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NEWSLETTER FROM DEPARTMENT OF PHARMACY, SUMANDEEP VIDYAPEETH DEEMED UNIVERSITY

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## CARTOON


## ASSOCIATE EDITORS VIEW:

Dr. Ashim Kumar Sen

Welcome to the 2nd issue of the sixth volume of PHARMAHORIZON. I am extremely honored and excited to share this issue with you. In the last issue, we focused on articles related to Covid 19 pandemic which we hope have helped to updated with recent developments in Covid-19 treatment. This issue brings together a diverse range of subjects. A on personalized medicine, artificial intelligence in pharma and a rare case report on Erdheim Chester Disease (ECD) been included. Evidence based update about the recent advancements in Covid-19 treatment, an article on Nobel Prize winner Jennifer Anne Doudna and favipiravir as molecule of the millennium are other highlights of this issue.

We have also tried to disseminate important updates about new drug molecules and various departmental activities held recently. Lastly, I would like to thank and congratulate all authors for their great contribution to this edition. Feel free to contact editorial coordinators for contributions, feedback and for any topics you'd like to see in future editions.

**Dr. Ashim Kumar Sen**
Professor, Department of Pharmacy

## TOLOSA HUNT SYNDROME – A RARE CASE REPORT IN INDIA

Tolosa Hunt syndrome (THS), also known as painful ophthalmoplegia, recurrent ophthalmoplegia, or ophthalmoplegia syndrome, is described as severe and unilateral periorbital headaches associated with painful and restricted eye movements. Tolosa Hunt syndrome is one of the rare disorders recognized by the National Organization for Rare Disorders (NORD). It is also included as one of the painful cranial neuropathies by the International Headache Society [IHS] in its headache classification. Tolosa Hunt syndrome is usually idiopathic and is thought to be from non-specific inflammation in the region of the cavernous sinus and/or superior orbital fissure. However, traumatic injury, tumors, or an aneurysm could be the potential triggers. It is usually diagnosed via exclusion, and laboratory tests. These tests include a CBC, TFT, and serum protein electrophoresis. Cerebrospinal fluid may also be beneficial in distinguishing between THS and conditions with similar signs and symptoms. Treatment includes immunosuppressive such as corticosteroids (methylprednisolone) and steroid-sparing agents like methotrexate or azathioprine.

Case description- A 60 year old diabetic male patient who recovered from covid-19 15 days before, came with complain of sharp and intense unilateral headache, ptosis, ophthalmoplegia and loss of vision in right eye since 10 days. He was admitted to another hospital where he was diagnosed with THS by MRI Brain and other laboratory tests. He was advised to start intravenous corticosteroid Methylprednisolone once a day for seven days; however, he took discharge against medical advice after 1st dose. After 5 days, the symptoms intensified and so he came to our hospital. Later, again his MRI study of brain with orbit was done which showed the minimal proptosis noted on the right side with mild edema in the right periorbital soft tissues and small enhancing soft tissue in the right cavernous sinus region which suggested the possibility of Tolosa Hunt Syndrome. The pharmacotherapy involved intravenous methylprednisolone (40mg) once a day with other supportive care therapy. Yet, there was no reversal of vision loss and ptosis. However, the headache subsided and the patient was discharged after 7 days. The discharge medication included Tab. Methylprednisolone (16mg) [2—0— 1] for 5 days then taper to [1—0—1] for 5 days, Cap. Pantoprazole (40mg) [1—0—0] and Tab. Paracetamol (650mg) [SOS].

Treatment- Glucocorticoids have been the mainstay of the treatment ever since the syndrome was first described. But there is no specific data to give recommendations about dose, duration, or route of administration. Spontaneous remission of symptoms is known to occur. Although orbital pain drastically improves with steroid treatment, there is no evidence to suggest cranial nerve palsies improve faster with it. As with any glucocorticoid regimen, treatment for Tolosa Hunt syndrome involves initial high-dose therapy for few days followed by a gradual taper over weeks to months. A very small percentage of patients will require immunosuppression with other agents, either to avoid side effects of long-term steroid therapy or for long-term suppression of the disease process itself. Azathioprine, methotrexate, mycophenolate mofetil, cyclosporine, and infliximab have been used as second-line therapy.

