology, Dermatopathology, Bone & Soft Tissue, University of Arkansas for Medical Sciences, Little Rock (Dr Gardner); and the Department of Pathology, Duke University Medical Center, Durham, North Carolina (Dr Jiang).

CONTEXT.—: Social media sites are increasingly used for education, networking, and rapid dissemination of medical information, but their utility for facilitating research has remained largely untapped.

OBJECTIVE.—: To describe in detail our experience using a social media platform (Twitter) for the successful initiation, coordination, and completion of an international, multi-institution pathology research study.

DESIGN.—: Following a tweet describing a hitherto-unreported biopsy-related histologic finding in a mediastinal lymph node following endobronchial ultrasound-guided transbronchial needle aspiration, a tweet was posted to invite pathologists to participate in a validation study. Twitter's direct messaging feature was used to create a group to facilitate communication among participating pathologists. Contributing pathologists reviewed consecutive cases of mediastinal lymph node resection following endobronchial ultrasound-guided transbronchial needle aspiration and examined them specifically for biopsy site changes. Data spreadsheets containing deidentified data and digital photomicrographs of suspected biopsy site changes were submitted via an online file hosting service for central review by 5 pathologists from different institutions.

RESULTS.—: The study recruited 24 pathologists from 14 institutions in 5 countries within 143 days of study conception, and a total of 297 cases were collected and analyzed. The time interval between study conception and acceptance of the manuscript for publication was 346 days.

CONCLUSIONS.—: To our knowledge, this is the first time that a social media

platform has been used to generate a research idea based on a tweet, recruit coinvestigators publicly, communicate with collaborating pathologists, and successfully complete a pathology study.

DOI: 10.5858/arpa.2019-0297-OA

PMID: 31846366

105: Loeb M, Dokainish H, Dans A, Palileo-Villanueva LM, Roy A, Karaye K, Zhu J, Liang Y, Goma F, Damasceno A, AlHabib KF, Yonga G, Mondo C, Almahmeed W, Al Mulla A, Yusuf S; IVVE investigators. Corrigendum to "Randomized controlled trial of influenza vaccine in patients with heart failure to reduce adverse vascular events (IVVE): Rationale and design" [212 (2019) 36-44]. *Am Heart J*. 2019 Dec 12. pii: S0002-8703(19)30323-0. doi: 10.1016/j.ahj.2019.11.008. [Epub ahead of print] PubMed PMID: 31839177.

106: Madhusudhan KS, Das P, Gunjan D, Srivastava DN, Garg PK. IgG4-Related Sclerosing Cholangitis: A Clinical and Imaging Review. *AJR Am J Roentgenol*. 2019 Dec;213(6):1221-1231. doi: 10.2214/AJR.19.21519. Epub 2019 Sep 11. PubMed PMID: 31509439.

**OBJECTIVE.** The purpose of this article is to present the pathologic and clinical features of IgG4-related sclerosing cholangitis (ISC), illustrate the associated imaging findings, and discuss treatment of the disorder. **CONCLUSION.** ISC is an inflammatory disorder involving the biliary system and resulting in strictures. Although often associated with autoimmune pancreatitis, it may be an isolated disease. Differentiation of ISC from other forms of cholangitis and cholangiocarcinoma is difficult but necessary for management. Imaging is important in diagnosing and assessing the extent of disease and planning a management strategy.

DOI: 10.2214/AJR.19.21519

PMID: 31509439

107: Magan D, Yadav RK. Physiological persona differences based on stress and inflammation between meditators and healthy controls. *J Complement Integr Med*. 2019 Dec 24. pii: /j/jcim.ahead-of-print/jcim-2019-0106/jcim-2019-0106.xml. doi: 10.1515/jcim-2019-0106. [Epub ahead of print] PubMed PMID: 31875490.

Background Nowadays, yoga is endorsed and advised routinely to stay fit and healthy, as well as control many chronic diseases including diabetes type 2, hypertension, coronary artery diseases, etc. Now, our assumption is that those who do regular yoga have different persona than who do not do yoga regularly. We planned to test our hypothesis scientifically, and therefore baseline physiological characteristics with stress and inflammation levels in long-term and short-term meditators and healthy novice controls were analyzed. Methods In this retrospective analysis, 97 male participants were included for their Baseline analysis. Fifteen apparently healthy subjects practicing preksha meditation (since >5years, at least 5days a week) were included as long-term meditators (LTMs); 58 subjects who attended one of our short-term yoga-based lifestyle intervention programs for 2weeks were included as short-term meditators (STMs); 24 male novice subjects, who did not participate in any yogic intervention, were included as healthy controls. Here, we analyzed the Baseline plasma levels of stress and inflammatory markers, cortisol,  $\beta$ -endorphin, interleukin (IL)-6 and tumor necrosis factor (TNF)- $\alpha$  in long-term meditators vs. short-term meditators vs. healthy controls. Outcome measures The study parameters body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), plasma levels of stress and immune markers, cortisol,  $\beta$ -endorphin ( $\beta$ -Ed),

interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), were assessed in all the three groups at baseline. Results Significant ( $p < 0.05$ ) differences were observed at baseline for plasma levels of stress and inflammatory markers as well as body mass index and systolic blood pressure among LTM vs. STM vs. healthy controls. Conclusions Our observations suggest that the subjects who do regular yoga-meditation practice have better stress & inflammation status than comparable age matched healthy controls.

DOI: 10.1515/jcim-2019-0106

PMID: 31875490

108: Magan D, Yadav RK, Bal CS, Mathur R, Pandey RM. Brain Plasticity and Neurophysiological Correlates of Meditation in Long-Term Meditators: A (18)Fluorodeoxyglucose Positron Emission Tomography Study Based on an Innovative Methodology. *J Altern Complement Med*. 2019 Dec;25(12):1172-1182. doi: 10.1089/acm.2019.0167. Epub 2019 Sep 26. PubMed PMID: 31556688.

Objective: Previous studies evaluating neurophysiological correlates of long-term meditation are constrained by some methodological limitations. The objective of this study was to measure changes in the regional cerebral glucose metabolism during meditation using a novel methodological approach. Design: The present study was a part of a larger, nonrandomized, single-center open-label study. Setting/location: The study was conducted at the Department of Physiology and Department of Nuclear Medicine and Positron Emission Tomography. A dedicated place was set up as a yoga room, away from the positron emission tomography (PET) scanning room in the Department of Nuclear Medicine and Positron Emission Tomography, where meditators performed meditation in a peaceful environment in a sitting posture with eyes closed. The electroencephalography (EEG) was recorded to affirm the meditation objectively. Subjects: Twenty-four sets of PET scans were obtained at 2 different occasions (baseline and postmeditation within 40 min of 18FDG [18fluorodeoxyglucose] injection) from 12 apparently healthy, male, right-handed long-term meditators practicing Preksha meditation (since >5 years, at least 5 days a week) who were recruited from a well-established meditation center in Delhi. Outcome measures: Changes in the regional cerebral glucose metabolism during meditation versus baseline. Results: Regional cluster analysis showed significantly activated well-defined areas of fronto-parieto-temporal regions of the right versus left hemisphere during meditation. Interestingly, right homolog of Broca's area and right lentiform nucleus were hyperactive during meditation in all the meditators. Conclusions: Long-term meditation might potentially enhance the explicit functions of specific parts of the right hemisphere, possibly due to neuroplastic changes in the brain. Importantly, results of the current study are encouraging and show a novel methodological approach to acquire 18FDG PET/CT (computed tomography) images. The study was registered at Clinical Trial Registry India (CTRI), CTRI/2009/091/000727.

DOI: 10.1089/acm.2019.0167

PMID: 31556688 [Indexed for MEDLINE]

109: Magoon R, Makhija N, Das D. Vasoplegic syndrome after cardiac surgery: Better the devil you know! *J Card Surg*. 2019 Dec;34(12):1679-1680. doi: 10.1111/jocs.14297. Epub 2019 Oct 26. PubMed PMID: 31654579.

110: Malapure SS, Mukherjee A, Bal C. Radioiodine Therapy of Graves' Disease and the Uptake Paradox. *Indian J Nucl Med*. 2020 Jan-Mar;35(1):17-20. doi: 10.4103/ijnm.IJNM\_158\_19. Epub 2019 Dec 31. PubMed PMID: 31949364; PubMed Central PMCID: PMC6958960.

**Purpose of the Study:** Radioiodine (<sup>131</sup>I) therapy is approved and well-accepted modality for the treatment of hyperthyroidism. The dosage of <sup>131</sup>I for successful treatment is based on many factors; however, an objective tool to determine the dose was missing. In a retrospective study, we found that high <sup>131</sup>I uptake values required more dose to achieve desirable results contrary to the belief.

**Materials and Methods:** Clinically and scintigraphically proven Graves' disease patients with high <sup>131</sup>I uptake (>50%) were accrued for this study and block randomized into low-dose (Group I) and high-dose (Group II) groups. Low activity (5 mCi) was administered in Group I and higher activity (10 mCi) in Group II. The patients were followed up after 3 months with thyroid function tests to determine the outcome.

**Results:** A total of 344 patients were analyzed at the end of 3 months, with 174 in low-dose group and 170 in high-dose group. Euthyroidism/hypothyroidism was achieved in significantly higher number of patients as compared to the low-dose group.

**Conclusion:** The higher dose of <sup>131</sup>I is required to achieve euthyroidism/hypothyroidism in patients with high <sup>131</sup>I uptake.

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DOI: 10.4103/ijnm.IJNM\_158\_19

PMCID: PMC6958960

PMID: 31949364

111: Malhotra R, Vaishya R. Revision arthroplasty in 2020. *J Clin Orthop Trauma*. 2020 Jan-Feb;11(1):1. doi: 10.1016/j.jcot.2019.12.007. Epub 2019 Dec 18. PubMed PMID: 32001975; PubMed Central PMCID: PMC6985162.

112: Malhotra S, Kalaivani M, Rath R, Prasad M, Vashist P, Gupta N, Senjam SS, Gupta SK. Use of spectacles for distance vision: coverage, unmet needs and barriers in a rural area of North India. *BMC Ophthalmol*. 2019 Dec 12;19(1):252. doi: 10.1186/s12886-019-1262-3. PubMed PMID: 31830950; PubMed Central PMCID: PMC6909564.

**BACKGROUND:** Uncorrected refractive errors contribute enormously to the burden of avoidable visual impairment worldwide. There is a huge disparity in different parts of the globe in context to spectacle coverage for distance vision. This study was undertaken with objectives of determining prevalence of spectacle coverage, unmet needs and associated factors among adults in a rural community of north India.

**METHODS:** A community-based cross-sectional study was carried out within selected clusters of Jhajjar district of Haryana. All participants aged >15 years underwent visual acuity assessment by LogMAR "E" screening chart. Participants with presenting visual acuity <6/12 in any eye and all current spectacle users underwent detailed ophthalmic examination and refraction. Additional details about spectacles, barriers for their use and willingness to pay for them were collected. Participants with met and unmet need for spectacle use at visual acuity >6/12 was computed. These are reported as proportions with 95% confidence intervals. Associated factors with unmet need were determined using bivariable and multivariable logistic regression analysis.

**RESULTS:** A total of 6910 participants were examined. The current spectacle use was 7.5% (95% Confidence Interval CI: 6.5, 8.7). The spectacle coverage was found in 33.3% (95% CI: 30.0, 36.7) participants among those in need. The unmet need was found in 10.8% of participants (95% CI: 10.1, 11.6). On multivariable analysis, odds of unmet need was associated with age, gender, level of education and marriage status. The most common barrier for refractive correction was lack

of perceived need for refraction and its correction.

**CONCLUSION:** There is substantial unmet need for distance vision spectacles in this population. It is imperative that multi-component intervention be implemented to improve spectacle coverage in this rural north Indian setting.

DOI: 10.1186/s12886-019-1262-3

PMCID: PMC6909564

PMID: 31830950

113: Manchanda S, Vora Z, Sharma R, Hari S, Das CJ, Kumar S, Kachhawa G, Khan MA. Quantitative Sonoelastographic Assessment of the Normal Uterus Using Shear Wave Elastography: An Initial Experience. *J Ultrasound Med.* 2019 Dec;38(12):3183-3189. doi: 10.1002/jum.15019. Epub 2019 May 11. PubMed PMID: 31077426.

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

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

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

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

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DOI: 10.1002/jum.15019

PMID: 31077426

114: Mann S, Sharma A, Sarkar A, Kharb R, Malhotra R, Datta B, Gupta RK, Biswas S. Evaluation of anti-inflammatory effects of *Choerospondias axillaris* fruit's methanolic extract in synoviocytes and CIA rat model. *Curr Pharm Biotechnol.* 2019 Dec 9. doi: 10.2174/1389201021666191210114127. [Epub ahead of print] PubMed PMID: 31820687.

**BACKGROUND:** Rheumatoid arthritis (RA) is an autoimmune, systemic disease mainly affecting joints. Presently, there is no specific treatment/ drug available for curing RA except few supportive medicines. Therefore, the focus has been diverted on medicinal plants for the treatment of such diseases. *Choerospondias axillaris* commonly known as Lupsi/Lapsi and have been reported to have several properties for treating various diseases.

**OBJECTIVE:** The present study has been undertaken to explore the anti-inflammatory effects of *Choerospondias axillaris* fruit extract on synoviocytes (FLS) and collagen-induced arthritis (CIA) rat model.

**METHOD:** Methanolic extract of the *Choerospondias axillaris* fruit was used for checking phytochemical, antioxidant and anti-inflammatory properties. Antioxidant

activity of *Choerospondias axillaris* fruit was measured via free radicals scavenging assays and bioactive compounds were identified via LC-MS/MS analysis. Anti-inflammatory effect was investigated in RA and Osteo arthritis (OA) primary cells and also in Collagen Induced Arthritis (CIA) rat models. Further, the medicinal properties of anti-inflammatory bioactive compounds were supported by docking studies.

RESULTS: In-vitro and in-vivo studies showed significant decrease in the levels of inflammatory cytokines. Docking analysis revealed that quercetin inhibits TNF- $\alpha$  having -9.1 kcal/mol binding energy and 10.13  $\mu$ M inhibitory constant. Quercetin also inhibits IL-6 having -6.6 kcal/mol binding energy and 21.9  $\mu$ M inhibitory constant.

CONCLUSION: Observed results suggests that the underutilized fruit *Choerospondias axillaris* can be used to reduce the inflammation of inflammatory diseases like RA.

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DOI: 10.2174/1389201021666191210114127

PMID: 31820687

115: Mathew R, Jamshed N, Aggarwal P, Patel S, Pandey RM. Profile of acute poisoning cases and their outcome in a teaching hospital of north India. *J Family Med Prim Care*. 2019 Dec 10;8(12):3935-3939. doi: 10.4103/jfmpc.jfmpc\_832\_19. eCollection 2019 Dec. PubMed PMID: 31879639; PubMed Central PMCID: PMC6924236.

Objectives: Aim of this study was to characterize acute poisoning and snakebite cases and their outcome in the Emergency Department (ED).

Methods: This was a prospective study done in the ED of a tertiary healthcare center. Study included 184 patients of acute poisoning and 16 cases of snakebite. Data regarding demographics, type, time, and mode of poisoning, lag time in reaching the hospital, initiation of treatment, first aid, in-hospital treatment, and comorbid illness were obtained. Data regarding requirement of antidote, duration of hospitalization, and outcome were also obtained.

Results: Out of 200 cases, 181 (90.5%) were adults and 19 (9.5%) were of pediatric age group. Poisoning was common among males (57%) than females (43%). Majority (40%) were from the age group of 21-30 years. Out of 200, 115 (57.5%) poisonings were suicidal, 68 (34%) were accidental, and 17 (8.5%) were homicidal. Acute poisonings included corrosive 54 (27%), drug overdose 26 (13%), organophosphorus compounds 20 (10%), rodenticides 20 (10%), and symptomatic snakebite 16 (8%). Seventy-two (36%) were admitted with a median hospital stay of 6 days with 5 (2.5%) deaths. Logistic regression analysis revealed poorer outcome for 15-30 years age [OR 12.6 (1.6-97.5), P = 0.015], males [OR 2.5 (1.4-4.4) P = 0.04], patients coming from >30 km [OR 4.3 (1.5-12.1), P = 0.006].

Conclusion: Our study demonstrated an increased incidence of corrosive ingestion. With increasing rates of suicidal ingestions, there is a need for holistic approach to manage mental health issues at primary care level.

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PMCID: PMC6924236

PMID: 31879639

116: Mathew R, Rl B, Mohindra R. Modified Sequential Organ Failure Assessment score in the emergency department. *Emerg Med Australas*. 2019 Dec;31(6):1123. doi: 10.1111/1742-6723.13359. Epub 2019 Jul 25. PubMed PMID: 31347286.

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**OBJECTIVE:** Resistance to colistin, a last resort antibiotic, has emerged in India. We investigated colistin-resistant *Klebsiella pneumoniae* (ColR-KP) in a hospital in India to describe infections, characterize resistance of isolates, compare concordance of detection methods, and identify transmission events.

**DESIGN:** Retrospective observational study.

**METHODS:** Case-patients were defined as individuals from whom ColR-KP was isolated from a clinical specimen between January 2016 and October 2017. Isolates resistant to colistin by Vitek 2 were confirmed by broth microdilution (BMD). Isolates underwent colistin susceptibility testing by disk diffusion and whole-genome sequencing. Medical records were reviewed.

**RESULTS:** Of 846 *K. pneumoniae* isolates, 34 (4%) were colistin resistant. In total, 22 case-patients were identified. Most (90%) were male; their median age was 33 years. Half were transferred from another hospital; 45% died.

Case-patients were admitted for a median of 14 days before detection of ColR-KP. Also, 7 case-patients (32%) received colistin before detection of ColR-KP. All isolates were resistant to carbapenems and susceptible to tigecycline. Isolates resistant to colistin by Vitek 2 were also resistant by BMD; 2 ColR-KP isolates were resistant by disk diffusion. Moreover, 8 multilocus sequence types were identified. Isolates were negative for mobile colistin resistance (*mcr*) genes. Based on sequencing analysis, in-hospital transmission may have occurred with 8 case-patients (38%).

**CONCLUSIONS:** Multiple infections caused by highly resistant, *mcr*-negative ColR-KP with substantial mortality were identified. Disk diffusion correlated poorly with Vitek 2 and BMD for detection of ColR-KP. Sequencing indicated multiple importation and in-hospital transmission events. Enhanced detection for ColR-KP may be warranted in India.

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PMID: 31625832

118: Meenu M, Reeta KH, Dinda AK, Kottarath SK, Gupta YK. Evaluation of sodium valproate loaded nanoparticles in acute and chronic pentylenetetrazole induced seizure models. *Epilepsy Res*. 2019 Dec;158:106219. doi: 10.1016/j.epilepsyres.2019.106219. Epub 2019 Oct 24. PubMed PMID: 31726286.

**BACKGROUND AND PURPOSE:** Efficacy of sodium valproate in epilepsy is limited by its poor blood brain barrier penetration and side effects. Nanoparticles may offer a better drug delivery system to overcome these limitations. This study evaluated the efficacy of sodium valproate encapsulated in nanoparticles in pentylenetetrazole (PTZ) induced acute and kindling models of seizures in male Wistar rats.