Conclusion- Unlike the typical headache, patients with the THS are managed with steroids and immunosuppressive agents. Despite treatment, recurrences are common and the overall quality of life is poor.. An inter- professional approach to the care of this disease will provide the best patient outcome.


References- NCBI, National Organization of Rare Disease [NORD]



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## Personalized Medicine

**Introduction :** Personalised medicine (PM) is considered as an expansion of standard approaches to diagnosing and treating certain disease. With the help of pharmacogenomics and gene testing, healthcare professional can choose a therapy or treatment protocol based on patient's molecular profile that minimize adverse effects and ensures desired outcome, it can also help contain costs compared with "trial-and-error" approach to disease treatment. PM is multiple aspect approach to patient care that not only enhances potential to diagnose and treat disease, but provides potential to detect disease as early as possible, when it is easier to treat effectively without complications. It has potential to change the way we think about, identify and manage health problems, also PM have great impact on both clinical research and patient care, and this impact will grow as our understanding and technologies improve. An optimal medical therapy could be reach for desired outcomes for individual, medication types and dosages may differ from patient to patient resulting in customization of patient.

**Pharmacogenomics :** It has been defined as the study of variability in drug response to individual due to heredity. It is the branch of pharmacology which deals with the effect of genetic variation on drug response in patients by correlating gene expression or single-nucleotide polymorphisms with a drug's efficacy or toxicity. It helps to generate rational means to optimize drug therapy, with respect to the patient's genotype, to ensure desired outcome with great efficacy and minimal side effects. Pharmacogenomics is the study of how an individual's genetic inheritance alters the body's response to drugs.

**Perspectives of PM :** Through five main perspectives, ICPerMed vision [1] affirms PM as medical practice centred on the individual's characteristics.
Perspective 1: Informed, empowered, engaged, and responsible citizens
Perspective 2: Informed, empowered, engaged, and responsible health providers
Perspective 3: Healthcare systems enable personally tailored, optimised health promotion and disease prevention, diagnosis, and treatment for benefit of patients
Perspective 4: Available health-related information for optimised treatment, care, prevention, and research
Perspective 5: Economic value by establishing next generation of medicine

**Applications of PM :** It has many advantages and applications in health care, it not only helps in early diagnosis and treatment of disease, but more important is it detects disease at an earlier stage, when it's easier to treat effectively. PM is rapidly developing because influence of individual characteristics on development of disease and efficacy of medicines is becoming more evident.

**Conclusion :** The recent phase of personalized medicine, which incorporates uniqueness of an individual with respect to pharmacokinetics and pharmacodynamics of a drug, shows a promising result by providing greater safety and efficacy in drug design and development.

**References :**
**(1)** Vicente AM, Ballensiefen W. How personalised medicine will transform healthcare by 2030: the ICPerMed vision. Journal of Translational Medicine. 2020 Dec; 18:1-4. **(2)** Meiliana A, Dewi NM, Wijaya A. Personalized Medicine: The Future of Health Care. The Indonesian Biomedical Journal. 2016 Dec 1;8(3):127-46.

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## ARTIFICIAL INTELLIGENCE IN PHARMA

Artificial intelligence in Pharma refers to the use of automated algorithms to perform tasks which traditionally rely on human intelligence. Traditionally, the manufacturing of the drug requires several years with the huge investment in time as well as money in order to bring the product in the market. Thus, to combat such challenges, these industries have adopted AI to accelerate their innovations.

**AI in drug discovery:** Various Pharmaceutical companies have collaborated with AI companies and created platforms to accelerate their drug discovery programmes. These platforms look for pattern in data and make use of algorithms that can make accurate predictions about the potential drug molecules based on computational structure analysis, drug target and data from in-vivo cell line studies. AI is playing a role in drug target identification and validation; target-based, phenotypic, as well as multi-target drug discoveries; drug repurposing; and biomarker identification.