**METHODS:** Poly lactic-co-glycolic acid (PLGA) based, polysorbate 80 stabilized sodium valproate loaded nanoparticles (nano sodium valproate) and rhodamine loaded nanoparticles (RLN) were formulated by double emulsion- solvent evaporation method and characterized for their size, shape, zeta potential and drug loading percentage. RLN was used to demonstrate blood brain barrier (BBB) permeability of nanoparticles. Serum drug levels were estimated using high performance liquid chromatography. The efficacy of standard sodium valproate (300mg/kg) and nano sodium valproate (~300, ~150 and ~75mg/kg of sodium

valproate) were evaluated in experimental animal models of seizures along with their effects on behavioral and oxidative stress parameters. Drugs were administered 60min before PTZ in acute model. In the kindling model, drugs were administered every day while PTZ was administered on alternate days 60min after drug administration. All the study drugs/compounds were administered intraperitoneally.

RESULTS: RLN were observed to be clustered in cortex which implied that the nanoparticles crossed BBB. Both standard sodium valproate and nano sodium valproate reached therapeutic serum level at 15min and 1h, but were undetectable in serum at 24h. In acute PTZ (60mg/kg) model, nano sodium valproate (~300mg/kg of sodium valproate) and standard sodium valproate showed protection against seizures till 6h and 4h, respectively. There were significant behavioral impairment and oxidative stress with standard sodium valproate in acute model as compared to nano sodium valproate at 6h. In kindling model, induced with PTZ (30mg/kg, every alternate day for 42 days), complete protection from seizures was observed with nano sodium valproate (~150mg/kg and ~75mg/kg of sodium valproate) and standard sodium valproate (300mg/kg). Similarly, significant protection from behavioral impairment and oxidative stress was observed with standard sodium valproate and nano sodium valproate as compared to PTZ.

CONCLUSION: When compared to conventional therapy, nano sodium valproate showed protection from seizures at reduced doses and for a longer duration in animal models of epilepsy. This study suggests the potential of nano sodium valproate in the treatment of epilepsy.

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PMID: 31726286

119: Mehta A, Bajaj MS, Pushker N, Chawla B, Pujari A, Grewal SS, Grewal SPS, Singh SR, Kishore A, Yadav NS. To compare intralesional and oral propranolol for treating periorbital and eyelid capillary hemangiomas. *Indian J Ophthalmol*. 2019 Dec;67(12):1974-1980. doi: 10.4103/ijo.IJO\_59\_19. PubMed PMID: 31755431; PubMed Central PMCID: PMC6896529.

Purpose: A pilot randomized control trial to compare the efficacy and side effects of intralesional and oral propranolol in periorbital and eyelid capillary hemangiomas.

Methods: Twenty patients were prospectively randomized to two groups of ten each. Group 1 was initiated on oral propranolol 1 mg/kg/day titrated to final dose of 3 mg/kg/day over 1 week which was continued for 6 months and then tapered over 1 week; Group 2 received 3 doses of direct intralesional propranolol hydrochloride 1 mg/ml; 0.2 ml/cm 4-6 weeks apart. Hemangioma area and corneal astigmatism were measured.

Results: Within each group at 6 months there was a significant reduction in area (group 1:  $83.48 \pm 11.67\%$ ,  $P= 0.0019$ ; group 2:  $67.78 \pm 21.71\%$ ,  $P= 0.0019$ ) and improvement in astigmatism (pre, post: group 1:  $2.98D @ 179.8^\circ$ ,  $1.13D @ 179.8^\circ$ ,  $P= 0.0045$ ; group 2:  $1.62D @ 90.16^\circ$ ,  $0.75D @ 179.9^\circ$ ,  $P= 0.0001$ ). There was no difference in area reduction ( $P = 0.056$ ), change in appearance ( $P = 0.085$ ), ptosis ( $P = 0.23$ ) and side effects (lethargy, poor feeding;  $P= 0.171$ ) between the two groups.

Conclusion: Efficacy and side effects with intralesional propranolol are comparable to oral propranolol for periorbital and eyelid lesions.

DOI: 10.4103/ijo.IJO\_59\_19  
PMCID: PMC6896529

PMID: 31755431

120: Mehtab W, Agarwal A, Singh N, Malhotra A, Makharia GK. All that a physician should know about FODMAPs. *Indian J Gastroenterol*. 2019 Oct;38(5):378-390. doi: 10.1007/s12664-019-01002-0. Epub 2019 Dec 4. Review. PubMed PMID: 31802437.

A diet low in poorly absorbed, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) is now considered as an effective strategy for symptoms control in patients with irritable bowel syndrome (IBS). The low FODMAP diet is administered in three phases, namely restriction of all dietary FODMAPs followed by rechallenge and then reintroduction of specific FODMAPs according to the tolerance of patients. A dietician should be involved in patients in whom a low FODMAP diet is planned. While restricting high FODMAPs, it is pertinent that patients are advised a well-balanced diet and suitable alternatives with low FODMAP contents in each food groups are prescribed. Strict adherence to a low FODMAP diet has been shown to improve symptoms, stool output, quality of life, and the overall well-being of patients with IBS. For those who do not respond to this dietary approach, a normal diet may be initiated and other treatment strategies (dietary or nondietary) should be considered. Interestingly, the low FODMAP diet has also been tried in other functional disorders, nonceliac gluten sensitivity, and even inflammatory bowel disease. Since the concept of FODMAP is relatively new, there is only limited data on the content of FODMAP in the Indian food items and there is a need to address this question. There is also a need for well-designed and adequately powered studies to explore the efficacy of low FODMAP diet in patients with IBS. In the present review article, we have compiled all the relevant information about FODMAPs with an objective to provide comprehensive information on FODMAPs to a physician.

DOI: 10.1007/s12664-019-01002-0

PMID: 31802437

121: Mishra B, Joshi MK, Tiwari R, Uniyal M. Complex chest wall wound managed by a novel technique of thoracoplasty. *BMJ Case Rep*. 2019 Dec 29;12(12). pii: e230782. doi: 10.1136/bcr-2019-230782. PubMed PMID: 31888917.

Thoracoplasty is a procedure to collapse the chest wall over a residual space in the thoracic cavity in order to abolish and avoid the complications associated with this dead space. Although effective in achieving this, the procedure is crippled by poor cosmetic appearance and functional outcome. We report a case of recalcitrant complex chest wall defect with a large cavity, marred by visible heart and poor availability of local muscles, that was successfully managed by a novel technique of thoracoplasty with acceptable postoperative appearance and function.

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DOI: 10.1136/bcr-2019-230782

PMID: 31888917

122: Mishra S, Rastogi YP, Jabin S, Kaur P, Amir M, Khatoon S. A bacterial phyla dataset for protein function prediction. *Data Brief*. 2019 Dec 18;28:105002. doi: 10.1016/j.dib.2019.105002. eCollection 2020 Feb. PubMed PMID: 31921945; PubMed Central PMCID: PMC6950771.

Protein function prediction has been the most worked upon and the most challenging problem for computational biologists. The vast majority of known proteins have yet not been characterised experimentally, and there is significant

gap between their structures and functions. New un-annotated sequences are being added to the public protein databases (e.g. UniprotKB) at an enormous pace [1]. Such proteins with unknown functions might play key role in the metabolism, growth and development regulation. Thus, if functions of unknown proteins left undiscovered, researchers may skip important information(s). Based on their sequence, structure, evolutionary history, and their association with other proteins, tools of computational biology can provide insights into the function of proteins [2]. For proteins with well characterised close relatives, it is trivial to infer function. Orphan proteins without discernible sequence relatives present a greater challenge [3]. Here the task of experimental characterisation is blind and becomes unwieldy. It is highly unlikely that all known proteins will ever be completely experimentally characterised [4]. Thus, there is an emergent need to develop fast and accurate computational approaches to fulfil this requirement. Towards this end, we prepared a dataset for protein function prediction by extracting protein sequences and annotations of reviewed prokaryotic proteins (total count 323,719 as accessed on date March 10, 2019) belonging to 9 bacterial phyla Actinobacteria, Bacteroidetes, Chlamydiae, Cyanobacteria, Firmicutes, Fusobacteria, Proteobacteria, Spirochaetes and Tenericutes. Corresponding to the most frequent 1739 Gene Ontology (Molecular Function) terms, samples were filtered, and 171,212 proteins were retrieved for feature generation. The Dataset was generated by calculating the sequence, sub-sequence, physiochemical, annotation-based features for each 171,212 reviewed proteins using method in [10]. These features constitute a total of 9890 attributes for each sequence of protein along with 1739 Gene Ontology terms. Each protein sequence is assigned one or more of 1739 Gene Ontology (Molecular Function) term as its target label. The Dataset contains the Entry and Entry name of each sequence corresponding to UniprotKB Database. This dataset being huge in size (171,212 samples X 9890 features, 1739 classes with multiple values) and equipped with enough number of positive and negative samples of each 1739 class, is good for testing efficiency of any upcoming deep learning models [5]. We divided the full dataset of 171,212 reviewed proteins in the ratio 3:1 to form Train/Test dataset 1; train dataset with 128,409 samples and test dataset with 42,803 samples to facilitate training of a deep learning model. The train and test datasets are stratified to contain good proportion of each 1739 classes. We then prepared a dataset 2 of pathogenic unreviewed proteins of the 9 bacterial phyla each with 9890 features same as train/train dataset of reviewed proteins but without target labels in order to predict their functions using deep learning model proposed in [5].

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123: Mishra S, Rastogi YP, Jabin S, Kaur P, Amir M, Khatun S. A deep learning ensemble for function prediction of hypothetical proteins from pathogenic bacterial species. *Comput Biol Chem.* 2019 Dec;83:107147. doi: 10.1016/j.compbiolchem.2019.107147. Epub 2019 Oct 19. PubMed PMID: 31698160.

Protein function prediction is a crucial task in the post-genomics era due to their diverse irreplaceable roles in a biological system. Traditional methods involved cost-intensive and time-consuming molecular biology techniques but they proved to be ineffective after the outburst of sequencing data through the advent of cost-effective and advanced sequencing techniques. To manage the pace of annotation with that of data generation, there is a shift to computational approaches which are based on homology, sequence and structure-based features, protein-protein interaction networks, phylogenetic profiles, and physicochemical

properties, etc. A combination of these features has proven to be promising for protein function prediction in terms of improving prediction accuracy. In the present work, we have employed a combination of features based on sequence, physicochemical property, subsequence and annotation features with a total of 9890 features extracted and/or calculated for 171,212 reviewed prokaryotic proteins of 9 bacterial phyla from UniProtKB, to train a supervised deep learning ensemble model with the aim to categorize a bacterial hypothetical/unreviewed protein's function into 1739 GO terms as functional classes. The proposed system being fully dedicated to bacterial organisms is a novel attempt amongst various existing machine learning based protein function prediction systems based on mixed organisms. Experimental results demonstrate the success of the proposed deep learning ensemble model based on deep neural network method with F1 measure of 0.7912 on the prepared Test dataset 1 of reviewed proteins.

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DOI: 10.1016/j.compbiolchem.2019.107147

PMID: 31698160 [Indexed for MEDLINE]

124: Mongia M, Gupta AK, Vijay A, Sadhu R. Management of stuttering using cognitive behavior therapy and mindfulness meditation. *Ind Psychiatry J.* 2019 Jan-Jun;28(1):4-12. doi: 10.4103/ipj.ipj\_18\_19. Epub 2019 Dec 11. Review. PubMed PMID: 31879440; PubMed Central PMCID: PMC6929220.

Stuttering is a speech fluency disorder with varied etiological explanations. It is important to identify symptoms early so that adequate and timely intervention can be delivered with focus on management and recovery. Stuttering, besides affecting speech fluency, might have a number of negative psychosocial consequences for the sufferer that may lead to immense anxiety, besides other symptoms. Therefore, it is thus imperative to include multiple dimensions in the holistic treatment of stuttering. Cognitive behavior therapy and mindfulness equip the client with the skills to manage the problems that occur as a result of stuttering. Since the rate of relapse in this condition is high, the chosen therapeutic paradigm must involve booster sessions over a long term. Periodic, detailed assessment would update the therapist about the barriers in treatment and would help in devising appropriate methods to get rid of these hindrances.

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PMCID: PMC6929220

PMID: 31879440

125: Mridha AR, Barwal I, Gupta A, Majeed A, Barwad AW, Kumar VS, Gamanagatti S, Yadav SC. Processing Techniques for Scanning Electron Microscopy Imaging of Giant Cells from Giant Cell Tumors of Bone. *Microsc Microanal.* 2019 Dec;25(6):1376-1382. doi: 10.1017/S1431927619014855. PubMed PMID: 31466545.

Giant cell tumor (GCT) of bone is a common benign lesion that causes significant morbidity due to the failure of modern medical and surgical treatment. Surface ultra-structures of giant cells (GCs) may help in distinguishing aggressive tumors from indolent GC lesions. This study aimed to standardize scanning electron microscopic (SEM) imaging of GC from GCT of bone. Fresh GCT collected in Dulbecco's Modified Eagle Medium was washed to remove blood, homogenized, or treated with collagenase to isolate the GCs. Mechanically homogenized and collagenase-digested GCs were imaged on SEM after commonly used drying methodologies such as air-drying, tetramethylsilane (TMS)-drying, freeze-drying, and critical point-drying (CPD) for the optimization of sample processing. The

collagenase-treated samples yielded a greater number of isolated GC and showed better surface morphology in comparison to mechanical homogenization. Air-drying was associated with marked cell shrinkage, and freeze-dried samples showed severe cell damage. TMS methodology partially preserved the cell contour and surface structures, although the cell shape was distorted. GC images with optimum surface morphology including membrane folding and microvesicular structures on the surface were observed only in collagenase-treated and critical point-dried samples. Collagenase digestion and critical point/TMS-drying should be performed for optimal SEM imaging of individual GCs.

DOI: 10.1017/S1431927619014855  
PMID: 31466545

126: Mulchandani R, Chandrasekaran AM, Shivashankar R, Kondal D, Agrawal A, Panniyammakal J, Tandon N, Prabhakaran D, Sharma M, Goenka S. Effect of workplace physical activity interventions on the cardio-metabolic health of working adults: systematic review and meta-analysis. *Int J Behav Nutr Phys Act.* 2019 Dec 19;16(1):134. doi: 10.1186/s12966-019-0896-0. Review. PubMed PMID: 31856826; PubMed Central PMCID: PMC6923867.

**BACKGROUND:** Adults in urban areas spend almost 77% of their waking time being inactive at workplaces, which leaves little time for physical activity. The aim of this systematic review and meta-analysis was to synthesize evidence for the effect of workplace physical activity interventions on the cardio-metabolic health markers (body weight, waist circumference, body mass index (BMI), blood pressure, lipids and blood glucose) among working adults.

**METHODS:** All experimental studies up to March 2018, reporting cardio-metabolic worksite intervention outcomes among adult employees were identified from PUBMED, EMBASE, COCHRANE CENTRAL, CINAHL and PsycINFO. The Cochrane Risk of Bias tool was used to assess bias in studies. All studies were assessed qualitatively and meta-analysis was done where possible. Forest plots were generated for pooled estimates of each study outcome.

**RESULTS:** A total of 33 studies met the eligibility criteria and 24 were included in the meta-analysis. Multi-component workplace interventions significantly reduced body weight (16 studies; mean diff: -2.61kg, 95% CI: -3.89 to -1.33) BMI (19 studies, mean diff: -0.42kg/m<sup>2</sup>, 95% CI: -0.69 to -0.15) and waist circumference (13 studies; mean diff: -1.92 cm, 95% CI: -3.25 to -0.60). Reduction in blood pressure, lipids and blood glucose was not statistically significant.

**CONCLUSIONS:** Workplace interventions significantly reduced body weight, BMI and waist circumference. Non-significant results for biochemical markers could be due to them being secondary outcomes in most studies. Intervention acceptability and adherence, follow-up duration and exploring non-RCT designs are factors that need attention in future research. Prospero registration number: CRD42018094436.

DOI: 10.1186/s12966-019-0896-0  
PMCID: PMC6923867  
PMID: 31856826

127: Muthukrishnan SP, Chandran DS, Afreen N, Bir M, Dastidar SG, Jayappa H, Mattoo B, Navneet A, Poorasamy J, Roy A, Sharma A, Ghosh D, Deepak KK. Planning, implementation, and evaluation of multicomponent, case-based learning for first-year Indian medical undergraduates. *Adv Physiol Educ.* 2019 Dec 1;43(4):504-511. doi: 10.1152/advan.00080.2019. PubMed PMID: 31553644.

Didactic lecture is an effective method to quickly pass on a high volume of information to a large number of students. However, if not well designed,

lectures can be monotonous and provide only passive learning, with little scope for higher order learning skills. To address this drawback of lectures, we supplemented it with case-based learning (CBL), which has been shown to promote self-learning. After giving an overview of gastrointestinal physiology through lectures, CBL on peptic ulcer disease was implemented for first-year Bachelor of Medicine, Bachelor of Surgery students. The present study aimed to evaluate the students' and teachers' opinions on the notion of supplementing lectures with CBL. In previous reports, discussion using clinical cases was primarily employed as the solitary component for conducting CBL. In the present study, three different but mutually exclusive components, such as case discussion, concept map, and critical thinking exercise on a specific topic in gastrointestinal pathophysiology, were integrated to form the multicomponent CBL (MC-CBL). Students reported that MC-CBL could promote application of the knowledge learned in lectures in a more appropriate context (92.42% positive response), enhance their learning efficiency (98.46% positive response), promote their active participation in the learning process (98.48% positive response), and help them in integrating physiological concepts with clinical science (98.46% positive response). Teachers observed that MC-CBL could promote active learning, analytic, and problem-solving skills of students. In conclusion, MC-CBL appeared to be an effective supplement for the lectures, providing an opportunity for the students to relate the knowledge learned during lectures.

DOI: 10.1152/advan.00080.2019  
PMID: 31553644

128: Naalla R, Murthy V, Chauhan S, Chinta K, Singhal M. Revisiting the Trapezius Flap as a Reconstructive Option for Cervico-Occipital and Thoracic Spine Regions. *Indian J Plast Surg.* 2019 Sep;52(3):322-323. doi: 10.1055/s-0039-3400677. Epub 2019 Dec 26. PubMed PMID: 31908371; PubMed Central PMCID: PMC6938435.

**Introduction** Reconstruction of complex soft tissue defects around the cervico-occipital and thoracic spine regions is a challenging task. We want to share our experience with trapezius flap for the reconstruction of these complex cases. **Materials and Methods** A retrospective analysis of patients who underwent reconstruction using trapezius flaps from January 2016 to June 2019 was performed. The indications, technique, complications, and outcomes were analyzed and presented. **Results** Six patients (three males and three females, >10 years of age) underwent seven reconstructions using trapezius flaps (one of the patients underwent reconstruction using a bilateral trapezius flap). Trapezius flap was used to resurface the parieto-occipital (n = 2), cervico-occipital (n = 2), cervicothoracic (n = 1), and thoracic (n = 1) regions. All flaps showed successful outcomes; one patient had wound dehiscence, and one patient had partial skin graft loss. **Conclusion** Trapezius flap is a reliable and good alternative to free flaps for the coverage of complex cervical-occipital and upper thoracic soft tissue defects.

DOI: 10.1055/s-0039-3400677  
PMCID: PMC6938435  
PMID: 31908371

129: Nagarathna R, Kaur N, Anand A, Sharma K, Dada R, Sridhar P, Sharma P, Kumar Singh A, Patil S, Nagendra HR. Distribution of glycated haemoglobin and its determinants in Indian young adults. *Diabetes Res Clin Pract.* 2019 Dec 14;159:107982. doi: 10.1016/j.diabres.2019.107982. [Epub ahead of print] PubMed PMID: 31846666.