**AI in genomics:** This technology helps in the formation of the gene maps which describes the certain genes that are responsible cause of the diseases. Further, it even suggests the drug molecule that can target such genes and eventually helps in curing the disease.

**AI in diseases identification:** By scanning medical images, AI has shown promising results in detecting conditions such as pneumonia, breast and skin cancers, and eye diseases. AI is used to analyse echocardiography scans that detect patterns of heartbeats and diagnose coronary heart disease.

**AI in drug repurposing:** AI platforms are a boon for budget-pressed pharma companies in terms of drug repurposing, in which the available data of drug molecules is evaluated to match new targets. AI-based technologies can deliver great value in this area as the chances of the ADR and other toxic effects during the human trials are less and even the cost of R&D process is low.

**AI in Rare diseases and personalised medicine:** On combing the information from body scans, patient biology and analytics of individual patient, AI is being used in various ways to detect diseases such as cancer, and even predict health issues people might face based on their genetics.AI is also being used to develop personalized drug treatments based on an individual's test results, reactions to past drugs and historical patient data for drug reactions. It reportedly examined millions of oncology research papers in 10 minutes after which it successfully diagnosed the patient and recommended a personalized treatment plan.

**AI in processing biomedical and clinical data:** AI designed algorithm is used to save time for the researches in the healthcare industry to read and interpret the large volume of the data generated during clinical trials. The use of AI has led to better analysis of data and generating appropriate hypothesis. Furthermore, it helps in enrolling patients even without their physical presence. It also helps in maintaining patient's log like the number of medications taken along with the other co-morbid conditions, any allergies or side-effects etc. which is useful for the cross-referencing of the data and easily extracting required data whenever needed.

**AI in marketing:** Pharma is considered to be sales-driven industry where AI can be a useful tool to refine marketing decision-making and strategies. Knowing which methods (print, digital, direct and other marketing activities) are most successful can be used by the companies to make profit. The technology charts a customer journey and helps to analyse data from past campaigns allows companies to invest in the most lucrative schemes

**References: (1)** Victoria Rees. Optimising artificial intelligence in the pharmaceutical industry European Pharmaceutical Review. Available from: https://www.europeanpharmaceuticalreview.com/article/107772/optimising-artificial-intelligence-in-the-pharmaceutical-industry/ **(2)** Rakesh Sharma. Artificial Intelligence-the future of pharma industry [Internet] Pharma express. Available from: https://www.expresspharma.in/amp/it-at-pharma/artificial-intelligence-the-future-of-pharma-industry/

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## Novel Coronavirus Medicine Update: Newer and Existing Treatment

Continuous research & clinical trials are underway to handle the current Covid-19 crisis. Evidence based update about the recent advancements in Covid-19 treatment.

**Favipiravir:** Antiviral: Chain terminator in Coronavirus & also inhibiting an enzyme called RNA dependent RNA polymerase. Current Status Worldwide: Granted approval in Japan for novel influenza strains, Unlicensed USA and UK. Current Status in India: DCGI granted approval for manufacturing & marketing to a pharmaceutical Company (Glenmark, Brand name: Fabiflu). People who are having mild-to moderate Coronavirus disease will get benefit from it.

**Remdesivir:** Antiviral: MOA is same as Favipiravir. Current Status Worldwide: Granted approval for Emergency Use Authorization (EUA) by FDA to treat adults & children hospitalized with severe COVID-19. Current Status in India: DCGI granted approval for manufacturing & marketing to a pharmaceutical Companies (Hetero Health Care, Brand name: Covifor) and (Cipla, Brand Name: Cipremi). Emergency use for the treatment of people hospitalized with COVID-19 will get benefit from it.