**AIM:** The aim of the present study is to understand the distribution of A1c in four different age groups in young adults and its relation to other co-variants.

**METHODS:** The countrywide data was collected in 2017 in Individuals with high risk analysed by Indian Diabetes Risk Score (IDRS) and self-declared diabetics were identified after screening a sample of 240,968 individuals from rural (4 villages of about 500 adults each) and urban (4 census enumeration blocks of about 500 adults each) population spanning 65 districts of 29 states/UTs of Indian subcontinent. Blood tests and other detailed assessments were carried out on this selected group. This study presents the analysis of the A1c values of 2862 young adults (<35 years).

**RESULTS:** In the age group of 31-34 years, the proportion of Diabetes (22.36%) and Prediabetes (9.86%) was higher in comparison with younger age groups. Also, Diabetes (7.3%) and Prediabetes (22%) were highest among those who had parental history of DM in both parents as compared to those with Diabetes history in one parent [Diabetes (7.1%) or Prediabetes (19.0%)] and no Diabetes Parental History (Diabetes (7.3%) and Prediabetes (18.3%) cases. BMI was found to play a significant positive correlation with Diabetes and Prediabetes ( $p < 0.001$ ) with range of A1c.

**CONCLUSION:** Age, BMI and parental history were found to be correlated with A1c levels in IDRS screened high-risk population. With increasing age, the proportion of Diabetics and Prediabetics also increased with positive correlation of age with A1c levels.

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PMID: 31846666

130: Nakra T, Roy M, Yadav R, Agarwala S, Jassim M, Khanna G, Das P, Jain D, Mathur SR, Iyer VK. Cytomorphology of hepatoblastoma with histological correlation and role of SALL4 immunocytochemistry in its diagnosis, subtyping, and prognostication. *Cancer Cytopathol.* 2019 Dec 27. doi: 10.1002/cncy.22231. [Epub ahead of print] PubMed PMID: 31880869.

**BACKGROUND:** Hepatoblastoma (HB) is the most common malignant pediatric liver tumor, and cytology material is often the only tissue available for evaluation before definitive therapy. Subcategorization of HB based on cytomorphological features thus carries an important role in its prognostication. Spalt-like transcription factor 4 (SALL4), a marker of embryonic stem cells that is also found in the fetal liver, is reactivated in certain liver tumors. Limited studies have evaluated its role in HB. This study was aimed at evaluating the cytomorphological features of HB and assessing the utility of SALL4 immunocytochemistry (ICC) in its subtyping and prognostication.

**METHODS:** Pretherapy fine-needle aspiration smears from patients diagnosed with HB over a period of 9 years were retrieved. Aspirates were subclassified on the basis of the cytomorphology and were correlated with the histology wherever it was available. ICC for SALL4 was performed in 33 cases, and nuclear staining was considered positive.

**RESULTS:** A total of 53 HB cases were included with 30 available postchemotherapy resection specimens. All the patients were diagnosed as epithelial HB on cytology, and the cases were subclassified as pure fetal (9 of 53), pure embryonal (2 of 53), or combined epithelial HB (42 of 53). There was good concordance between cytology and histology for subtyping. SALL4 immunostaining displayed strong and diffuse nuclear positivity in the embryonal component while focal and weak to negative staining in fetal cells.

**CONCLUSIONS:** Fine-needle aspiration cytology serves as a rapid and effective tool for a correct diagnosis of HB before the implementation of chemotherapy, and SALL4 may serve as a useful diagnostic and prognostic marker.

DOI: 10.1002/cncy.22231  
PMID: 31880869

131: Nanda D, Nangia S, Thukral A, Yadav CP. A new clinical respiratory distress score for surfactant therapy in preterm infants with respiratory distress. *Eur J Pediatr*. 2019 Dec 18. doi: 10.1007/s00431-019-03530-5. [Epub ahead of print] PubMed PMID: 31853688.

The guidelines for surfactant therapy are largely based on studies done in developed countries wherein the facility infrastructure, patient profile, and clinical practices are different from low- and middle-income countries (LMICs). Though SRT is widely practiced in developing countries, there exists variability in clinical practice. Our objective was to identify the factors which would predict the need of surfactant administration and develop a "clinical respiratory distress (RD) score" for surfactant administration in preterm neonates with respiratory distress. A prospective observational study was conducted in 153 preterm infants (260/7 to 346/7 weeks gestation) with respiratory distress who were managed with CPAP and/or surfactant where indicated. Gestation < 32 weeks, no antenatal corticosteroid (ANS), hypothermia at admission, Apgar score < 3 at 1 minute, and Silverman score > 2 at 2 hours were found to be the significant factors in predicting surfactant requirement in multivariate regression analysis. A seven point scale was developed and categorized into two categories as < 4 and  $\geq 4$ . The sensitivity, specificity, PPV, and NPV were 67%, 87%, 86%, and 68%, respectively, with a cutoff score  $\geq 4$ . The positive likelihood ratio was 5.07 (95% CI 2.71-9.48), and negative likelihood ratio was 0.38 (95% CI 0.28-0.52). The observed rate of surfactant administration was found to be around 32% when the composite score was below four, and the rate increased to almost 86% when the composite score was  $\geq 4$ . The predictive accuracy of the model was subsequently evaluated in a cohort of 56 preterm infants with respiratory distress.. Sensitivity, specificity and positive and negative predictive value during the validation phase were 97%, 73%, 85%, and 94%, respectively. With a composite score less than 4, the observed rate of surfactant administration was 6% (95% CI 1%-28%) as against the model predicted rate of 24%, while with composite score  $\geq 4$ , the observed rate was 85% (95% CI 69%-94%) as against the model predicted rate of 90%. Conclusion: "Clinical RD score" is a simple score, which can be utilized for decision-making for early surfactant administration for preterm infants (260/7 to 346/7 weeks gestation) with respiratory distress. Trial Registration: NCT03273764 What is Known: • Both CPAP and surfactant therapy are effective in management of preterm infants with RDS. • The efficacy of surfactant replacement therapy is better when it is administered early in the course of disease. What is New: • Many of the known risk factors for RDS do not predict surfactant requirement. • "Composite RD score" comprising of five independent predictors of surfactant requirement with a numeric cutoff may help decide which preterm neonates with respiratory distress need early surfactant administration in low- and middle-income countries.

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PMID: 31853688

132: Panda S, Kumar R, Konkimalla A, Thakar A, Singh CA, Sikka K, Sharma SC, Kakkar A, Bhasker S. Rationale behind thyroidectomy in total laryngectomy: analysis of endocrine insufficiency and oncological outcomes. *Indian J Surg Oncol*. 2019 Dec;10(4):608-613. doi: 10.1007/s13193-019-00935-4. Epub 2019 May 22. PubMed PMID: 31857751; PubMed Central PMCID: PMC6895295.

Thyroidectomy conventionally accompanies total laryngectomy. This study intends

to analyze the incidence and factors leading to thyroid gland involvement in carcinoma larynx and hypopharynx. Retrospective chart review from March 2011 to December 2016 of all patients who had undergone total laryngectomy at our institute. A total of 125 patients entered into the analysis. Subsites involved were glottis (n= 32), supraglottis (n =28), transglottis (n =52), pyriform sinus (n =12), and subglottis (n =1). TNM distribution according to AJCC 7th edition is as follows: T2 (n=1), T3 (n =34), T4 (n =90); N0 (n=97), N1 (n=13), N2a (n=5), N2b (n=5), N2c (n=4), and N3 (n=1). Total thyroidectomy was performed in 16 patients, near total thyroidectomy in 5, and hemithyroidectomy in 104. Histopathologically thyroid gland involvement was seen in 11/125 (8.8%). The overall incidence of hypothyroidism was 48% (hemithyroidectomy, 43/104; total thyroidectomy, 16/16; near total thyroidectomy, 1/5). The incidence of permanent hypoparathyroidism was 12.8% (total thyroidectomy, 11; hemithyroidectomy, 5). On multivariate analysis (Cox proportional hazards model), extralaryngeal spread into level 6 (HR=5.5, p=.006, C.I=1-18.8) and extracapsular extension (HR=9.3, p =0.02, C.I=1.29-67.5) were statistically significant predictors for thyroid gland involvement. Survival analysis of patients with thyroid gland involvement (n =11) revealed 5-year overall survival (OS) of 100% and 5-year disease-free survival (DFS) of 59.3% compared with patients without thyroid gland involvement, 71% and 51.7%, respectively (median follow-up, 30 months). Thyroid gland involvement did not show a statistically significant effect on OS/DFS on multivariate analysis. In view of the endocrine abnormalities and lack of survival benefit seen, thyroidectomy should be performed judiciously during total laryngectomy.

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PMCID: PMC6895295 [Available on 2020-12-01]

PMID: 31857751

133: Pandey D, Patel SKS, Singh R, Kumar P, Thakur V, Chand D. Solvent-Tolerant Acyltransferase from *Bacillus* sp. APB-6: Purification and Characterization. *Indian J Microbiol.* 2019 Dec;59(4):500-507. doi: 10.1007/s12088-019-00836-8. Epub 2019 Nov 4. PubMed PMID: 31762514; PubMed Central PMCID: PMC6842382.

Amidase from *Bacillus* sp. APB-6 with very good acyltransferase activity was purified to homogeneity with a purification fold of 3.68 and 53.20% enzyme yield. The purified protein's subunit molecular mass was determined approximately 42 kDa. Hyperactivity of the enzyme was observed at pH 7.5 (150 mM, potassium-phosphate buffer) and 50 °C of incubation. An enhancement in activity up to 42% was recorded with ethylenediaminetetraacetic acid and dithiothreitol. The kinetic parameter  $K_m$  values for substrates: acetamide and hydroxylamine-hydrochloride were 73.0 and 153 mM, respectively. Further, the  $V_{max}$  for acyltransferase activity was 1667 U/mg of protein and the  $K_i$  for acetamide was calculated as 37.0 mM. The enzyme showed tolerance to various organic solvents (10%, v/v) and worked well in the biphasic reaction medium. The acyltransferase activity in presence of solvents i.e. biphasic medium may prove highly favorable for the transformation of hydrophobic amides, which otherwise is not possible in simple aqueous phase.

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PMID: 31762514

134: Pandey G, Bakhshi S, Kumar M, Thakur B, Jain P, Kaur P, Chauhan SS. Prognostic and therapeutic relevance of cathepsin B in pediatric acute myeloid leukemia. *Am J Cancer Res.* 2019 Dec 1;9(12):2634-2649. eCollection 2019. PubMed PMID: 31911851; PubMed Central PMCID: PMC6943344.

AML, the second most common childhood leukemia is also one of the deadliest cancers. High mortality rate in AML is due to high incidence of relapse after complete remission with chemotherapy and inadequate prognostic assessment of patients. Moreover, there is dearth of therapeutic targets for treatment of this malignancy. Previous pilot study (n = 24) by our group revealed strong association between cathepsin B (CTSB) overexpression in peripheral blood mononuclear cells (PBMCs) and poor survival outcome in pediatric AML patients. To further explore the clinical utility and role of this protease in pediatric AML, we measured its enzymatic activity and mRNA expression in PBMCs as well as bone marrow mononuclear cells (BMMCs) of patients (n = 101) and PBMCs of healthy controls. Our results revealed elevated CTSB activity (P < 0.01) and overexpression of its mRNA (P < 0.01) in AML patients. Interestingly CTSB in BMMCs of patients emerged as an independent prognostic marker when compared with other known risk factors. Moreover, chemical inhibition of CTSB activity compromised survival, and induced apoptosis in an AML cell line THP-1. We further demonstrate the inhibition of CTSB activity by chemotherapeutic agent doxorubicin in these cells. Docking and simulation studies suggested the binding of doxorubicin to CTSB with higher affinity than its known specific inhibitor CA-074 Me, thereby indicating that cell death induced by this drug may at least partly be mediated by CTSB inhibition. CTSB, therefore, may serve as a prognostic marker and an attractive chemotherapeutic target in pediatric AML.

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PMCID: PMC6943344  
PMID: 31911851

135: Pandey H, Singh K, Ranjan R, Pandey SK, Sharma A, Kishor K, Seth T, Mahapatra M, Saxena R. Clinical variability and molecular characterization of Hbs/G $\Gamma^3$  (A $\Gamma^3$ I $\Gamma^2$ ) $\Gamma^0$ -thal and Hbs/HPFH in Indian sickle cell disease patients: AIIMS experience. *Hematology.* 2019 Dec;24(1):349-352. doi: 10.1080/16078454.2019.1579985. Erratum in: *Hematology.* 2019 Dec;24(1):354. PubMed PMID: 30777489.

**INTRODUCTION:** In sickle cell disease (SCD) patients, among the predictors of survival, HbF levels play a significant role in lowering the morbidity and mortality. Coinheritance of  $\delta\beta$  thalassemia and hereditary persistence of fetal hemoglobin (HPFH) may contribute to variable HbF levels in SCD patients, thus influencing their clinicopathological profile. Such cases are sparsely documented in the literature and thus, we screened the presence of  $\delta\beta$  thalassemia and HPFH in 126 cases of SCD with high HbF.

**MATERIAL AND METHODS:** A total 126 SCD individuals with raised HbF levels were the study subject. Capillary zone electrophoresis (CZE) was done for the quantitative assessment of hemoglobin variants. HbSC, HbSD, HbAS and HbSE cases were excluded. Asian Indian G $\gamma$ (A $\gamma$  $\delta\beta$ ) $\Gamma^0$ -thal,  $\delta\beta^0$ -thal (Sicilian, 13.4 kb), (Chinese, 100 kb), HPFH-1 (Black, 106 kb), HPFH-2 (Ghanaian, 105 kb), HPFH-3 (Indian, 48.5 kb) were done by GAP-PCR.

**RESULTS:** Out of 126, 78 cases (62%) were homozygous for SCD. The remaining 48 cases suspected to be heterozygous were furthered screened and 6/48 cases (12.5%) were found to be compound heterozygous. Out of these 6 cases, 4 (66.66%) had HbS/ $\delta\beta$ - G $\gamma$ (A $\gamma$  $\delta\beta$ ) $\Gamma^0$  and 2 (33%) had HbS/HPFH compound heterozygous condition. None of

the patients had  $\delta\beta 0$ -thal (Sicilian, 13.4 kb), (Chinese, 100 kb), HPFH-1 (Black, 106 kb), HPFH-2 (Ghanaian, 105 kb).

CONCLUSION: This study highlights the importance of understanding the complex patho-physiology of compound heterozygous cases of HbS/HPFH and HbS/ $\delta\beta$  thalassemia, as these infrequent conditions lead to change in phenotype and clinical severity of the disease. Insight into more such cases will open the window to better analyze the disease pathogenesis in these rare compound heterozygous conditions, as this will be beneficial to formulate proper management protocol in these patients.

DOI: 10.1080/16078454.2019.1579985

PMID: 30777489 [Indexed for MEDLINE]

136: Pandey NN, Sinha M, Sharma A, Kumar S. Anomalous left vertebral artery from descending thoracic aorta with juxtaductal coarctation of aorta. *BMJ Case Rep.* 2019 Dec 10;12(12). pii: e232949. doi: 10.1136/bcr-2019-232949. PubMed PMID: 31826908.

137: Pandey NN, Sinha M, Sharma A, Kumar S. Empty left atrioventricular groove: congenital atresia of left circumflex artery. *Acta Cardiol.* 2019 Dec;74(6):549-550. doi: 10.1080/00015385.2018.1539374. Epub 2018 Dec 4. PubMed PMID: 30513262.

138: Patel A, Kaur H, Xess I, Michael JS, Savio J, Rudramurthy S, Singh R, Shastri P, Umabala P, Sardana R, Kindo A, Capoor MR, Mohan S, Muthu V, Agarwal R, Chakrabarti A. A multicentre observational study on the epidemiology, risk factors, management and outcomes of mucormycosis in India. *Clin Microbiol Infect.* 2019 Dec 4. pii: S1198-743X(19)30621-4. doi: 10.1016/j.cmi.2019.11.021. [Epub ahead of print] PubMed PMID: 31811914.

OBJECTIVES: To describe the epidemiology, management and outcome of individuals with mucormycosis; and to evaluate the risk factors associated with mortality.

METHODS: We conducted a prospective observational study involving consecutive individuals with proven mucormycosis across 12 centres from India. The demographic profile, microbiology, predisposing factors, management and 90-day mortality were recorded; risk factors for mortality were analysed.

RESULTS: We included 465 patients. Rhino-orbital mucormycosis was the most common (315/465, 67.7%) presentation followed by pulmonary (62/465, 13.3%), cutaneous (49/465, 10.5%), and others. The predisposing factors included diabetes mellitus (342/465, 73.5%), malignancy (42/465, 9.0%), transplant (36/465, 7.7%), and others. *Rhizopus* species (231/290, 79.7%) were the most common followed by *Apophysomyces variabilis* (23/290, 7.9%), and several rare Mucorales. Surgical treatment was performed in 62.2% (289/465) of the participants. Amphotericin B was the primary therapy in 81.9% (381/465), and posaconazole was used as combination therapy in 53 (11.4%) individuals. Antifungal therapy was inappropriate in 7.6% (30/394) of the individuals. The 90-day mortality rate was 52% (242/465). On multivariate analysis, disseminated and rhino-orbital (with cerebral extension) mucormycosis, shorter duration of symptoms, shorter duration of antifungal therapy, and treatment with amphotericin B deoxycholate (versus liposomal) were independent risk factors of mortality. A combined medical and surgical management was associated with a better survival.

CONCLUSIONS: Diabetes mellitus was the dominant predisposing factor in all forms of mucormycosis. Combined surgical and medical management was associated with better outcomes. Several gaps surfaced in the management of mucormycosis. The rarer Mucorales identified in the study warrant further evaluation.

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DOI: 10.1016/j.cmi.2019.11.021  
PMID: 31811914

139: Pathak M, Dwivedi SN, Deo SVS, Thakur B, Sreenivas V, Rath GK. Effectiveness of Added Targeted Therapies to Neoadjuvant Chemotherapy for Breast Cancer: A Systematic Review and Meta-analysis. *Clin Breast Cancer*. 2019 Dec;19(6):e690-e700. doi: 10.1016/j.clbc.2019.06.001. Epub 2019 Jun 20. Review. PubMed PMID: 31337531.

Over the past several years, targeted therapy has been increasingly used in the management of breast cancer. Reported results for targeted therapies are variable, as some randomized controlled trials (RCTs) reported a strong effect, whereas others reported no or minimal effect on the outcomes. Accordingly, the present study aimed to assess the effect of the addition of targeted therapies to neoadjuvant chemotherapy on tumor response rates, breast conserving surgeries, and survival outcomes. PubMed and the Cochrane register of clinical trials were searched on April 28, 2017 for RCTs comparing addition of targeted therapies to neoadjuvant chemotherapy. Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, the screening of records and data extraction were performed by 2 independent reviewers. Publication bias and risk of bias were assessed by the Egger test and the Cochrane tool for risk of bias assessment, respectively. The fixed effect method or random effect method were used to synthesize the results depending on the heterogeneity assessed by the I<sup>2</sup> statistic. A total of 17 RCTs including trastuzumab (n = 5), bevacizumab (n = 7), and other targeted therapies (n = 5) were found eligible. Pathologic complete response was significantly higher with trastuzumab (relative risk [RR], 2.20; 95% confidence interval [CI], 1.62-2.99) and bevacizumab (RR, 1.23; 95% CI, 1.11-1.37), but not with other targeted therapies. Bevacizumab for human epidermal growth factor receptor 2 (HER2)-negative breast cancer was found to be associated with improved overall (hazard ratio, 0.69; 95% CI, 0.53-0.90) and disease-free survival (hazard ratio, 0.83; 95% CI, 0.67-1.03). The addition of targeted therapies may not significantly increase breast conserving surgery rates (RR, 1.04; 95% CI, 0.97-1.12). The addition of targeted therapies, especially trastuzumab for patients with HER2-positive breast cancer and bevacizumab for patients with HER2-negative breast cancer significantly increased pathologic complete response, overall response, and clinical complete response but not breast conserving surgery rates.

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DOI: 10.1016/j.clbc.2019.06.001  
PMID: 31337531

140: Patnaik U, Panda S, Thakar A. Audit of Complications in an Otolaryngology Led Skull-Base Surgical Practice. *J Neurol Surg B Skull Base*. 2019 Dec;80(6):586-592. doi: 10.1055/s-0038-1676793. Epub 2018 Dec 26. PubMed PMID: 31754595; PubMed Central PMCID: PMC6864432.

**Objective** This study was aimed to classify and study complications of surgery of the cranial base, primarily from an otorhinolaryngology perspective. **Design** This study was designed with consecutive cohort of skull base surgical cases. **Setting** Tertiary referral academic center. **Participants** Patients having skull-base surgery at a otorhinolaryngology based skull-base unit, from 2002 to 2015. **Main Outcome Measures** Enumeration of complications is the main outcome of this study. Surgical procedures, categorized for complexity as per a unified system, are

applicable to endoscopic and open procedures. Complications were categorized as per the British Association of Otolaryngologists coding of surgical complications. Complication classified as major if life-threatening, causing permanent disability, or compromising the result of surgery. Results A total of 342 patients (n =342) were operated; 13 patients' records were excluded due to <6 months posttreatment follow-up. The study group constituted 204 anterior skull-base (endoscopic, 120; open/external, 84) and 125 lateral skull-base procedures. Complication rates noted to increase in both groups with increasing complexity of surgical intervention. Anterior skull-base surgery (total complications, 11%; major, 3%; death, 0.5%) noted to have significantly less surgical complications than lateral skull-base surgery (total complications, 33%; major, 15%; death, 1.6%; p <0.001). Among the anterior procedures no significant difference noted among endoscopic and external approaches when compared across similar surgical complexity. Conclusion Despite improvement in surgical and perioperative care, the overall major complication rate in a contemporary otolaryngology led, primarily extradural, skull-base practice is noted at 8%. Perioperative mortality, though rare, was encountered in 1%. A standard method for categorization of surgical complexity and the grade of complications as reported here is recommended.

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PMID: 31754595

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**BACKGROUND:** Tuberculosis (TB) represents a worldwide cause of mortality (it infects one third of the world's population) affecting mostly developing countries, including India, and recently also developed ones due to the increased mobility of the world population and the evolution of different new bacterial strains capable to provoke multi-drug resistance phenomena. Currently, antitubercular drugs are unable to eradicate subpopulations of *Mycobacterium tuberculosis* (MTB) bacilli and therapeutic vaccinations have been postulated to overcome some of the critical issues related to the increase of drug-resistant forms and the difficult clinical and public health management of tuberculosis patients. The Horizon 2020 EC funded project "In Silico Trial for Tuberculosis Vaccine Development" (STriTuVaD) to support the identification of new therapeutic interventions against tuberculosis through novel in silico modelling of human immune responses to disease and vaccines, thereby drastically reduce the cost of clinical trials in this critical sector of public healthcare.

**RESULTS:** We present the application of the Universal Immune System Simulator (UISS) computational modeling infrastructure as a disease model for TB. The model is capable to simulate the main features and dynamics of the immune system activities i.e., the artificial immunity induced by RUTI<sup>®</sup> vaccine, a

polyantigenic liposomal therapeutic vaccine made of fragments of *Mycobacterium tuberculosis* cells (FCMtb). Based on the available data coming from phase II Clinical Trial in subjects with latent tuberculosis infection treated with RUTI® and isoniazid, we generated simulation scenarios through validated data in order to tune UISS accordingly to STriTuVaD objectives. The first case simulates the establishment of MTB latent chronic infection with some typical granuloma formation; the second scenario deals with a reactivation phase during latent chronic infection; the third represents the latent chronic disease infection scenario during RUTI® vaccine administration.

**CONCLUSIONS:** The application of this computational modeling strategy helpfully contributes to simulate those mechanisms involved in the early stages and in the progression of tuberculosis infection and to predict how specific therapeutical strategies will act in this scenario. In view of these results, UISS owns the capacity to open the door for a prompt integration of *in silico* methods within the pipeline of clinical trials, supporting and guiding the testing of treatments in patients affected by tuberculosis.

DOI: 10.1186/s12859-019-3045-5

PMCID: PMC6904993

PMID: 31822272

143: Prabhu M, Shakya S, Ballal S, Shamim SA, Bal C. Long-term Clinicopathological Features of a Family with Multiple Endocrine Neoplasia Type 2A Caused by C634R RET Gene Mutation. *Indian J Nucl Med.* 2020 Jan-Mar;35(1):48-53. doi: 10.4103/ijnm.IJNM\_168\_19. Epub 2019 Dec 31. PubMed PMID: 31949369; PubMed Central PMCID: PMC6958961.

Type 2 multiple endocrine neoplasia (MEN2A) is a variant of hereditary medullary thyroid carcinoma (MTC). MEN2A is characterized by the presence of the following: MTC, hyperparathyroidism, and pheochromocytoma (PHEO). The pathogenesis includes RET proto-oncogene mutation; the most frequently observed mutation is in exon 11 codon 634. We report pedigree of a large Indian family involving three generations including 21 members with MEN2A, in whom RET mutation status was determined. We then analyzed their clinical follow-up details, with a median duration of follow-up of 60 months (range: 9-276 months). Calcitonin (Ctn) levels were routinely checked during the follow-up. The index case was found to carry p.C634R mutation involving exon 11 of the RET gene. RET mutation was positive in 12 members in the family (12/21, i.e., 57%), was negative in 7 patients, and was not tested in 2 patients, as they were not available for the genetic test. Thirteen were clinically affected with MTC and 10 members had PHEO. At the last follow-up, the median Ctn level was 14.3 pg/mL (range: 2-12655 pg/mL). Four patients developed lymph nodal recurrence during follow-up, for which they underwent re-operations with median duration to recurrence being 48 months (range: 9-156 months). We highlight in this article that early diagnosis, adequate surgery, and appropriate genetic counseling with genetic screening are essential to improve the outcome of persons with MTC. Every case of MTC should be seen as familial or index case of hereditary MTC unless otherwise RET mutation excludes it.

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PMCID: PMC6958961

PMID: 31949369

144: Prajapati B, Fatma M, Fatima M, Khan MT, Sinha S, Seth PK. Identification of lncRNAs Associated With Neuroblastoma in Cross-Sectional Databases: Potential Biomarkers. *Front Mol Neurosci.* 2019 Dec 12;12:293. doi:

10.3389/fnmol.2019.00293. eCollection 2019. PubMed PMID: 31920530; PubMed Central PMCID: PMC6920248.

Long non-coding RNAs (lncRNAs) have emerged as an important regulatory control in biological systems. Though the field of lncRNA has been progressing rapidly, a complete understanding of the role of lncRNAs in neuroblastoma pathogenesis is still lacking. To identify the abrogated lncRNAs in primary neuroblastoma and in the metastasized as well as the relapsed form of neuroblastoma, we analyzed an RNA-seq dataset on neuroblastoma that is available online to identify the lncRNAs that could potentially be contributing to the biology of neuroblastoma. The identified lncRNAs were further scrutinized using a publicly available epigenetic dataset of neuroblastoma and a cancer database. After this cross-sectional study, we were able to identify three significant lncRNAs, CASC15, PPP1R26-AS1, and USP3-AS1, which could serve as potential biomarkers in clinical studies of neuroblastoma pathogenesis.

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DOI: 10.3389/fnmol.2019.00293

PMCID: PMC6920248

PMID: 31920530

145: Praveen PA, Madhu SV, Mohan V, Das S, Kakati S, Shah N, Chadha M, Bhadada SK, Kaur T, Dhaliwal RS, Das AK, Yajnik CS, Tandon N. Demographic and clinical profile of youth onset diabetes patients in India- Results from the baseline data of a clinic based registry of people with diabetes in India with young age at onset (YDR) - [YDR-02]. *Pediatr Diabetes*. 2019 Dec 29. doi: 10.1111/pedi.12973. [Epub ahead of print] PubMed PMID: 31885113.

**BACKGROUND:** We here report the demographic and clinical profile of the patients enrolled in the Indian Council of Medical Research funded Registry of people with diabetes in India with Young age at onset (YDR) from first January 2000 to 31st July 2011.

**METHODS:** The YDR registry recruits all diabetes cases (newly diagnosed or treated) reporting on or after January 1, 2000 with age of diagnosis  $\leq 25$  years, and residing within the assigned geographical area of the reporting centres. A baseline proforma was used to obtain information on demographic and clinical details at registration.

**RESULTS:** The registry has enrolled 5546 patients (49.5% male; 50.5% female) with youth onset diabetes from 205 reporting centres linked to 8 regional collaborating centres (RCC) across India. T1DM (63.9%; n = 3545) and T2DM (25.3%; n = 1401) were the commonest variants of youth onset diabetes, though their relative proportion varied across RCCs. The mean (SD) age at diagnosis for T1DM was 12.9 (6.5) years, while that for T2DM was 21.7 (3.7) years. Nearly half the T1DM patients were registered within 6 months of the onset of disease. Most cases of T2DM (47.3%) were registered after 3 years from their date of diagnosis. 56.1% of patients had at least one episode of hospitalization at registration.

**CONCLUSION:** The observations from YDR registry indicate the need to establish a surveillance system in India to monitor diabetes in youth, not only to understand its complex etiology and natural history but also due to its detrimental socio economic impact. This article is protected by copyright. All rights reserved.

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DOI: 10.1111/pedi.12973

PMID: 31885113

146: Pujari A, Sharma N. Assessment of posterior capsular integrity on optical coherence tomography. *Can J Ophthalmol*. 2019 Dec;54(6):e302-e305. doi: 10.1016/j.jcjo.2019.04.005. Epub 2019 May 31. PubMed PMID: 31836121.

147: Pushker N, Meel R, Bajaj MS. Levator-Muller's recession using labial mucosa as a spacer in severe eyelid retraction. *Can J Ophthalmol*. 2019 Dec;54(6):678-681. doi: 10.1016/j.jcjo.2019.04.004. Epub 2019 May 31. PubMed PMID: 31836099.

**OBJECTIVE:** To evaluate the use of labial mucosa as a spacer for levator-Muller's recession in correction of severe eyelid retraction.

**DESIGN:** Retrospective interventional study.

**PARTICIPANTS:** We retrospectively reviewed records of 4 patients with severe upper eyelid retraction not associated with cicatricial diseases of the conjunctiva.

**METHOD:** Surgical correction of eyelid retraction was performed by Levator-Muller's recession using autologous mucosal graft (from lip) as a spacer through transconjunctival approach. Eyelid height and contour were the main outcome measures evaluated after surgery.

**RESULTS:** There was resolution of dry eye symptoms in all 4 cases. In 2 cases the corrected eyelid height was within 1 mm of the desired lid position. The lid contour was good in 2 cases and satisfactory in 2 cases because of mild lateral flare. The eyelid height remained stationary till the last follow-up, which ranged from Eyelid height and contour were the main outcome measures evaluated after surgery. 6-30 months (mean: 18 months).

**CONCLUSIONS:** Labial mucosal graft as a spacer for levator-Muller's recession is a good option for correction of severe upper eyelid retraction. It provides stable eyelid position within 3 months of surgery with no corneal complications.

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DOI: 10.1016/j.jcjo.2019.04.004  
PMID: 31836099

148: Raghav S, Niveditha M, Ravi S, Shashwat M. Neglected Traumatic Atlantoaxial Rotatory Dislocation in Adult. *Int J Spine Surg*. 2019 Dec 31;13(6):531-535. doi: 10.14444/6071. eCollection 2019 Dec. PubMed PMID: 31970048; PubMed Central PMCID: PMC6962011.

Atlantoaxial rotatory dislocations (AARD) are common in the pediatric population and rarely seen in adults. We describe a case of neglected AARD and subsequent management. A 25-year-old man developed a Fielding type 1 AARD following a road traffic accident. He was managed conservatively for 1.5 months before being referred to us. The patient underwent surgery 1.5 months after the accident. Closed reduction failed, and C1-2 fixation with the Harms technique was performed after intraoperative reduction, resulting in correction of deformity. Delay of treatment makes intraoperative reduction more difficult and increases the possibility of the chronic permanent change of neck muscles and ligaments. Hence, a high index of suspicion with a thorough clinical examination and judicious use of radiological investigations is paramount to the appropriate management of such cases.

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PMCID: PMC6962011  
PMID: 31970048

149: Rai G, Das S, Ansari MA, Singh PK, Pandhi D, Tigga RA, Bhattacharya SN, Gupta C, Dar SA. The interplay among Th17 and T regulatory cells in the immune dysregulation of chronic dermatophytic infection. *Microb Pathog.* 2019 Dec 10;139:103921. doi: 10.1016/j.micpath.2019.103921. [Epub ahead of print] PubMed PMID: 31830582.

The delineation of the pathogenic interaction between the host skin immune responses and dermatophytes has remained indigent. The obscure enigma in host-dermatophyte immunopathogenic interactions is the T regulatory (Treg) and T-helper (Th) 17 cell role in maintaining immune homeostasis. We attempted to understand the regulation and recognition of lineage-specific response in chronic dermatophytic skin infection patients. The percentages of Th17 (CD4+CD161+IL23R+) and Treg (CD4+CD25+FoxP3+) cell subpopulations in the peripheral circulation of thirty chronic dermatophytic skin infection patients and twenty healthy individuals was determined. The serum cytokine levels were estimated for disease correlation. The mean duration of the disease was  $10.68 \pm 8.72$  months, with *Trichophyton mentagrophytes* complex as the major pathogen. Total serum IgE level of patients was significantly higher compared to healthy controls ( $305 \pm 117$  vs  $98.53 \pm 54.55$  IU/ml;  $p < 0.01$ ). Expression of Th17 and Treg cell markers on CD4+ T cells was significantly elevated in patients than controls ( $p < 0.05$ ). Comparatively, serum interleukin (IL)-4 and interferon (IFN)- $\gamma$  levels were increased, with low IL-10 levels in patients. Our data envisages a complex immune dysfunction in chronic dermatophytosis, arising either as a result of dermatophyte exposure or paradoxical precedence of disease establishment. Designing new treatment strategies and preventing recurrences are challenges for future research.

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DOI: 10.1016/j.micpath.2019.103921  
PMID: 31830582

150: Rajagopalan V, Chouhan RS, Pandia MP, Lamsal R, Rath GP. Effect of Intraoperative Blood Loss on Perioperative Complications and Neurological Outcome in Adult Patients Undergoing Elective Brain Tumor Surgery. *J Neurosci Rural Pract.* 2019 Oct;10(4):631-640. doi: 10.1055/s-0039-3399487. Epub 2019 Dec 11. PubMed PMID: 31831982; PubMed Central PMCID: PMC6906102.

**Background** Major blood loss during neurosurgery can lead to several complications, including life-threatening hemodynamic instabilities. Studies addressing these complications in patients undergoing intracranial tumor surgery are limited. **Materials and Methods** During the study period, 456 patients who underwent elective craniotomy for brain tumor excision were categorized into four groups on the basis of estimated intraoperative blood volume loss: Group A (<20%), Group B (20-50%), Group C (>50-100%), and Group D (more than estimated blood volume). The occurrence of various perioperative complications was correlated with these groups to identify if there was any association with the amount of intraoperative blood loss. **Results** The average blood volume loss was  $11\% \pm 5.3\%$  in Group A,  $29.8\% \pm 7.9\%$  in Group B,  $68.3\% \pm 13.5\%$  in Group C, and  $129.1\% \pm 23.9\%$  in Group D. Variables identified as risk factors for intraoperative bleeding were female gender ( $p < 0.001$ ), hypertension ( $p = 0.008$ ), tumor size >5 cm ( $p < 0.001$ ), high-grade glioma ( $p = 0.004$ ), meningioma ( $p < 0.001$ ), mass effect ( $p = 0.002$ ), midline shift ( $p = 0.014$ ), highly vascular tumors documented on preoperative imaging ( $p < 0.001$ ), extended craniotomy approach ( $p = 0.002$ ), intraoperative colloids use >1,000 mL ( $p < 0.001$ ), intraoperative brain bulge ( $p = 0.03$ ), intraoperative appearance as highly vascular tumor ( $p < 0.001$ ), and duration of surgery >300 minutes ( $p <$

0.001). Conclusions Knowledge of these predictors may help anesthesiologists anticipate major blood loss during brain tumor surgery and be prepared to mitigate these complications to improve patient outcome.

DOI: 10.1055/s-0039-3399487

PMCID: PMC6906102

PMID: 31831982

151: Ramprasad A, Rastogi N, Xess I, Singh G, Ranjan P, Jadon R, Ray A, Vikram N. Disseminated phaeohyphomycosis by *Exophiala jeanselmei*. QJM. 2019 Dec 5. pii: hcz304. doi: 10.1093/qjmed/hcz304. [Epub ahead of print] PubMed PMID: 31803917.

152: Rastogi S, Kalra K, Manasa P, Rajawat M, Mehta V. Long lasting response of trabectedin in patient with gastric leiomyosarcoma with liver metastasis: an update to previous report. Future Sci OA. 2019 Dec 9;6(1):FSO432. doi: 10.2144/fsoa-2019-0085. PubMed PMID: 31915533; PubMed Central PMCID: PMC6920747.

Leiomyosarcoma of the stomach is an extremely rare malignancy for which treatment in advanced disease is hardly reported. Here, we report a case of a 48-year-old man with metastatic gastric Leiomyosarcoma who had previously received a combination of gemcitabine and docetaxel followed by pazopanib after detection of metastasis. The patient was started on trabectedin as per protocol and had disease control continuing for 17 cycles of trabectedin. His quality of life and absence of significant toxicities highlight the noncumulative nature of trabectedin and potential benefit in responding cases.

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DOI: 10.2144/fsoa-2019-0085

PMCID: PMC6920747

PMID: 31915533

153: Razik A, Das CJ, Gupta A, Wanamacher D, Verma S. Urinary diversions: a primer of the surgical techniques and imaging findings. Abdom Radiol (NY). 2019 Dec;44(12):3906-3918. doi: 10.1007/s00261-019-02179-w. PubMed PMID: 31440802.

**OBJECTIVE:** The article attempts to describe the indications, classification, and surgical anatomy of the commonly performed urinary diversion procedures, followed by the imaging protocol and radiological appearances of the normal postoperative anatomy and complications related to these procedures.

**CONTENTS:** Diversion procedures are used to reroute urine after cystectomy and in patients with refractory neurogenic or outlet obstruction of the urinary bladder. Broadly, these can be classified as continent and incontinent diversions.

Patients with urinary diversions frequently undergo radiological investigations for the detection of complications. Commonly, a loopogram or pouchogram is performed few weeks after the surgery to look for leak, whereas CT or MRI is used for long-term follow-up. Postoperative complications can be early (within 30 days of the surgery) or delayed and include leaks, collections, strictures, calculi, parastomal hernia, small bowel obstruction, and oncologic recurrence.