**Dexamethasone:** Steroid: Works by suppressing the massive immune response evoked by the coronavirus, which may cause damage to lungs and other organs. Current Status Worldwide: Granted Approval in UK to treat all people hospitalized with COVID-19, who require oxygen, including those on ventilators. Unlicensed in USA, exclusive recommendations for use of dexamethasone in people with COVID-19 have been released by the National Institutes of Health. Current Status in India: The Ministry of Health and Family Welfare has included dexamethasone in the updated clinical management protocol for COVID-19, after considering the latest available evidence and expert's consultations.

**Hydroxychloroquine:** Antimalarial: Works by interfering with the process of viral entry into the body's cells. Current Status Worldwide: WHO has stopped clinical trial on HCQ on 17th June 2020. Current Status in India: Phase 3 trial is being conducted to check role of HCQ for prevention of new infection & adverse outcomes following COVID-19. Only approved for prophylaxis in high-risk exposures. People will get benefit for Prevention of infection in asymptomatic healthcare workers, frontline workers and high-risk household contacts of confirmed positive cases.

**Ivermectin:** Anthelmintics: Acts by inhibiting the host importin alpha/beta-1 nuclear transport proteins, which are part of a key intracellular transport process that viruses hijack to enhance infection by suppressing the host's antiviral response. In addition, ivermectin docking may interfere with the attachment of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein to the human cell membrane. Ivermectin may be effective for the treatment of early-onset mild COVID-19 in adult patients. Early viral clearance of SARS-CoV-2 was observed in ivermectin treated patients. There are insufficient data for the COVID-19 Treatment Guidelines Panel to recommend either for or against the use of ivermectin for the treatment of COVID-19. Results from adequately powered, well-designed, and well-conducted clinical trials are needed to provide more specific, evidence-based guidance on the role of ivermectin in the treatment of COVID-19.

**References:** Hydroxychloroquine & COVID-19. WHO. Clinical Trials Registry, India. RECOVERY Trial, Oxford University News Release. COVID-19 Clinical Management Protocol. MoHFW.

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## ERDHEIM CHESTER DISEASE (ECD): A RARE CASE REPORT IN AN INDIAN HOSPITAL

ECD is a rare form of non-Langerhans cell histiocytosis. It involves the excessive production of histiocytes, which are a type of WBC. It is not believed to be contagious or hereditary. The cause is not known. The first two cases of ECD were reported by scientists Jakob Erdheim and William Chester in 1930. In 1972, Dr. Ronald Jaffe reported a third case & coined the name ECD. Because this is a very rare disease, no large studies have been performed & no treatment plan has been established that is widely accepted. **Symptoms:** Varies greatly from patient to patient. **Diagnosis:** Because it is so rare, ECD is often difficult to diagnose. Patients may go for months and even years after symptoms start until they are properly diagnosed.

**Case description:** A 12-year-old female child came to our hospital with the complains of seizure which was associated with up rolling of eyeballs, clenching of teeth and frothing from mouth which was lasted for 15 minutes. She also had fever and vomiting in the last 2 days. Seizures were recovered after medication which was given at outside setting. When she came to our hospital, she had neck rigidity and found febrile at a time of admission and for that she was given 0.9% DNS (56 ml/hour) with 100% maintenance, Inj. Ceftriaxone (8.5 cc + 10 cc NS) (IV) (BD) (100 mg/kg/ day), Inj. Phenytoin (0.9 cc + up to 5 cc NS) (IV) (BD) (100 mg/kg/day), Inj. Pantoprazole (1 ampoule + 100 cc NS) (IV) (BD) and Inj. Febrinyl (0.6 cc + up to 3 cc NS) (IV) (SOS). In past she had multiple hospitalization. She was diagnosed for Tubercular Meningitis with Hydrocephalus 2 years back. At that period, they noted that size of head is increasing and diagnosed with hydrocephalus with help of MRI. Her CT Thorax were showing the signs of patchy consolidation and ground glass appearance in both lungs and was confirmed for Pulmonary Koch's with help of Chest X-ray PA view. As patient were showing the signs of ECD she was scanned for PET-CT Impression it confirmed for Erdheim-Chester Disease with involvement of central nervous system, pulmonary, renal and skeletal system. In our hospital setting she was treated with Tab. Fosium (5 mg) (0-0-1), Syrup Sodium Valproate (1.5 ml) (PO) (TDS), Tab. Lenalidomide (10 mg) (1 TAB) (OD), Tab. Fluconazole (150 mg) (1/3 TAB) (OD).

**Treatment:** Various treatments have been used by individual doctors with different levels of success. These include: Systemic corticosteroids, Immunotherapy, Chemotherapy, Radiation & Surgery. Drugs usually given in the vein to control the over-production of histiocytes. This may include vinblastine (Velban), vincristine (Oncovin), cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), and cladribine (2CdA). Other drugs such as methotrexate, Gleevec, Tamoxifen, Imuran, and CellCept have also been used. New therapies which target the chemicals (cytokines) produced in excessive amounts in patients with ECD have been tested in a very small number of patients with ECD and may prove beneficial in the future but would be considered experimental at present. FDA Approved Treatment: Vemurafenib (Brand name: Zelboraf): Manufactured by Genentech, Inc. FDA-approved indication: Treatment of patients with Erdheim-Chester Disease with BRAF V600 mutation. Other drugs such as methotrexate, and Tamoxifen, have also been used.

**Conclusion:** It is important to remember that while these treatments may control the symptoms and growth of the disease, to date, there is no known "cure" for Erdheim-Chester. This case is concluding the treatment and management of the rare disease ECD. It can be utilized as evidence for similar like cases. There is need of more case series.

**References:** ECD Global Alliance. ECD Histiocytosis Association. Genetic & Rare Disease Information Center. UpToDate & Micromedex.

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## PROMINENT RESEARCHERS

Jennifer Doudna, in full **Jennifer Anne Doudna**, (born February 19, 1964, Washington, D.C.), American biochemist best known for her discovery, with French microbiologist Emmanuelle Charpentier, of a molecular tool known as clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9. After earning a degree in chemistry in 1985 from Pomona College in California, she went to Harvard University. There she worked in the laboratory of English-born American biochemist and geneticist Jack W. Szostak (who won the 2009 Nobel Prize for Physiology or Medicine) and in 1989 completed a Ph.D. in biochemistry. In 1994, following postdoctoral studies at the University of Colorado under the direction of American biochemist and molecular biologist Thomas R. Cech (who received a share of the 1989 Nobel Prize for Chemistry), she joined the faculty at Yale University. In 2002 she moved to the University of California, Berkeley, where she served as professor of biochemistry and molecular biology.

The discovery of CRISPR-Cas9, made in 2012, provided the foundation for gene editing, enabling researchers to make specific changes to DNA sequences in a way that was far more efficient and technically simpler than earlier methods. Using the CRISPR-Cas9 system, scientists were able to alter DNA to correct genetic defects in animals and modify DNA sequences in embryonic stem cells, an advance that opened the path to germ-line (sperm and egg) genome modification in humans. Doudna and Charpentier shared the 2020 Nobel Prize in Chemistry for their discovery and development of gene editing technologies