**CONCLUSION:** A variety of urinary diversion procedures are commonly performed and interpretation of the postsurgical anatomy can be overwhelming for the general radiologist. This article provides a basic understanding of the normal anatomy as well as a thorough discussion on the imaging protocol and radiological appearances of the potential complications associated with these procedures.

DOI: 10.1007/s00261-019-02179-w

PMID: 31440802

154: Sahoo T, Sivanandan S, Thomas D, Verma A, Thukral A, Sankar MJ, Agarwal R, Deorari AK. Predictors of Mortality among Neonates with Congenital Diaphragmatic Hernia: Experience from an Inborn Unselected Cohort in India. *Indian Pediatr.* 2019 Dec 15;56(12):1037-1040. PubMed PMID: 31884435.

**OBJECTIVE:** To evaluate the clinical profile and predictors of mortality in neonates with congenital diaphragmatic hernia (CDH).

**METHODS:** Demographic and clinical parameters of neonates with congenital diaphragmatic hernia (n=37) between January 2014 and October, 2017 were reviewed, and compared among those who survived or expired in hospital.

**RESULTS:** Median (range) gestation and birthweight were 38 (37-39) weeks and 2496 (2044-2889) g, respectively. Persistent pulmonary hypertension (PPHN) was documented in 19 (51%) neonates and 10 (27%) had associated malformations. Surgery could be performed in 18 (49%), overall mortality was 60%. On univariate analysis, low Apgar scores, presence of malformations, PPHN, need for higher initial peak inspiratory pressure/high frequency ventilation, and requirement of a patch for closure were associated with increased mortality. On multivariate analysis, PPHN remained the only significant risk factor [adjusted RR 3.74 (95% CI 1.45-9.68)].

**CONCLUSIONS:** The survival of infants with CDH is low, and PPHN is an important predictor of mortality.

PMID: 31884435

155: Sain A, Sharma V, Farooque K, V M, Pattabiraman K. Dual Plating of the Distal Femur: Indications and Surgical Techniques. *Cureus.* 2019 Dec 27;11(12):e6483. doi: 10.7759/cureus.6483. Review. PubMed PMID: 31903313; PubMed Central PMCID: PMC6935741.

Dual-plating of the distal femur is required in some cases to achieve stable fixation. The indications of a medial plate in addition to the lateral plate are medial supracondylar bone loss, low trans-condylar bicondylar fractures, medial Hoffa fracture, peri-prosthetic distal femur fractures, non-union after failed fixation with single lateral plate, poor bone quality and comminuted distal femur fractures (AO type C3). We recommend orthogonal plate configuration with locked plates by a single incision or dual incision approach as per surgeon choice.

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DOI: 10.7759/cureus.6483

PMCID: PMC6935741

PMID: 31903313

156: Saluja G, Samdani A, Bhatia P. Importance of clinical tests in ocular myasthenia. *BMJ Case Rep.* 2019 Dec 8;12(12). pii: e231296. doi: 10.1136/bcr-2019-231296. PubMed PMID: 31818887.

A 24-year-old otherwise healthy male presented to us with unilateral ptosis and contralateral lid retraction with limitation of extraocular movements; the disease had a gradual chronic course, which raised a suspicion of ocular myasthenia. Ice pack test was performed, which improved the ptosis; further investigations confirmed the diagnosis of ocular myasthenia. Patient was started on pyridostigmine and oral prednisolone which improved the extraocular movements and ptosis.

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DOI: 10.1136/bcr-2019-231296  
PMID: 31818887

157: Selvan H, Gupta S, Puri P, Sen S, Gupta V. The immortal Ologen: persisting 10 years after trabeculectomy. *Can J Ophthalmol*. 2019 Dec;54(6):e305-e308. doi: 10.1016/j.jcjo.2019.03.004. Epub 2019 Apr 30. PubMed PMID: 31836122.

158: Selvan H, Pujari A. In Reply: Smartphone Disc Photography Versus Standard Stereoscopic Disc Photography as a Teaching Tool. *J Glaucoma*. 2019 Dec;28(12):e174-e175. doi: 10.1097/IJG.0000000000001384. PubMed PMID: 31633621.

159: Selvan H, Gupta V, Gupta S. Cyclodialysis: an updated approach to surgical strategies. *Acta Ophthalmol*. 2019 Dec;97(8):744-751. doi: 10.1111/aos.14210. Epub 2019 Aug 6. Review. PubMed PMID: 31386805.

Cyclodialysis is a rare occurrence and is difficult to treat, it being concealed behind the iris. In view of the varied success outcomes of the different available surgical repair techniques, there is at present no clear consensus regarding their management strategies. Through this article, we intend to appraise the established surgical methods, update the novel techniques in vogue, discuss their outcomes and propose a uniform system to codify these corrective techniques. They have been reclassified under the terms 'exocyclohexy', 'endocyclohexy', 'exocyclotamponade' and 'endocyclotamponade' based on the approach used and their mode of action. The ab-interno techniques (endocyclohexy and endocyclotamponade) are easier to perform, offer good success rates and better safety profiles such that they may be considered as a viable alternative to the standard exocyclohexy in either cataractous or pseudophakic and aphakic eyes.

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DOI: 10.1111/aos.14210  
PMID: 31386805

160: Sethi A, Priyadarshi M, Agarwal R. Mineral and bone physiology in the foetus, preterm and full-term neonates. *Semin Fetal Neonatal Med*. 2019 Dec 16:101076. doi: 10.1016/j.siny.2019.101076. [Epub ahead of print] Review. PubMed PMID: 31882392.

Mother is the major source of minerals in foetal life with placenta actively transporting against a concentration and electrochemical gradient. The foetal serum mineral concentration is thereby higher as compared to maternal values, which possibly help in its rapid accretion in developing bones and for counteracting postnatal fall in calcium levels at birth. Parathyroid hormone related peptide (PTHrP) and parathyroid hormone (PTH) play a major role in mineral physiology during foetal life with hormones like calcitriol, calcitonin, FGF-23 and sex steroids having minimal role. PTHrP and PTH also play a major role in endochondral bone formation and mineralization of skeleton. At the birth, as the cord is clamped, there is loss of active transport of minerals through placenta and the neonate has to rely on enteral intake of minerals to meet the demands of growing bones and metabolisms. The calcium levels fall after birth, reaching a nadir at 24-48 h and gradually rise to adult values over several days, probably resulting from a fall in PTHrP levels and hyporesponsiveness of

parathyroid glands. As PTH and calcitriol levels increase postnatally, there is a rise in calcium levels with maturation in functioning of kidneys and intestines. However, there may be significant delay in intestinal maturation in preterm infants along with an increased demand for mineral accretion, which predispose them to osteopenia of prematurity.

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PMID: 31882392

161: Shakya S, Kumari R, Suroliya V, Tyagi N, Joshi A, Garg A, Singh I, Kalikavil Puthanveedu D, Cherian A, Mukerji M, Srivastava AK, Faruq M. Whole exome and targeted gene sequencing to detect pathogenic recessive variants in early onset cerebellar ataxia. *Clin Genet*. 2019 Dec;96(6):566-574. doi: 10.1111/cge.13625. Epub 2019 Sep 1. PubMed PMID: 31429931.

Over 100 genetically distinct causal known loci for hereditary ataxia phenotype poses a challenge for diagnostic work-up for ataxia patients in a clinically relevant time and precision. In the present study using next-generation sequencing, we have investigated pathogenic variants in early-onset cerebellar ataxia cases using whole exome sequencing in singleton/family-designed and targeted gene-panel sequencing. A total of 98 index patients were clinically and genetically (whole exome sequencing (WES) in 16 patients and targeted gene panel of 41 ataxia causing genes in 82 patients) evaluated. Four families underwent WES in family based design. Overall, we have identified 24 variants comprising 20 pathogenic and four likely-pathogenic both rare/novel, variations in 21 early onset cerebellar ataxia patients. Among the identified variations, SACS (n = 7) and SETX (n = 6) were frequent, while ATM (n = 2), TTPA (n = 2) and other rare loci were observed. We have prioritized novel pathogenic variants in RARS2 and FA2H loci through family based design in two out of four families.

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DOI: 10.1111/cge.13625

PMID: 31429931

162: Shankar SH, Kumar P, Madhusudan KS. Arterial and venous thrombosis with right ventricular thrombus in Crohn's disease. *Turk J Gastroenterol*. 2019 Dec;30(12):1070-1071. doi: 10.5152/tjg.2019.19323. PubMed PMID: 31854315; PubMed Central PMCID: PMC6924601.

163: Sharma A, Sinha M, Pandey NN, Chandrashekhara SH. Stem cell therapy in critical limb ischemia: Current scenario and future trends. *Indian J Radiol Imaging*. 2019 Oct-Dec;29(4):397-403. doi: 10.4103/ijri.IJRI\_385\_19. Epub 2019 Dec 31. PubMed PMID: 31949342; PubMed Central PMCID: PMC6958876.

Critical limb ischemia (CLI) represents the most severe manifestation of peripheral arterial disease (PAD). It imposes a huge economic burden and is associated with high short-term mortality and adverse cardiovascular outcomes. Prompt recognition and early revascularization, surgical or endovascular, with the aim of improving the inline bloodflow to the ischemic limb, are currently the standard of care. However, this strategy may not always be feasible or effective; hence, evaluation of newer pharmacological or angiogenic therapies for alleviating the symptoms of this alarming condition is of utmost importance. Cell-based therapies have shown promise in smaller studies; however, large-scale studies, demonstrating definite survival benefits, are entailed to ascertain

their role in the management of CLI.

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DOI: 10.4103/ijri.IJRI\_385\_19

PMCID: PMC6958876

PMID: 31949342

164: Sharma A, Tyagi S, Gautam SK, Abid M, Kanga U. HLA-A\*33:03:01:06 allele identified in an individual from the Kashmiri Brahmin population of North India. *HLA*. 2019 Dec;94(6):524-526. doi: 10.1111/tan.13703. Epub 2019 Oct 7. PubMed PMID: 31576660.

165: Sharma A, Kaushik P, Singh TP, Patel C. Focal pulmonary uptake on myocardial perfusion scintigraphy due to iatrogenic microembolism. *J Nucl Cardiol*. 2019 Dec;26(6):2133-2135. doi: 10.1007/s12350-018-01553-3. Epub 2018 Dec 4. PubMed PMID: 30515746.

166: Sharma A, Pandey NN, Kumar S. Pacemaker site pseudoaneurysm from superior thoracic artery: an uncommon offender. *Acta Cardiol*. 2019 Dec;74(6):538-539. doi: 10.1080/00015385.2018.1530403. Epub 2018 Dec 4. PubMed PMID: 30513255.

167: Sharma P, Sagar R, Deep R, Mehta M, Subbiah V. Assessment for familial pattern and association of polymorphisms in KIAA0319 gene with specific reading disorder in children from North India visiting a tertiary care centre: A case-control study. *Dyslexia*. 2019 Dec 8. doi: 10.1002/dys.1642. [Epub ahead of print] PubMed PMID: 31814229.

Genetic association studies have identified KIAA0319 gene as a possible susceptibility locus for reading disorder; however, very few studies are available from India. The study was planned to investigate the familial pattern and association of KIAA0319 polymorphisms among children with reading disorder visiting a tertiary centre in North India. This is a case-control, familial, and genetic association study on 30 children diagnosed with reading disorder (ICD-10) and 30 matched healthy controls and their families. The Aggregate Neurobehavioral Student Health and Educational Review System was administered on parents of probands and controls for reading problems in their siblings, and Adult Reading Questionnaire was administered for parents of both groups. The blood sample was taken from probands, and DNA was isolated. Four KIAA0319 coding sequence single nucleotide polymorphisms (SNPs; rs4504469, rs6935076, rs2038137, and rs2179515) were genotyped using SNaPshot single nucleotide extension. The incidence of reading problem was significantly higher in families of probands as compared with families of controls. There were no significant differences in both groups regarding the frequency of alleles of four SNPs. The reading disorder showed a significant familial pattern, but KIAA0319 gene did not appear to be a susceptibility factor. Future replications with larger samples and whole genome studies are warranted.

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DOI: 10.1002/dys.1642

PMID: 31814229

168: Sharma R. Use of Smartphone Applications in Children with Type 1 Diabetes Mellitus. *Indian J Pediatr*. 2019 Dec;86(12):1087-1088. doi:

10.1007/s12098-019-03108-x. Epub 2019 Nov 11. PubMed PMID: 31713208.

169: Sharma S, Anwar MF, Dinda A, Singhal M, Malik A. In Vitro and in Vivo Studies of pH-Sensitive GHK-Cu-Incorporated Polyaspartic and Polyacrylic Acid Superabsorbent Polymer. ACS Omega. 2019 Nov 19;4(23):20118-20128. doi: 10.1021/acsomega.9b00655. eCollection 2019 Dec 3. PubMed PMID: 31815212; PubMed Central PMCID: PMC6893953.

The main aim of this study was to evaluate the in vitro and in vivo efficiency of the polyaspartic acid- and acrylic acid-based superabsorbent polymer. The synthesized polymer was first investigated to check the blood compatibility by protein adsorption and blood clotting tests. Further, the GHK-Cu peptide was incorporated within the polymer and release studies were performed to evaluate the drug-delivery efficiency of the superabsorbent polymer. The polymer with best peptide release results were further used for in vivo analysis for wound healing. The healing efficiency of polymer with and without peptide was analyzed using wound closure, biochemical assay, histopathological, and toxicity studies.

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DOI: 10.1021/acsomega.9b00655

PMCID: PMC6893953

PMID: 31815212

170: Shewade HD, Gupta V, Ghule VH, Nayak S, Satyanarayana S, Dayal R, Mohanty S, Singh S, Biswas M, Reddy KK, Mallick G, Bera OP, Pandey P, Pandurangan S, Rao R, Prasad BM, Kumar AMV, Chadha SS. Impact of Advocacy, Communication, Social Mobilization and Active Case Finding on TB Notification in Jharkhand, India. J Epidemiol Glob Health. 2019 Dec;9(4):233-242. doi: 10.2991/jegh.k.190812.002. PubMed PMID: 31854164.

Community-level benefits of screening for active tuberculosis (TB) disease remain uncertain. Project Axshya (meaning free of TB) conducted advocacy, communication, social mobilization, and active case finding among vulnerable/marginalized populations of India. Among 15 districts of Jharkhand state, the project was initiated in 36 subdistrict level administrative units - tuberculosis units (TUs) in a staggered manner between April 2013 and September 2014, and continued till the end of 2015. Seven TUs did not implement the project. We assessed the relative change in the quarterly TB case finding indicators ( $n = 4$ ) after inclusion of a TU within the project. By fitting four multilevel models (mixed-effects maximum likelihood regression using random intercept), we adjusted for secular (over previous five quarters) and seasonal trends, baseline differences within Axshya and non-Axshya TUs, and population size and clustering within districts and within TUs. After inclusion of a TU within the project, we found a significant increase [95% confidence interval (CI)] in TU-level presumptive TB sputum examination rate, new sputum-positive TB Case Notification Rate (CNR), sputum-positive TB CNR, and all forms TB CNR by 12 (5.5, 18.5), 1.1 (0.5, 1.7), 1.3 (0.6, 2.0), and 1.2 (0.1, 2.2) per 100,000 population per quarter, respectively. Overall, the project resulted in an increase (95% CI) in sputum examination and detection of new sputum-positive TB, sputum-positive TB and all forms of TB patients by 22,410 (10,203, 34,077), 2066 (923, 3210), 2380 (1162, 3616), and 2122 (203, 4059), respectively. This provides evidence for implementing project Axshya over and above the existing passive case finding.

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DOI: 10.2991/jegh.k.190812.002

PMID: 31854164

171: Sihota R, Sen S, Mohanty S, Ahmad M, Ravi A, Gupta V, Bhatla N. Effect of intracameral human cord blood-derived stem cells on lasered rabbit trabecular meshwork. *Int Ophthalmol*. 2019 Dec;39(12):2757-2766. doi: 10.1007/s10792-019-01120-w. Epub 2019 May 28. PubMed PMID: 31140023.

**BACKGROUND:** This study aimed to investigate the effect of intracameral human cord blood stem cells on lasered rabbit trabecular meshwork.

**METHODS:** Immediately following diode laser application to the trabecular meshwork, human cord blood stem cells were injected intracamerally, in one eye of 12 albino rabbits. The other eye of ten rabbits was lasered controls and two eyes were normal controls. Rabbits were killed after 4, 8 and 12 weeks.

**RESULTS:** Lasered control rabbit eyes showed significant disruption of trabecular architecture, loss and pleomorphism of trabecular endothelial cells and progressive narrowing of trabecular spaces till 12 weeks. In contrast, lasered eyes, concurrently injected with human cord blood stem cells, showed relatively preserved endothelial cellularity and structure of the trabecular meshwork, at all time points. Human CD34- and CD44-positive cells were identified in 7/8 eyes treated with stem cells, at 4 and 8 weeks, and 2 of 3 at 12 weeks. Many PKH26-labeled human cord blood cells were visible throughout the trabecular area at 4 weeks. They gradually decreased in number by 8 weeks, and at 12 weeks, they appeared to be oriented along trabecular beams.

**CONCLUSIONS:** There was a relative preservation of cellularity and architecture of the trabecular meshwork in eyes injected with human cord blood stem cells, as compared to lasered control eyes up to 12 weeks, without significant inflammation. This suggests a probable role for such stem cells in eyes with glaucoma, having trabecular dysfunction.

DOI: 10.1007/s10792-019-01120-w

PMID: 31140023

172: Sindhu D, Jorwal P, Gupta N, Xess I, Singh G, Soneja M, Nischal N, Sethi P, Ray A, Biswas A, Wig N. Clinical spectrum and outcome of hospitalized patients with invasive fungal infections: a prospective study from a medical ward/intensive care unit of a teaching hospital in North India. *Infez Med*. 2019 Dec 1;27(4):398-402. PubMed PMID: 31846989.

The aim of the study was to determine the clinical spectrum and outcome of invasive fungal infections (IFIs) in hospitalized patients. A prospective study was conducted in a teaching hospital in North India between December 2016 and December 2018. Patients diagnosed with IFIs were enrolled. Their clinical and laboratory parameters were recorded using a pre-defined clinical report form. They were followed up till discharge or death and a 60-day outcome was recorded. A total of 110 IFI cases were identified, which included invasive aspergillosis (39%), invasive candidiasis (16%), cryptococcosis (14%) and mucormycosis (12%). Pneumonia (63%) was the most common final diagnosis in these patients. Diabetes mellitus, chronic kidney disease and chronic obstructive pulmonary disease were the most common risk factor for all four diseases. Additionally, most patients with cryptococcosis had human immunodeficiency virus infection. Mortality was observed in 73% of the patients. Overall, IFIs are an important cause of morbidity and mortality in critically ill patients admitted to medical wards and ICUs.

173: Singh A, Kumar R, Sagar P. Herald Cell: The Gateway to Posterior Tympanotomy-A Cadaveric Study. *Indian J Otolaryngol Head Neck Surg*. 2019 Dec;71(4):517-519. doi: 10.1007/s12070-019-01692-0. Epub 2019 Jun 26. PubMed PMID: 31750113; PubMed Central PMCID: PMC6838255.

Posterior tympanotomy is the avenue to the facial recess of the middle ear from mastoid antrum. The entry into the facial recess in many cases is heralded by a distinct air cell before approaching the facial-chordal plane. The current study was undertaken to determine the prevalence of this 'Herald Cell' in an adult cadaveric population. It was a human cadaveric temporal bone dissection study. The bones were dissected to carry out cortical mastoidectomy and posterior tympanotomy using standard otologic drills under microscopic visualization (Leica M320 F12). Appropriate snapshots were taken to document the presence or absence of Herald cell. A total of 51 temporal bones were dissected (26 right, 25 left sided). The Herald cell was found to be present in 22 bones (43.1%). Herald cell, when present, is a convenient and reliable landmark to carry out a safe posterior tympanotomy.

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PMCID: PMC6838255 [Available on 2020-12-01]

PMID: 31750113

174: Singh A, Gupta N, Ganger A, Singh D, Kashyap S, Tandon R. Sutureless Customized Lamellar Corneal Transplant in a Patient with Gelatinous Drop-Like Corneal Dystrophy. *Exp Clin Transplant*. 2019 Dec;17(6):844-848. doi: 10.6002/ect.2019.0043. Epub 2019 Jul 19. PubMed PMID: 31324138.

Patients with gelatinous drop-like corneal dystrophy need to be effectively managed as the disease is severely debilitating in view of associated pho-topobia and glare. Here, we report a rare case of gelatinous drop-like corneal dystrophy effectively managed by intraoperative anterior segment optical coherence tomography-guided manual deep anterior lamellar keratoplasty in 1 eye and sutureless fibrin glue-aided, microkeratome-assisted automated lamellar therapeutic keratoplasty in the other eye. The patient, a 22-year old man, presented with gradual diminution of vision associated with foreign body sensation, glare, photophobia, and watering due to corneal lesions, which were consistent with a diagnosis of gelatinous drop-like corneal dystrophy. Visual acuity at pre-presentation was 4/60 and 3/60 in the right and left eye, respectively. The patient received customized component lamellar keratoplasty in both eyes, and host tissue was sent for histopathologic examination. Treatment resulted in a best-corrected distance visual acuity of 6/9 and 6/12 in the right and left eye, respectively. The graft was clear and well apposed, with minimal interface haze bilaterally. The histopathologic report suggested intralamellar amyloid deposition in the form of homogenous, acellular eosinophilic deposits in the epithelium and anterior corneal stroma. This is a first report of the exclusive use of a fibrin-protinin tissue adhesive to stabilize a donor corneal lamellar graft as a treatment modality for a patient with gelatinous drop-like corneal dystrophy, suggesting that this treatment could supplant the need for sutures.

DOI: 10.6002/ect.2019.0043

PMID: 31324138

175: Singh AD, Mian A. Letter to the Editor: Some TIPS for future decompensations! *Hepatology*. 2019 Dec 16. doi: 10.1002/hep.31066. [Epub ahead of print] PubMed PMID: 31841218.

In the September 12th , 2019 issue of *Hepatology*, Billey et al published a study assessing laboratory, echocardiographic and right heart catheter based parameters to predict cardiac decompensation in patients undergoing Trans jugular

intrahepatic Porto systemic shunts (TIPS) procedure (1). A total of 100 patients who were evaluated with serum NT-proBNP levels and echocardiography were included.

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DOI: 10.1002/hep.31066

PMID: 31841218

176: Singh BP, Khan WF, Rathore YS, Pol MM. Incidental Carcinoma Gallbladder: Incidence, Risk Factors, and Factors Affecting Survival-5-Year Experience from a Tertiary Care Institute. *J Gastrointest Cancer*. 2019 Dec 5. doi: 10.1007/s12029-019-00347-1. [Epub ahead of print] PubMed PMID: 31808057.

**INTRODUCTION:** Carcinoma gallbladder is a very lethal disease. It can get detected incidentally after laparoscopic cholecystectomy. The overall outcome of incidentally detected carcinoma gallbladder is a matter of debate in literature. **AIM:** To estimate the overall incidence of the incidental gallbladder carcinoma, the various risk factors associated with it and factors affecting overall survival in patients who underwent laparoscopic cholecystectomy with eventual histology turning out to be carcinoma gallbladder.

**METHODS:** Data of all the patients undergoing laparoscopic cholecystectomies in one surgical unit under the Department of Surgery at All India Institute of Medical Sciences, New Delhi, India, between January 2014 and December 2018 was retrospectively analyzed. All patients with incidental carcinoma gallbladder were followed up and completion radical cholecystectomy was performed. The demographic profile, preoperative imaging, intra-operative finding, histopathology of primary surgery, and median interval between two surgeries were analyzed to look for various risk factors associated with incidental carcinoma gallbladder and factors affecting overall survival.

**RESULTS:** Incidence of the incidental carcinoma gallbladder was 0.51% with a female/male ratio of 4:1 and mean age of 47.2 years. Preoperative imaging of most of them was suggestive of chronic cholecystitis; however, one patient had multiple gallbladder polyps. Six patients had uneventful laparoscopic cholecystectomy, while four had bile spillages intraoperatively. All the patients had adenocarcinoma on histopathology. Pathological staging of four patients was pT1b and six patients had pT2 tumor. The median interval between cholecystectomy and completion radical cholecystectomy in this series was 8 weeks. At the end of 19-month median follow-up, overall survival was 55.5%.

**CONCLUSION:** Incidence of incidental carcinoma gallbladder is 0.51%, most commonly affecting middle-aged females. Risk factors associated with incidental carcinoma gallbladder were found to be multiple gallbladder calculi, single large stone, and gallbladder polyps. Survival is better in males, young patients with uneventful primary surgery and better-differentiated pathology.

DOI: 10.1007/s12029-019-00347-1

PMID: 31808057

177: Singh M, Sankar J, Kumar A, Kumar UV, Lodha R, Kabra SK. Predictors of Mortality in Children Admitted to the Pediatric Intensive Care Unit with Acute Gastroenteritis with Severe Dehydration. *Indian J Pediatr*. 2019 Dec;86(12):1142-1145. doi: 10.1007/s12098-019-03094-0. Epub 2019 Nov 7. PubMed PMID: 31701427.

The objective of the present study was to identify risk factors for mortality at admission in children admitted to the Pediatric Intensive Care Unit (PICU) with acute gastroenteritis (AGE) with severe dehydration and shock. This was a retrospective chart review of all cases of AGE with severe dehydration and shock

admitted to the PICU from 2012 to 2017. Children who died during hospital stay were compared with those who survived. A total of 62 children were admitted with AGE to the PICU during this period. Twenty-four children (39%) died. The following variables were found to be significantly associated with death on univariate analysis: clinical pallor ( $p=0.01$ ), thrombocytopenia ( $p=0.018$ ), elevated leucocyte count ( $p=0.02$ ), hypoalbuminemia ( $p=0.02$ ) and severe acute malnutrition (SAM) ( $p=0.04$ ). On multivariate analysis, only hypoalbuminemia {RR [95% CI: 2.6 (1.27 to 9.21)]; 0.039} and SAM {RR [95% CI: 4.9 (1.12 to 10)]; 0.045} remained statistically significant. Children admitted with severe dehydration and shock had high mortality rates. These children were a sicker subset with probable sepsis. Severe acute malnutrition and hypoalbuminemia were associated with increased risk of death in these patients.

DOI: 10.1007/s12098-019-03094-0

PMID: 31701427

178: Singh MK, Singh L, Chosdol K, Pushker N, Saini N, Meel R, Bakhshi S, Sen S, Kashyap S. Differential expression of p52 and RelB proteins in the metastatic and non-metastatic groups of uveal melanoma with patient outcome. *J Cancer Res Clin Oncol*. 2019 Dec;145(12):2969-2982. doi: 10.1007/s00432-019-03052-5. Epub 2019 Oct 14. PubMed PMID: 31612319.

**PURPOSE:** Non-canonical NF $\kappa$ B (NC-NF $\kappa$ B) pathway plays an influential role in metastasis, which promotes cancer proliferation and progression. The aim of the study was to examine the expression of NC-NF $\kappa$ B proteins and their correlation with clinicopathological factors associated with metastatic cases of uveal melanoma (UM) and with the patient outcome.

**METHOD:** Expression of NC-NF $\kappa$ B proteins (p52, RelB, and co-expression of p52/RelB) was evaluated in 75 formalin-fixed cases of uveal melanoma by immunohistochemistry. Validation of nuclear immunoreactivity was done by western blotting. Transcriptional status of NC-NF $\kappa$ B genes was assessed in 60 fresh tumor tissues by quantitative real-time PCR. Co-immunoprecipitation was performed to determine the presence of native p52/RelB heterodimer in UM. Prognostic relevance was determined using Cox proportional hazard and Kaplan-Meier methods.

**RESULTS:** Immunohistochemical expression of p52, RelB, and their co-expression was observed in 81%, 68.7%, 56.2% of metastatic cases, respectively, while their expression was seen only in 38%, 33% and 30% of non-metastatic cases. Loss of BAP-1 was correlated with expression of p52 and RelB proteins.

Co-immunoprecipitation assay confirmed the putative interaction of p52 with RelB protein in metastatic cases of uveal melanoma. Co-expression of p52/RelB and expression of p52 protein was significantly correlated with decreased metastasis-free survival (MFS) ( $p=0.004$ ;  $p=0.002$ ) and overall survival (OS) ( $p=0.004$ ;  $p=0.032$ ), while the RelB expression only correlated with reduced MFS ( $p=0.003$ ).

**CONCLUSION:** Our data showed that non-canonical NF $\kappa$ B proteins were significantly higher in metastatic cases and associated with poor outcome of the patients. Furthermore, the p52 protein could be used as a potential therapeutic biomarker for metastatic cases in uveal melanoma.

DOI: 10.1007/s00432-019-03052-5

PMID: 31612319 [Indexed for MEDLINE]

179: Singh MK, Singh L, Chosdol K, Pushker N, Meel R, Bakhshi S, Sen S, Kashyap S. Clinicopathological relevance of NF $\kappa$ B1/p50 nuclear immunoreactivity and its relationship with the inflammatory environment of uveal melanoma. *Exp Mol Pathol*. 2019 Dec;111:104313. doi: 10.1016/j.yexmp.2019.104313. Epub 2019 Sep 15. PubMed PMID: 31533021.

**PURPOSE:** To analyze the activation of NFκB1/p50 in the inflammatory and non-inflammatory environment of uveal melanoma and its association with clinicopathological factors and patient outcome.

**METHODS:** Activation of NFκB1/p50 was evaluated in 75 cases of uveal melanoma by immunohistochemistry. mRNA expression in 58 fresh UM specimen was measured by quantitative reverse-transcriptase PCR (qRT-PCR). Western blotting was performed to validate the immunohistochemistry results in representative cases.

**RESULTS:** Forty-five cases showed both cytoplasmic and nuclear immunoreactivity of NFκB1/p50. Increased level of NFκB1/p50 activation was more frequent in the inflammatory environment group as compared to non-inflammatory environment group at both transcriptional and translational level. In multivariate analysis, infiltrating macrophages and nuclear immunoreactivity of NFκB1/p50 ( $p < .05$ ) in tumor cells were found to be an independent prognostic factor for poor survival.

**CONCLUSION:** Our results suggest that nuclear immunoreactivity NFκB1/p50 may serve as a useful marker in assessing the prognosis of uveal melanoma patients.

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DOI: 10.1016/j.yexmp.2019.104313

PMID: 31533021

180: Singh PK, Yadav VK, Kalia M, Sharma D, Pandey D, Agarwal V. *Pseudomonas aeruginosa* quorum-sensing molecule N-(3-oxo-dodecanoyl)-L-homoserine lactone triggers mitochondrial dysfunction and apoptosis in neutrophils through calcium signaling. *Med Microbiol Immunol*. 2019 Dec;208(6):855-868. doi: 10.1007/s00430-019-00631-8. Epub 2019 Aug 3. PubMed PMID: 31377870.

*Pseudomonas aeruginosa* is an opportunistic pathogen that utilizes the quorum-sensing (QS) process to regulate the production of different virulence factors and biofilm. N-3-oxo-dodecanoyl-L-homoserine lactone (C12) is a key QS molecule of *P. aeruginosa* which interacts with the mammalian immune cells and modulates their function. Here, we investigated the molecular mechanism of C12-induced apoptosis in neutrophils. Our data show that C12 causes apoptosis in neutrophils through an elevation in cytosolic and mitochondrial Ca<sup>2+</sup> levels. Besides, C12 induces phosphatidylserine (PS) exposure, mitochondrial membrane potential (MMP) depolarization, mitochondrial permeability transition pore (MPTP) formation and mitochondrial reactive oxygen species (mROS) generation. C12-induced rise in intracellular Ca<sup>2+</sup> level is majorly contributed by endoplasmic reticulum store through the activation of inositol 1, 4, 5-triphosphate receptor. Intracellular calcium chelation inhibited C12-induced mitochondrial dysfunction and apoptosis. Further, inhibition of mitochondrial Ca<sup>2+</sup> uniporter by ruthenium red or Ru360 abrogated C12-induced mitochondrial Ca<sup>2+</sup> uptake, MMP loss, MPTP opening, mROS production, and PS exposure. These mechanistic insights are expected to provide a better understanding of the role of C12 in *P. aeruginosa* pathogenesis.

DOI: 10.1007/s00430-019-00631-8

PMID: 31377870

181: Singh S, Dahiya N, Singh AB, Kumar R, Balhara YPS. Gaming disorder among medical college students from India: Exploring the pattern and correlates. *Ind Psychiatry J*. 2019 Jan-Jun;28(1):107-114. doi: 10.4103/ipj.ipj\_96\_18. Epub 2019 Dec 11. PubMed PMID: 31879456; PubMed Central PMCID: PMC6929222.

**Background:** In the extant literature, apart from few published case reports describing patients with severe form of gaming disorder (GD), there is a lack of studies describing the pattern and correlates of GD existing in the Indian

settings. Thus, the present study aimed to explore the extent and pattern of gaming behavior in a sample of medical college students from India and explore its association with the sociodemographic, psychological (depressive symptoms), and Internet gaming characteristics.

**Materials and Methods:** This Internet-based cross-sectional study was conducted as an online survey among 306 medical students by the Behavioral Addictions Clinic at a tertiary care teaching college in India. The severity of problematic gaming behavior and depressive symptoms was assessed using the Internet GD Scale-Short Form (IGDS9-SF) and Patient Health Questionnaire-9 (PHQ-9). A semi-structured questionnaire was used to collect information regarding sociodemographic and Internet gaming characteristics of the participants. Statistical analysis was done using SPSS software version 21.0, with two-tailed  $P < 0.05$  taken as significant and  $P < 0.01$  as highly significant results.

**Results:** We identified 173 (55.6%) current gamers, with 11 (3.6%) Internet GD gamers based on the Diagnostic and Statistical Manual of Mental Disorders -5 criteria in the current study sample. A preference for multiplayer online gaming pattern ( $\beta = 0.17$ ,  $P = 0.005$ ), spending greater amount of time in playing digital games ( $\beta = 0.53$ ,  $P < 0.01$ ), and higher PHQ-9 scores ( $\beta = 0.25$ ,  $P < 0.01^{**}$ ) representing greater depressive symptom severity were associated with statistically significantly greater scores on the IGDS9-SF, indicative of a higher risk for having GD.

**Conclusions:** GD is a cause of concern among medical students in India. There is an urgent need to create awareness about it among students and concerned authorities. Further, there is a need to develop effective screening and treatment strategies suited for our population. The risk factors identified in the current study can be utilized to screen those at high risk of developing the same.

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DOI: 10.4103/ipj.ipj\_96\_18

PMCID: PMC6929222

PMID: 31879456

182: Singh S, Kumar S, Mahal P, Vishwakarma A, Deep R. Self-reported medication adherence and its correlates in a lithium-maintained cohort with bipolar disorder at a tertiary care centre in India. *Asian J Psychiatr.* 2019 Dec;46:34-40. doi: 10.1016/j.ajp.2019.09.015. Epub 2019 Sep 23. PubMed PMID: 31590007.

**BACKGROUND:** Lithium remains a cornerstone of prophylaxis in bipolar disorder (BD), but adherence continues to be a major clinical challenge and merits a closer attention. There is scant literature available in Indian as well as Asian context.

**METHODS:** This study was conducted at Department of Psychiatry, AIIMS, New Delhi with an aim to assess the self-reported medication adherence and its correlates among a naturalistic, lithium-maintained cohort ( $n=76$ ) with bipolar disorder. Subjects were included if they were on lithium therapy  $\geq 1$  year, met DSM-5 diagnosis of bipolar disorder and were in clinical remission ( $\geq 1$  month). Besides sociodemographic and clinical performance, participants were assessed on medication adherence rating scale (MARS), lithium questionnaire for knowledge and lithium attitude questionnaire (LAQ).

**RESULTS:** Mean age was  $35.7 \pm 10.6$  years (males: 59.2%); median duration of illness and lithium therapy was 84 months and 24.5 months, respectively. Mean MARS score was  $6.95 \pm 2.81$ . Regression analysis (with MARS total as dependent variable) found LAQ score to be the single most significant predictor variable ( $\beta = -0.681$ ,  $p < 0.0001$ ), explaining over 75% of the total variance. In regression model with MARS factor-1 score as dependent variable, the 'LAQ score' ( $\beta = -0.601$ ,

$p < 0.0001$ ) and 'being accompanied by family during psychiatric visits (always/mostly) in the past year' ( $\beta = 0.193$ ,  $p = 0.010$ ) emerged as significant predictor variables.

CONCLUSION: Adherence in lithium-maintained treatment-seeking cohort of patients with BD remains far from ideal as observed in this naturalistic setting. Lithium-related attitudes and being accompanied by family during psychiatric visits were found to be significant predictors for adherence.

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DOI: 10.1016/j.ajp.2019.09.015

PMID: 31590007

183: Singh VK, Yadav D, Garg PK. Diagnosis and Management of Chronic Pancreatitis: A Review. JAMA. 2019 Dec 24;322(24):2422-2434. doi: 10.1001/jama.2019.19411. Review. PubMed PMID: 31860051.

Importance: Chronic pancreatitis (CP) is a chronic inflammatory and fibrotic disease of the pancreas with a prevalence of 42 to 73 per 100 000 adults in the United States.

Observations: Both genetic and environmental factors are thought to contribute to the pathogenesis of CP. Environmental factors associated with CP include alcohol abuse (odds ratio [OR], 3.1; 95% CI, 1.87-5.14) for 5 or more drinks per day vs abstainers and light drinkers as well as smoking (OR, 4.59; 95% CI, 2.91-7.25) for more than 35 pack-years in a case-control study involving 971 participants. Between 28% to 80% of patients are classified as having "idiopathic CP." Up to 50% of these individuals have mutations of the trypsin inhibitor gene (SPINK1) or the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

Approximately 1% of people diagnosed with CP may have hereditary pancreatitis, associated with cationic trypsinogen (PRSS1) gene mutations. Approximately 80% of people with CP present with recurrent or chronic upper abdominal pain. Long-term sequelae include diabetes in 38% to 40% and exocrine insufficiency in 30% to 48%. The diagnosis is based on pancreatic calcifications, ductal dilatation, and atrophy visualized by imaging with computed tomography, magnetic resonance imaging, or both. Endoscopic ultrasound can assist in making the diagnosis in patients with a high index of suspicion such as recurrent episodes of acute pancreatitis when imaging is normal or equivocal. The first line of therapy consists of advice to discontinue use of alcohol and smoking and taking analgesic agents (nonsteroidal anti-inflammatory drugs and weak opioids such as tramadol). A trial of pancreatic enzymes and antioxidants (a combination of multivitamins, selenium, and methionine) can control symptoms in up to 50% of patients. Patients with pancreatic ductal obstruction due to stones, stricture, or both may benefit from ductal drainage via endoscopic retrograde cholangiopancreatography (ERCP) or surgical drainage procedures, such as pancreaticojejunostomy with or without pancreatic head resection, which may provide better pain relief among people who do not respond to endoscopic therapy.