. https://www.britannica.com/biography/Jennifer-Doudna

## LATEST RESEARCH

For thousands of years, humans have used honey, propolis, and venom from the European honeybee Apis mellifera as medicines.
More recently, scientists have discovered that honeybee venom and its active component, melittin, are toxic to a wide range of tumors — including melanoma, lung, ovarian, and pancreatic cancers — in laboratory tests.For the first time, researchers have investigated the effect of melittin and honeybee venom on a range of breast cancers, including two of the most aggressive and hard-to-treat types.Breast cancer is the most common cancer in women. The two aggressive types, known as triple-negative breast cancer and HER2-enriched breast cancer, are associated with the poorest outcomes. They tend to develop resistance to existing treatments.
Scientists at the Harry Perkins Institute of Medical Research in Perth, Australia, and the University of Western Australia, also in Perth, found that melittin and honeybee venom rapidly kill these cancer types, with negligible effects on normal cells.The study also showed that venom from bumblebees, which contains no melittin, did not kill the cancer cells — even at high concentrations. The scientists reported their work in the journal of Precision Oncology.
Melittin can kill cells in under 1 hour by punching holes in their outer membrane. However, within 20 minutes of administration, it also disrupts the passing of chemical messages that the cells need to grow and divide.The scientists discovered that melittin does this by preventing the activation of receptors for growth factors in the cells' membrane. One of the reasons that HER2-enriched cancer cells and some triple-negative breast cancers grow uncontrollably is that they have large numbers of these receptors.By preventing these growth signals from getting through, melittin halts the cells' proliferation.

https://www.medicalnewstoday.com/articles/honeybee-venom-kills-aggressive-breast-cancer-cells

## MOLECULE OF MILLENNIUM

A research-led integrated drug company namely Glenmark Pharmaceuticals announced the launch of an antiviral drug namely Flavipiravir with brand name FabiFlu which will help to treat the COVID-19 patients from mild to moderate symptoms. According to Glenmark, Favipiravir drug shows clinical improvements of up to 88% in COVID-19 with a rapid reduction in viral load by 4 days. Further told that the clinical improvement noted across the age groups 20 to>90 years including the patients with co-morbid conditions like diabetes and heart disease suffering from mild to moderate COVID-19.
The drug also provides faster symptomatic and radiological improvement. The pharmaceutical company Glenmark successfully developed the active pharmaceutical ingredient (API) and the formulation for FabiFlu through its own in-house R&D team. With India's drug regulator DCGI, Glenmark filed the product for clinical trial and became the first pharmaceutical company in India to receive approval for phase 3 trial conducting on mild to moderated COVID-19 patients.

**How Favipiravir drug works?**

Since 2014, Favipiravir is approved in Japan for the treatment of novel or re-emerging influenza virus infections. It has a unique or different mechanism of action that is it is converted into an active phosphoribosylated form (favipiravir-RTP) in cells and recognised as a substrate by viral RNA polymerase and therefore inhibits RNA polymerase activity. Most of the patients having mild to moderate symptoms of COVID-19 can be benefit from FabiFlu drug use. Glenmark, earlier last month, also announced about another clinical test. It was to gauge the efficacy of two antivirals Favipiravir and Umifenovir as a combination therapy in moderate hospitalised adult COVID-19 patients in India.
Also according to some experts, it is not a specific drug made for COVID-19 and has been found to be useful, but the real efficacy will be known when administered on a large scale.



https://www.cnbctv18.com/healthcare/glenmark-launches-favipiravir-for-treatment-of-mild-to-moderate-covid-19-patients-6176191.htm

## NEW DRUG APPROVAL

**Dofetilide Bulk and Dofetilide Capsules 125 mcg, 250 mcg, 500mcg**

"Dofetilide is indicated for the maintenance of normal sinus rhythm (delay in time to recurrence of atrial fibrillation/ arterial flutter [AF/AFI] in patient with atrial fibrillation/ atrial flutter of greater than one week duration who have been converted to normal sinus rhythm).

**Drug dosing: Atrial Fibrillation and Flutter with or without Chemical Cardioversion**

- Individualize dose according to CrCl and QTc or QT ( if heart rate less than 60 beat/min)
  - CrCl Greater than 60 ml/min and QTc or QT 440 msec or less) Initial dose, 500 mcg orally twice daily.
  - Maintenance dose: If QTc or QT increases by more than 15% or is greater than 500 msec reduce dose to 250 mcg orally twice daily; MAX dose 500 mcg orally twice daily.

**Side effects:** Chest Pain, Dizziness, Headache, Heart block, Torsade's De Pointes, Ventricular Arrhythmia, Ventricular Fibrillation, Ventricular Tachycardia.