Conclusions and Relevance: Chronic pancreatitis often results in chronic abdominal pain and is most commonly caused by excessive alcohol use, smoking, or genetic mutations. Treatment consists primarily of alcohol and smoking cessation, pain control, replacement of pancreatic insufficiency, or mechanical drainage of obstructed pancreatic ducts for some patients.

DOI: 10.1001/jama.2019.19411

PMID: 31860051 [Indexed for MEDLINE]

184: Singh VV, Gupta S, Sarkar S, Chatterjee B. Problematic dicyclomine use: A case report and narrative review. Asian J Psychiatr. 2019 Dec 6;48:101891. doi:

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186: Sinha M, Chandrashekhara SH, Sharma A. Aortopulmonary window with unreported interesting pulmonary artery intersection. *Asian Cardiovasc Thorac Ann*. 2020 Jan;28(1):71-72. doi: 10.1177/0218492319895105. Epub 2019 Dec 10. PubMed PMID: 31821764.

187: Sneha A, Pawan T, Randeep G, Anant M, Mani K, Hadda V, Madan K. Acute Phase Proteins as Predictors of Survival in Patients With Acute Exacerbation of Chronic Obstructive Pulmonary Disease Requiring Mechanical Ventilation. *COPD*. 2019 Dec 10:1-7. doi: 10.1080/15412555.2019.1698019. [Epub ahead of print] PubMed PMID: 31820666.

Few studies have tried to assess prognostic variables in chronic obstructive pulmonary disease (COPD) patients requiring mechanical ventilation (MV). We evaluated serum C reactive protein, (CRP) pre-albumin (PA) and transferrin (TR) levels in AE-COPD patients requiring MV as prognostic markers of in hospital mortality. 93 AE-COPD patients on MV were evaluated. Detailed clinical evaluation was done daily. Serum CRP & PA were measured on admission, 3rd, 8th and 16th day; TR was measured on admission, 8th and 16th day. Demographics, baseline parameters, CRP, PA and TR were correlated with mortality. Of 93 patients, 49 (52.69%) survived whereas 44 patients (47.31%) died. APACHE II, serum urea & albumin were similar in survivors & non-survivors. Baseline CRP ( $\geq 10.5$ mg/dl) had sensitivity of 60.5%, specificity of 60.2%, with area under curve (AUC) of 0.62 as predictor of mortality. CRP ( $\geq 7$ mg/dl) on day 3 had sensitivity (65.5%) and specificity (63.3%) with AUC 0.70 as predictor of mortality. Baseline serum prealbumin was 11.00 (0.09-29.26) mg/dl, and similar in survivors & non-survivors ( $p=0.7$ ). Prealbumin at day 8 ( $n=50$ )  $< 13.5$ mg/dl had sensitivity 54.6%, and specificity 51.4% with AUC 0.54 (95% CI 0.34-0.75) as predictor of mortality. Transferrin at day 8 ( $n=50$ ) of  $< 148.9$  had sensitivity 63.4% and specificity 61.4% with AUC 0.61 with respect to mortality. High CRP levels at baseline, persistently elevated CRP (on day 3) may predict mortality in AE-COPD patients requiring MV. Further studies are required to establish prognostic variables in this patient population.

DOI: 10.1080/15412555.2019.1698019

PMID: 31820666

188: Solanki SL, Mukherjee S, Agarwal V, Thota RS, Balakrishnan K, Shah SB, Desai N, Garg R, Ambulkar RP, Bhorkar NM, Patro V, Sinukumar S, Venketeswaran MV, Joshi MP, Chikkalingegowda RH, Gottumukkala V, Owusu-Agyemang P, Saklani AP, Mehta SS, Seshadri RA, Bell JC, Bhatnagar S, Divatia JV. Society of Onco-Anaesthesia and Perioperative Care consensus guidelines for perioperative management of patients for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC). *Indian J Anaesth*. 2019 Dec;63(12):972-987. doi: 10.4103/ija.IJA\_765\_19. Epub 2019 Dec 11. PubMed PMID: 31879421; PubMed Central PMCID: PMC6921319.

Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC)

for primary peritoneal malignancies or peritoneal spread of malignant neoplasm is being done at many centres worldwide. Perioperative management is challenging with varied haemodynamic and temperature instabilities, and the literature is scarce in many aspects of its perioperative management. There is a need to have coalition of the existing evidence and experts' consensus opinion for better perioperative management. The purpose of this consensus practice guideline is to provide consensus for best practice pattern based on the best available evidence by the expert committee of the Society of Onco-Anaesthesia and Perioperative Care comprising perioperative physicians for better perioperative management of patients of CRS-HIPEC.

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PMCID: PMC6921319

PMID: 31879421

189: Soni D, Takkar B, Pillay G, Rathi A. Novel optical coherence tomography findings in idiopathic choroidal folds. *Clin Exp Optom*. 2019 Dec 5. doi: 10.1111/cxo.13023. [Epub ahead of print] PubMed PMID: 31805603.

190: Sonwani NS, Ateriya N, Kumar A. Dying from haemorrhagic cardiac tamponade - a case series. *Med Leg J*. 2019 Dec;87(4):210-214. doi: 10.1177/0025817219867268. Epub 2019 Oct 4. PubMed PMID: 31584847.

Cardiac tamponade is a condition produced by the rapid accumulation of pericardial fluid, which restricts the filling of the heart. Often the forensic pathologist comes across different naturally occurring sudden deaths. Cardiovascular causes are the most common. Death due to cardiac tamponade can cause sudden cardiac death. Acute cardiac tamponade is almost invariably fatal, unless the pressure is relieved by removing the pericardial fluid, either by needle pericardiocentesis or surgical procedures. Cardiac tamponade is more commonly associated with cases of trauma, operative procedures, secondary to myocardial infarction or intra pericardial rupture of great vessels. Previous literature showed an association of cardiac tamponade with many other pathological conditions such as malignancy, central venous catheterisation, open heart surgery, dissecting aneurysm of the aorta, myocardial abscess, infective endocarditis, etc. We report a series of three cases where cardiac tamponade was given as the cause of death on autopsy secondary to post-myocardial infarction wall rupture.

DOI: 10.1177/0025817219867268

PMID: 31584847

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192: Suhail A, Rizvi ZA, Mujagond P, Ali SA, Gaur P, Singh M, Ahuja V, Awasthi A, Srikanth CV. DeSUMOylase SENP7-Mediated Epithelial Signaling Triggers Intestinal Inflammation via Expansion of Gamma-Delta T Cells. *Cell Rep*. 2019 Dec 10;29(11):3522-3538.e7. doi: 10.1016/j.celrep.2019.11.028. PubMed PMID: 31825833.

Inflammatory bowel disease (IBD) is a complex autoimmune disorder recently shown to be associated with SUMOylation, a post-translational modification mechanism.

Here, we have identified a link between epithelial deSUMOylases and inflammation in IBD. DeSUMOylase SENP7 was seen to be upregulated specifically in intestinal epithelial cells in both human IBD and a mouse model. In steady state, but not IBD, SENP7 expression was negatively regulated by a direct interaction and ubiquitination by SIAH2. Upregulated SENP7 in inflamed tissue displayed a distinct interactome. These changes led to an expansion of localized proinflammatory  $\gamma\delta$  T cells. Furthermore, in vivo knockdown of SENP7 or depletion of  $\gamma\delta$  T cells abrogated dextran sulfate sodium (DSS)-induced gut inflammation. Strong statistical correlations between upregulated SENP7 and high clinical disease indices were observed in IBD patients. Overall, our data reveal that epithelial SENP7 is necessary and sufficient for controlling gut inflammation, thus highlighting its importance as a potential drug target.

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193: Suresh MV, Dolgachev VA, Zhang B, Balijepalli S, Swamy S, Mooliyil J, Kralovich G, Thomas B, Machado-Aranda D, Karmakar M, Lalwani S, Subramanian A, Anantharam A, Moore BB, Raghavendran K. TLR3 absence confers increased survival with improved macrophage activity against pneumonia. *JCI Insight*. 2019 Dec 5;4(23). pii: 131195. doi: 10.1172/jci.insight.131195. PubMed PMID: 31801911; PubMed Central PMCID: PMC6962028.

Toll-like receptor 3 (TLR3) is a pathogen recognition molecule associated with viral infection with double-stranded RNA (dsRNA) as its ligand. We evaluated the role of TLR3 in bacterial pneumonia using *Klebsiella pneumoniae* (KP). WT and TLR3<sup>-/-</sup> mice were subjected to a lethal model of KP. Alveolar macrophage polarization, bactericidal activity, and phagocytic capacity were compared. RNA-sequencing was performed on alveolar macrophages from the WT and TLR3<sup>-/-</sup> mice. Adoptive transfers of alveolar macrophages from TLR3<sup>-/-</sup> mice to WT mice with KP were evaluated for survival. Expression of TLR3 in postmortem human lung samples from patients who died from gram-negative pneumonia and pathological grading of pneumonitis was determined. Mortality was significantly lower in TLR3<sup>-/-</sup>, and survival improved in WT mice following antibody neutralization of TLR3 and with TLR3/dsRNA complex inhibitor. Alveolar macrophages from TLR3<sup>-/-</sup> mice demonstrated increased bactericidal and phagocytic capacity. RNA-sequencing showed an increased production of chemokines in TLR3<sup>-/-</sup> mice. Adoptive transfer of alveolar macrophages from the TLR3<sup>-/-</sup> mice restored the survival in WT mice. Human lung samples demonstrated a good correlation between the grade of pneumonitis and TLR3 expression. These data represent a paradigm shift in understanding the mechanistic role of TLR3 in bacterial pneumonia.

DOI: 10.1172/jci.insight.131195

PMCID: PMC6962028

PMID: 31801911

194: Surve A, Azad S, Venkatesh P, Kumar V, Chawla R, Gupta V, Vohra R. Choroidal Vascular Pattern in Cases of Sturge-Weber Syndrome. *Ophthalmol Retina*. 2019 Dec;3(12):1091-1097. doi: 10.1016/j.oret.2019.07.009. Epub 2019 Jul 22. PubMed PMID: 31523035.

**PURPOSE:** To study the choroidal vascular pattern in patients with Sturge-Weber syndrome (SWS) using swept-source OCT (SS-OCT).

**DESIGN:** Prospective comparative observational study.

**PARTICIPANTS:** All patients with SWS with no history of prior treatment for posterior segment pathology were included.

**METHODS:** Both eyes of all patients were studied using fundus imaging, SS-OCT, fundus fluorescein angiography (FFA), and indocyanine green angiography (ICG) by 2 independent observers.

**MAIN OUTCOME MEASURES:** The FFA and ICG were screened for any vascular abnormalities. The SS-OCT was evaluated for choroidal changes.

**RESULTS:** A total of 34 eyes of 17 patients with diagnosed SWS in the age group 9 to 26 years were studied. The FFA and ICG in 7 and 11 patients, respectively, showed some vascular abnormalities. SS-OCT was performed in all patients. The diffuse choroidal hemangioma (DCH) was characterized by loss of the choroidal vascular pattern, increase in the choroidal thickness and loss of visualization of the sclerochoroidal interface. Based on the FFA, ICG, and SS-OCT imaging, there were 3 patients with no DCH, 5 with bilateral DCH, and the remaining 9 patients had unilateral DCH. The detection rate was 50% clinically: 52.94% with FFA, 82.35% with ICG, and 86.36% with SS-OCT. There was substantial agreement between the 2 observers for all 3 investigations.

**CONCLUSION:** SS-OCT is a reliable noninvasive imaging modality for early diagnosis and follow-up of DCH over time.

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195: Tamhankar AJ, Nachimuthu R, Singh R, Harindran J, Meghwanshi GK, Kannan R, Senthil Kumar N, Negi V, Jacob L, Bhattacharyya S, Sahoo KC, Mahadik VK, Diwan V, Sharma M, Pathak A, Khedkar SU, Avhad D, Saxena S, Nerkar S, Venu V, Kumar S, Shandeepan G, Ranjit Singh K, Gashnga R, Kumar A. Characteristics of a Nationwide Voluntary Antibiotic Resistance Awareness Campaign in India; Future Paths and Pointers for Resource Limited Settings/Low and Middle Income Countries. *Int J Environ Res Public Health*. 2019 Dec 16;16(24). pii: E5141. doi: 10.3390/ijerph16245141. PubMed PMID: 31888272; PubMed Central PMCID: PMC6950494.

Antibiotic resistance has reached alarming proportions globally, prompting the World Health Organization to advise nations to take up antibiotic awareness campaigns. Several campaigns have been taken up worldwide, mostly by governments. The government of India asked manufacturers to append a 'redline' to packages of antibiotics as identification marks and conducted a campaign to inform the general public about it and appropriate antibiotic use. We investigated whether an antibiotic resistance awareness campaign could be organized voluntarily in India and determined the characteristics of the voluntarily organized campaign by administering a questionnaire to the coordinators, who participated in organizing the voluntary campaign in India. The campaign characteristics were: multiple electro-physical pedagogical and participatory techniques were used, 49 physical events were organized in various parts of India that included lectures, posters, booklet/pamphlet distribution, audio and video messages, competitions, and mass contact rallies along with broadcast of messages in 11 local languages using community radio stations (CRS) spread all over India. The median values for campaign events were: expenditure-3000 Indian Rupees/day (US\$~47), time for planning-1 day, program spread-4 days, program time-4 h, direct and indirect reach of the message-respectively 250 and 500 persons/event. A 2 min play entitled 'Take antibiotics as prescribed by the doctor' was broadcast 10 times/day for 5 days on CRS with listener reach of ~5 million persons. More than 85% of coordinators thought that the campaign created adequate awareness about appropriate antibiotic use and antibiotic resistance. The voluntary campaign has implications for resource limited settings/low and middle income countries.

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PMCID: PMC6950494

PMID: 31888272

196: Tapera T, Willis N, Madzeke K, Napei T, Mawodzeke M, Chamoko S, Mutsinze A, Zvirawa T, Dupwa B, Mangombe A, Chimwaza A, Makoni TM, Mandewo W, Senkoro M, Owiti P, Tripathy JP, Kumar AMV. Effects of a Peer-Led Intervention on HIV Care Continuum Outcomes Among Contacts of Children, Adolescents, and Young Adults Living With HIV in Zimbabwe. *Glob Health Sci Pract*. 2019 Dec 23;7(4):575-584. doi: 10.9745/GHSP-D-19-00210. Print 2019 Dec 23. PubMed PMID: 31852741; PubMed Central PMCID: PMC6927836.

**BACKGROUND:** Africaid Zvandiri, in partnership with the Ministry of Health and Child Care (MOHCC) in Zimbabwe, implemented a comprehensive, peer-led program, focused on children, adolescents, and young adults living with HIV aged 0-24 years. The peers, known as community adolescent treatment supporters (CATS), are people living with HIV (PLHIV) aged 18-24 years who are trained and mentored to support their peers throughout the HIV care continuum through support groups, home visits, phone call reminders, and messages. We report the HIV care continuum outcomes (HIV testing uptake, antiretroviral therapy [ART] uptake, retention, and viral suppression) in a cohort of household contacts and sexual partners (aged younger than 25 years) of index children, adolescents, and young adults living with HIV identified by CATS from October 2017 to September 2018 in 24 districts of Zimbabwe.

**METHODS:** This was a retrospective cohort study involving analysis of routine program data, extracted from electronic databases consisting of data on contacts of index PLHIV and ART outcomes. We used April 30, 2019, as the censor date for all analyses.

**RESULTS:** A total of 15,223 household contacts and sexual partners with unknown HIV status (linked to 9,353 index PLHIV) were identified and referred for HIV testing. Of these, 12,114 (79.6%) were tested and 1,193 (9.8%) were HIV-positive. Of the latter, 1,153 (96.6%) were initiated on ART with 99% starting on the day of diagnosis. Of those on ART, 1,151 (99.8%) were alive on ART at 6 months and 2 (0.2%) died. A total of 1,044 (91%) children, adolescents, and young people living with HIV underwent viral load testing at 6 months or later, of whom 1,037 (99.3%) were virally suppressed (<1000 copies/ml).

**CONCLUSION:** These findings add to the global evidence demonstrating the effectiveness of peer-led interventions in children, adolescents, and young adults living with HIV and justify the decision of the MOHCC in Zimbabwe to scale-up the model nationally. Future research should aim to understand the reasons for the gaps in HIV testing and viral load testing using qualitative research.

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PMCID: PMC6927836

PMID: 31852741

197: Thakur CK, Chaudhry R, Gupta N, E V V, Singh V, Das BK, Jadon RS, Wig N, Lodha R, Kabra SK, Dey AB, Chhabra M. Scrub typhus in patients with acute febrile illness: a five-year study from India. *QJM*. 2019 Dec 2. pii: hcz308. doi: 10.1093/qjmed/hcz308. [Epub ahead of print] PubMed PMID: 31790119.

**BACKGROUND:** Scrub typhus was once thought to be a disease of rural origin and was confined to specific pockets in South Asia. Early diagnosis and treatment is extremely important as it is associated with high mortality if left untreated. **AIM:** To delineate the clinical and molecular epidemiology of scrub typhus in patients presenting with acute febrile illness from various parts of India.

**METHOD:** During the study period of five years (October, 2013 to October, 2018), a total of 1742 patients with acute febrile illness <15 days were enrolled after taking informed consent. Patients were diagnosed using IgM Enzyme linked immunosorbent assay (ELISA) based on the pre-determined region specific cut-offs. Patients with positive IgM ELISA were also subjected to IgM Immunofluorescence assay (IFA) and nested polymerase chain reaction assay (PCR). The demographic and relevant clinical details of the patients were documented and analyzed.

**RESULT:** A total of 210 (12.1%) patients were diagnosed with scrub typhus. Of these, nested PCR was positive in only 85 patients. Sequencing and phylogenetic analysis showed that the predominant circulating genotypes were Gilliam and Karp. On multivariate analysis, acute respiratory distress syndrome, myocarditis, encephalitis/encephalopathy, jaundice and splenomegaly were significantly more common in those patients who were diagnosed with scrub typhus. A total of 14 patients diagnosed with scrub typhus succumbed to the illness.

**CONCLUSION:** Patients with fever, headache, pulmonary manifestations, CNS manifestations, myocarditis, transaminitis or thrombocytopenia presenting in the monsoon and post-monsoon season should be evaluated for scrub typhus irrespective of the geographical location in India.

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DOI: 10.1093/qjmed/hcz308  
PMID: 31790119

198: Thota R, Kumar R, Kumar R, Jat B. Navigation-assisted endonasal endoscopic optic nerve decompression in fibrous dysplasia. *BMJ Case Rep.* 2019 Dec 29;12(12). pii: e230621. doi: 10.1136/bcr-2019-230621. PubMed PMID: 31888916.

A 12-year-old girl presented with left-sided decreased vision of 2-month duration. Clinical evaluation and imaging revealed fibrous dysplasia compressing the left optic nerve with no underlying endocrinological abnormalities. Best-corrected visual acuity showed progressive deterioration of vision over 2-month follow-up. She underwent navigation-assisted endonasal endoscopic optic nerve decompression. Post-surgery there was improvement in vision and it became normal (6/6). Six-month follow-up showed stable vision with no further complications.