**Contraindications & Caution:** Hypersensitivity, Congenital or acquired long QT syndromes (QTc interval greater than 440 msec or 500 msec for patients with ventricular conduction abnormalities), Severe renal impairment.

**Pregnancy:** Fetal risk cannot be ruled out, Infant risk cannot be ruled out.

**Source: 1. List of new drugs approved in the year 2020**

https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NjYwMA==

https://www.micromedexsolutions.com

## WHO GUIDELINES ON THE MANAGEMENT OF CHRONIC PAIN IN CHILDREN BY GUIDELINE DEVELOPMENT GROUP (GDG)

**Recommendation 1**: In Children with chronic pain, physical therapies may be used, either alone or in combination with other treatments (Conditional recommendation, very low certainty evidence).

**Rationale:** When compared to non-physical therapy interventions or to wait-listed controls, physical therapy interventions for children with chronic pain due to various etiologies had a moderate effect on pain intensity post-treatment (very low certainty evidence). Benefits were not demonstrated at longer-term follow-up however, in the small number of available studies (very low certainty evidence). Functional disability and activity participation were improved post-treatment when used in the management of chronic pain of varying etiologies (very low certainty evidence). Adverse events were poorly reported in the studies examined; however, the events that were reported were generally minor or of short duration and did not require treatment. While physical therapy interventions were generally considered feasible and acceptable to children, parents and caregivers, views were mixed.

**Recommendation 2: Recommendation 2a.** In children with chronic pain, psychological management through cognitive behavioral therapy and related interventions (acceptance and commitment therapy, behavioral therapy and relaxation therapy) may be used (conditional recommendation, moderate certainty evidence).

**Recommendation 2b.** Psychological therapy may be delivered either face-to-face or remotely, or using a combined approach (conditional recommendation, moderate certainty evidence).

Rationale: The GDG agreed that cognitive behavioral therapy, acceptance and commitment therapy, behavioral therapy or relaxation Therapy have shared features in terms of their purpose, mechanism and delivery. At longer-term follow-up, there were beneficial effects on 50% pain reduction and functional disability. The systematic review of qualitative evidence reported that children had mixed views about the acceptability of psychological therapies. Children and parents perceived benefits (improved sleep, mood, quality of life and family communication, and less anxiety).

**Recommendation 3:** In children with chronic pain, appropriate pharmacological management, tailored to specific indications and conditions, may be used (conditional recommendation, low certainty evidence).

Rationale: The systematic review of the evidence reported small reductions in several pain measures post-treatment with several pharmacotherapies when used for the management of chronic pain of various etiologies in children. Although the balance of benefits and harms was difficult to determine based on the available evidence in children, particularly for specific drugs and indications, the GDG felt that pharmacotherapy has potential benefit for children with chronic pain, following individualized risk assessment. The costs of pharmacological therapy interventions are likely to vary across countries and specific settings, although the potential costs of not appropriately managing chronic pain could be high. Although analysis of these potential benefits compared to costs was not systematically reviewed across a range of settings, it was the GDG's opinion that these costs could be substantial, including healthcare utilization (in- and outpatient medical and mental health services) and the costs to parents of lost work time.

**Recommendation 4: Recommendation 4a.** Appropriate pharmacological management tailored to specific indications may include the use of morphine under the principles of opioid stewardship, for end-of-life-care (conditional recommendation, very low certainty evidence).

**Recommendation 4b.** In children with chronic pain associated with life-limiting conditions, morphine may be given by appropriately trained healthcare providers, under the principles of opioid stewardship (conditional recommendation, very low certainty evidence). Life-limiting conditions are illnesses for which there is no cure and an early death is expected, but with which a person may continue to live for several more years.