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DOI: 10.1136/bcr-2019-230621  
PMID: 31888916

199: Tomar A, Kaushik S, Khan SI, Bisht K, Nag TC, Arya DS, Bhatia J. The dietary isoflavone daidzein mitigates oxidative stress, apoptosis, and inflammation in CDDP-induced kidney injury in rats: Impact of the MAPK signaling pathway. *J Biochem Mol Toxicol.* 2019 Dec 13:e22431. doi: 10.1002/jbt.22431. [Epub ahead of print] PubMed PMID: 31833131.

Cisplatin-induced nephrotoxicity persists as a clinical problem despite several supportive measures to alleviate renal damage. Daidzein (DZ), a dietary isoflavone having antioxidant and anti-inflammatory activity, is investigated in this study for protective effects against cisplatin-induced renal injury in rats. DZ (25, 50, or 100mg/kg; intraperitoneally; 10 days) was administered along with Cisplatin, single dose, on the 7th day of the experiment. On the 11th day, the rats were euthanized, and different samples were collected for analysis.

Biochemical, histopathological, and molecular parameters were assessed to evaluate the effect of daidzein. Cisplatin injection resulted in renal dysfunction, lipid peroxidation that led to consumption of antioxidants, exaggerated apoptosis, and inflammation. These changes were associated with increase in the signaling proteins. DZ attenuated the toxic effects of cisplatin on the kidney at 100mg/kg dose. The study concludes with the finding that daidzein imparts protection against the nephrotoxic effect of Cisplatin and can be considered as a novel, potential therapy.

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DOI: 10.1002/jbt.22431

PMID: 31833131

200: Tomar AK, Agarwal R, Kundu B. Most Variable Genes and Transcription Factors in Acute Lymphoblastic Leukemia Patients. *Interdiscip Sci.* 2019 Dec;11(4):668-678. doi: 10.1007/s12539-019-00325-y. Epub 2019 Apr 10. PubMed PMID: 30972690.

Acute lymphoblastic leukemia (ALL) is a hematologic tumor caused by cell cycle aberrations due to accumulating genetic disturbances in the expression of transcription factors (TFs), signaling oncogenes and tumor suppressors. Though survival rate in childhood ALL patients is increased up to 80% with recent medical advances, treatment of adults and childhood relapse cases still remains challenging. Here, we have performed bioinformatics analysis of 207 ALL patients' mRNA expression data retrieved from the ICGC data portal with an objective to mark out the decisive genes and pathways responsible for ALL pathogenesis and aggression. For analysis, 3361 most variable genes, including 276 transcription factors (out of 16,807 genes) were sorted based on the coefficient of variance. Silhouette width analysis classified 207 ALL patients into 6 subtypes and heat map analysis suggests a need of large and multicenter dataset for non-overlapping subtype classification. Overall, 265 GO terms and 32 KEGG pathways were enriched. The lists were dominated by cancer-associated entries and highlight crucial genes and pathways that can be targeted for designing more specific ALL therapeutics. Differential gene expression analysis identified upregulation of two important genes, JCHAIN and CRLF2 in dead patients' cohort suggesting their possible involvement in different clinical outcomes in ALL patients undergoing the same treatment.

DOI: 10.1007/s12539-019-00325-y

PMID: 30972690

201: Trikha V, Veeresh V, Mittal S, Ganesh V, Bansal H. A new method in sacral fracture fixation. *Injury.* 2019 Dec 17. pii: S0020-1383(19)30815-0. doi: 10.1016/j.injury.2019.12.026. [Epub ahead of print] PubMed PMID: 31879173.

202: Trikha V, Kumar A, Mittal S, Passey J, Gaba S, Kumar A. Morphometric analysis of the anterior column of the acetabulum and safety of intramedullary screw fixation for its fractures in Indian population: a preliminary report. *Int Orthop.* 2019 Dec 14. doi: 10.1007/s00264-019-04428-5. [Epub ahead of print] PubMed PMID: 31838545.

INTRODUCTION: Morphometric variations of the anterior column of the acetabulum have been described in the literature for its complex structure, which can influence the safe containment of intramedullary screw for fixation of its fractures. The purpose of this CT-based study is to present a preliminary report on the morphometric variations and safety of intramedullary screw fixation of the

anterior column of the acetabulum in the Indian population.

**METHODS:** CT-based data from 102 uninjured pelvis were retrospectively analyzed in iPlan® BrainLab AG, Feldkirchen, Germany. Narrowest zones around acetabulum and superior pubic ramus were measured. We calculated the axis of the anterior column of the acetabulum by joining the centres of these narrowest zones. Standard screws trajectories were directed along this axis. Screw length up to the first cortical perforation, the distance of the exit point from the pubic symphysis, and the length of the anterior column up to the pubic tubercle were measured.

**RESULTS:** The osseous corridor of the anterior column of acetabulum had variable cross-section along its length with two constriction zones, first in the acetabular region and second in the superior pubic ramus. Only 54% of our cases allowed safe applicability of 6.5-mm-diameter screw trajectories with safety margin of 2 mm on either side of the screw. Significant morphometric and screw applicability-related differences were observed among male and female cases with males having a wider osseous corridor in general. Elimination of safety margin results in a significant increase in the screw applicability.

**CONCLUSION:** The osseous corridor of the anterior column varies in its dimensions from individual to individual. Standard screws of 6.5-mm and 7.3-mm diameters may not be safe for intramedullary screw fixation in every patient and carry a risk of cortical violation when a 2 mm of width around the screw is considered as a safety margin. However, with a precise screw placement within the extents of the cortices of the anterior column, 6.5-mm screws can be applied in most of the female cases and 7.3-mm screws can be applied in most of the male cases for anterior column fixation.

DOI: 10.1007/s00264-019-04428-5

PMID: 31838545

203: Tripathi P, Mishra P, Ranjan R, Tyagi S, Seth T, Saxena R. Factor VII deficiency - an enigma; clinicohematological profile in 12 cases. Hematology. 2019 Dec;24(1):97-102. doi: 10.1080/10245332.2018.1518799. Epub 2018 Sep 7. PubMed PMID: 30191763.

**OBJECTIVE:** Factor VII deficiency is the commonest of the rare bleeding disorders with limited knowledge on clinical profile. The objective of this study was to study the prevalence and clinico-hematological profile of factor VII-deficient patients.

**METHODS:** It is a retrospective observational study of probable inherited factor VII deficiency covering 18 months. Their clinical profile, family history, investigation and treatment records were studied in detail.

**RESULTS:** The study group comprised of total 12 factor VII deficiency cases with mean age of 17.5 years of onset of symptoms. The commonest symptom was menorrhagia (41.6%) followed by epistaxis (25%) and easy bruisability (16.6%). These 12 patients when categorized according to bleeding severity: severe bleeding - 2, moderate bleeding - 3, mild bleeding - 6 and asymptomatic - 1. All cases had prolonged prothrombin time (PT) with mean PT of 35.4 seconds (range 18-50 seconds) and mean prolongation of PT from upper limit of normal - 19.4 seconds (range 2-34 seconds). Factor VII levels ranged from < 1-40% in these patients. Clinical symptoms were not in concordance with factor levels. Of 12 patients, required treatment other than local measures.

**DISCUSSION AND CONCLUSION:** Inherited factor VII deficiency is the commonest autosomally inherited factor deficiency with marked variation in the age of presentation and clinical symptoms. The laboratory results in form of PT and factor VII levels do not correlate with the severity of clinical presentation. A comprehensive evaluation to exclude acquired causes of factor VII deficiency, e.g. obesity, liver diseases, vitamin K deficiency and acquired inhibitors is required before labeling it as inherited in the absence of family history and

molecular studies.

DOI: 10.1080/10245332.2018.1518799  
PMID: 30191763 [Indexed for MEDLINE]

204: Tripathy S, Behera A, Kumar A, Subudhi K, Bal C. Adrenocortical Carcinoma with Inferior Vena Cava Thrombus on (18)F-FDG-PET-Computed Tomography. *Indian J Nucl Med.* 2020 Jan-Mar;35(1):87-88. doi: 10.4103/ijnm.IJNM\_107\_19. Epub 2019 Dec 31. PubMed PMID: 31949384; PubMed Central PMCID: PMC6958943.

Adrenocortical carcinoma (ACC) is a rare and highly aggressive malignant neoplasm which can produce intravascular extension into the inferior vena cava (IVC) and can rarely extend into the right atrium. We describe the 18F Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography findings of a 57-year-old man diagnosed with ACC with IVC thrombus extending up to the right atrium.

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DOI: 10.4103/ijnm.IJNM\_107\_19  
PMCID: PMC6958943  
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205: Tripathy S, Parida GK, Naswa N, Jha P, Reddy S, Arun Raj ST. Right Ventricle Metastasis from Carcinoma Rectum: Findings on (18)F-Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography. *Indian J Nucl Med.* 2020 Jan-Mar;35(1):78-79. doi: 10.4103/ijnm.IJNM\_15\_19. Epub 2019 Dec 31. PubMed PMID: 31949380; PubMed Central PMCID: PMC6958966.

Rectal adenocarcinoma metastasizes most commonly to the lungs and liver. Metastasis to heart, although described in literature, is a very rare phenomenon. We describe the 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET-CT) findings of a 45-year-old male who was a biopsy-proven case of adenocarcinoma rectum. Apart from metastatic disease involving liver, lungs, bone marrow, and lymph nodes, metastasis to right ventricle was also seen on PET-CT scan.

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DOI: 10.4103/ijnm.IJNM\_15\_19  
PMCID: PMC6958966  
PMID: 31949380

206: Tyagi A, Dass C, Rao NT, Soni KD. Emergency anesthetic management of an achondroplastic elderly gravida with polytrauma. *Int J Crit Illn Inj Sci.* 2019 Oct-Dec;9(4):191-193. doi: 10.4103/IJCIIS.IJCIIS\_56\_19. Epub 2019 Dec 11. PubMed PMID: 31879607; PubMed Central PMCID: PMC6927133.

A 42-year-old pregnant female, diagnosed with achondroplasia, presented to our trauma center with multiple injuries after being involved in a motor vehicle accident. During her hospitalization, she underwent multiple surgeries and required admission in the intensive care unit. We describe the emergency anesthetic management of this patient, highlighting the effects of skeletal dysplasia on airway, cardiorespiratory system, and ventilatory mechanics. These effects, when superimposed upon with physiological changes of pregnancy, can lead to an unanticipated ventilatory challenge as we describe in this report.

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DOI: 10.4103/IJCIIS.IJCIIS\_56\_19  
PMCID: PMC6927133  
PMID: 31879607

207: Tyagi A, Pramanik R, Bakhshi R, Vishnubhatla S, Bakhshi S. Genetic Landscape of Mitochondrial Regulatory Region in Pediatric Acute Myeloid Leukemia: Changes from Diagnosis to Relapse. *J Pediatr Genet*. 2019 Dec;8(4):193-197. doi: 10.1055/s-0039-1696976. Epub 2019 Sep 12. PubMed PMID: 31687256; PubMed Central PMCID: PMC6824899.

This prospective study aimed to compare the pattern of mitochondrial deoxyribonucleic acid D-loop (mt-DNA D-loop) variations in 41 paired samples of de novo pediatric acute myeloid leukemia (AML) (baseline vs. relapse) patients by Sanger's sequencing. Mean mt-DNA D-loop variation was 10.1 at baseline as compared with 9.4 per patients at relapse. In our study, 28 (68.3%) patients showed change in number of variations from baseline to relapse, 11 (26.8%) patients showed increase, 17 (41.6%) patients showed decrease, and 7 (17.1%) patients who suffered a relapse had a gain at position T489C. No statistically significant difference was observed in the mutation profile of mt-DNA D-loop region from baseline to relapse in the evaluated population of pediatric AML.

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PMCID: PMC6824899 [Available on 2020-12-01]  
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208: Ung L, Acharya NR, Agarwal T, Alfonso EC, Bagga B, Bispo PJ, Burton MJ, Dart JK, Doan T, Fleiszig SM, Garg P, Gilmore MS, Gritz DC, Hazlett LD, Iovieno A, Jhanji V, Kempen JH, Lee CS, Lietman TM, Margolis TP, McLeod SD, Mehta JS, Miller D, Pearlman E, Prajna L, Prajna NV, Seitzman GD, Shanbhag SS, Sharma N, Sharma S, Srinivasan M, Stapleton F, Tan DT, Tandon R, Taylor HR, Tu EY, Tuli SS, Vajpayee RB, Van Gelder RN, Watson SL, Zegans ME, Chodosh J. Infectious corneal ulceration: a proposal for neglected tropical disease status. *Bull World Health Organ*. 2019 Dec 1;97(12):854-856. doi: 10.2471/BLT.19.232660. Epub 2019 Nov 1. PubMed PMID: 31819296; PubMed Central PMCID: PMC6883276.

209: Vaithiyam V, Jadon RS, Ray A, Manchanda S, Meena VP, Ranjan P, Vikram NK. Metronidazole induced encephalopathy: A rare side effect with a common drug. *Indian J Radiol Imaging*. 2019 Oct-Dec;29(4):431-434. doi: 10.4103/ijri.IJRI\_330\_19. Epub 2019 Dec 31. PubMed PMID: 31949347; PubMed Central PMCID: PMC6958887.

In hospitals, seizures and encephalopathy are one of the common complications observed in critically ill patients. Drug intoxication, metabolic derangements, and anatomical abnormalities can cause altered mental status. We encountered an uncommon case with a diagnostic dilemma due to persistent encephalopathy, where metronidazole toxicity was an etiological factor. A 45-year-old male, who was admitted with the diagnosis of ruptured amoebic liver abscess. During the course of his management, he developed seizures and altered sensorium. After excluding other etiologies for in-hospital de novo seizure, a suspicion of metronidazole toxicity was considered. MRI brain was done which suggested the same. Metronidazole induced encephalopathy (MIE) is an uncommon adverse effect of treatment with metronidazole. Diagnosis is made by identifying specific radiological findings. It characteristically affects the cerebellum and subcortical structures. While the clinical and neuroimaging changes are usually reversible, persistent encephalopathy with poor outcomes may occur as seen in our

case.

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DOI: 10.4103/ijri.IJRI\_330\_19

PMCID: PMC6958887

PMID: 31949347

210: Vani PC, Arthi G, Jessy JP, Rani N, Jhajhria SK. Vascular foramina of talus: an anatomical study with reference to surgical dissection. *Surg Radiol Anat.* 2019 Dec 21. doi: 10.1007/s00276-019-02394-6. [Epub ahead of print] PubMed PMID: 31865434.

**PURPOSE:** To study the distribution and morphometry of vascular foramina of adult human talus in Indian population.

**METHODS:** The study was carried out by using 56 adult human tali. The location, size, number and foraminal index of vascular foramina on head, neck and body of each bone were examined macroscopically. The difference in location of vascular foramina was further studied in relation to the pattern of calcaneal articular facets on talus.

**RESULTS:** The vascular foramina were present on the superior neck, inferior neck and medial surface of talar body in all (100%) the bones. The Kruskal-Wallis test followed by series of Mann-Whitney test for post hoc analysis showed the number of vascular foramina was significantly greater on inferior surface of neck and medial surface of body. The number of vascular foramina ranged from 0 to 25.

About 77.05% of foramina were  $\geq 0.5$  mm in size. The mean foraminal index of the closest foramina on inferior surface of neck and medial surface of body was 47.90% and 37.23%, respectively. The mean foraminal index of the farthest foramina on inferior surface of neck and medial surface of body was 75.08% and 71.35%, respectively.

**CONCLUSION:** The present study has provided additional information on the vascular foramina of tali. This knowledge is important to the orthopedic, vascular and podiatric surgeons while performing the surgeries of hind foot. We opine that the lateral approach would be more beneficial in the surgical procedures to talus.

DOI: 10.1007/s00276-019-02394-6

PMID: 31865434

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This communication describes the concept, rationale, and potential of social prescription in diabetes care. It calls for use of strategy to harness the strengths of the South Asian socio-cultural milieu, and contain the diabetes epidemic.

PMID: 31853131

212: Vidhubala E, Shewade HD, Niraimathi AK, Ramkumar S, Ramaswamy G, Nagalekshmi G, Sankar Mahadevan B. Call for Systematic Population-Based Cervical Cancer Screening: Findings from Community-Based Screening Camps in Tamil Nadu, India. *Asian Pac J Cancer Prev.* 2019 Dec 1;20(12):3703-3710. doi: 10.31557/APJCP.2019.20.12.3703. PubMed PMID: 31870112.

**BACKGROUND:** In India, systematic cervical cancer screening under the national programme is yet to cover the entire population and therefore opportunistic or camp based approach is commonly practiced screening mode currently. This study

presents the proportion of screen-positive women [positive visual inspection of the cervix with acetic acid (VIA) and/or Papanicolaou (Pap) smear results] and its associated factors from a rural community-based cervical cancer screening conducted in a service setting.

**METHODS:** In this cross-sectional study involving record review, data was drawn from free screening camps conducted by a non-governmental organization in two rural districts of Tamil Nadu, India between March 2015 and March 2017. The associations were assessed using adjusted prevalence ratio with 95% confidence interval.

**RESULTS:** A total of 5,207 women were screened from 307 camps. The mean age was 39.5 years (SD: 8.6). At least one symptom was observed among 2,245 women (43.1%). Of 5,207 women, 19.4% (n=1,009, 95% CI: 18.3%, 20.5%) were screen-positive. Screen positivity in women.

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213: Vijayakumar S, Anandan S, Ms DP, Kanthan K, Vijayabaskar S, Kapil A, Ray P, Sistla S, Bhattacharya S, Wattal C, Thirunarayan, Deotale V, Mathur P, Walia K, Ohri VC, Veeraraghavan B. Insertion sequences and sequence types profile of clinical isolates of carbapenem-resistant *A. baumannii* collected across India over four year period. *J Infect Public Health*. 2019 Dec 21. pii: S1876-0341(19)30361-2. doi: 10.1016/j.jiph.2019.11.018. [Epub ahead of print] PubMed PMID: 31874816.

**OBJECTIVES:** *Acinetobacter baumannii* emerged as a major nosocomial pathogen responsible for infections. In this study, we report the molecular characterization, association of insertion sequences and sequence types of clinical isolates of carbapenem resistant *A. baumannii*.

**MATERIALS AND METHODS:** A total of 763 non-duplicate isolates of *A. baumannii* received from 8 centres across India during January 2014 to December 2017 were studied. Susceptibility testing was done by Kirby-Bauer method. PCR was performed for detection of extended spectrum  $\beta$ -lactamases, metallo  $\beta$ -lactamases, oxacillinases and ISAbal. Mapping PCR was performed to identify the position of ISAbal with respect to blaOXA-23 like and blaOXA-51 like gene. MLST was performed to identify the sequence type. Whole genome sequencing was done to decipher the genetic arrangement of ISAbal with blaOXA-23 like and with blaOXA-51 like.

**RESULTS:** All the isolates were resistant to imipenem and meropenem. blaOXA-23 like was the predominant carbapenemase. All isolates were positive for ISAbal. The common sequence types were ST848, ST451 and ST1305 which belongs to International clone II. Whole genome sequencing showed considerable variation in the insertion site location.

**CONCLUSIONS:** In conclusion, high prevalence of blaOXA-23 like in *A. baumannii* and its association with ISAbal and sequence types belonging to IC-II facilitates the successful dissemination of these extremely drug resistant strains.

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