**Rationale:** There were no comparative studies identified in the systematic review of the evidence on the use of morphine or other opioids in children with chronic pain. There was moderate confidence that parents' attitude towards the use of morphine for their children with chronic pain due to cancer was positive and accepting, though some healthcare providers were reluctant to give opioids due to fear of their addictiveness (low confidence evidence). Some healthcare providers believed pain went untreated because of this fear, and that children needed better pain management. Overall, the GDG felt that access to morphine for children in end-of-life care, and in specific and limited situations for children with life-limiting conditions, was essential for adequate management of their pain.

Source: https://www.who.int/publications/i/item/9789240017870

## DRUGS IN CLINICAL TRIALS:

**Dupixent (dupilumab) significantly reduced severe asthma attacks in children and demonstrated improvement in children's lung function in a randomized Phase 3 trial:**

( October 2020 ) Regeneron Pharmaceuticals, Inc and Sanofi announced that a pivotal phase 3 randomized, double-blind, placebo-controlled trial of Dupixent (dupilumab) met its primary and all key secondary endpoints in children aged 6 to 11 years with uncontrolled moderate-to-severe asthma. In a broad type 2 inflammatory asthma patient population, defined as having elevated eosinophils (EOS) or elevated fractional exhaled nitric oxide (FeNO), Dupixent added to standard of care, significantly reduced asthma attacks (exacerbations) and improved lung function, as early as two weeks after the first dose, compared to standard of care alone.

Source: https://www.sanofi.com/en/media-room/press-releases/2020/2020-10-13-07-00-00

**Commenced patient dosing in phase 1b trial of camidanlumab tesirine in combo with pembrolizumab to treat advanced solid tumors:**

( November 2020 ) ADC Therapeutics announced that the first patient has been dosed with Camidanlumab tesirine (Cami, formerly ADCT-301) in combination with Pembrolizumab, a checkpoint inhibitor, in an ongoing Phase 1b clinical trial in patients with selected advanced solid tumors. The ongoing, multicenter, open-label, dose-escalation and dose-expansion Phase 1b trial is evaluating the safety, tolerability, pharmacokinetics and antitumor activity of Cami as monotherapy or in combination with Pembrolizumab in patients with selected advanced solid tumors.

Source: https://ir.adctherapeutics.com/press-releases/press-release-details/2020/ADC-Therapeutics-Announces-First-Patient-Dosed-with-Camidanlumab-Tesirine-Cami-in-Combination-with-Pembrolizumab-in-Ongoing-Phase-1b-Clinical-Trial-in-Selected-Solid-Tumors/default.aspx

**Dosing Starts in Phase 2 trial of Bryostatin-1 for Alzheimer's:**

( October 2020 ) Neurotrope Bioscience announced that dosing of patients has started in its Phase 2 clinical trial to further evaluate Bryostatin-1, for the treatment of moderate to severe Alzheimer's disease. The randomized, double-blind, and placebo-controlled Phase 2 study (NCT03560245) is comparing Bryostatin to placebo in individuals not receiving Namenda (memantine), for a six-month period, which will include two 11-week dosing cycles. Patients who went through a wash-out period of 30 days without talking Namenda were enrolled. The study will focus on assessing sustained cognitive benefit as measured by the Severe Impairment Battery (SIB) score.

Source: http://www.pharmabiz.com/NewsDetails.aspx?aid=131646&sid=2

## DIETARY RESEARCH:

**Omega 3 increases likelihood of developing Atrial fibrillation:**

According to a analysis by the European Society of Cardiology, omega-3 fatty acid supplements are associated with an increased likelihood of developing atrial fibrillation (AFib) in people with high triglyceride levels. The analysis looked at five randomized controlled trials and investigated the effects of omega-3 fatty acid supplementation on cardiovascular outcomes. Study participants had high triglyceride levels. They were at elevated risk of cardiovascular disease or had already received a diagnosis of it. More than 50,000 participants were given fish oils (a source of omega-3s) or a placebo. Researchers followed them up for up to 7.4 years. The dosage of fish oil was between 0.84 grams and 4 grams daily. Researchers found that omega-3 fatty acid supplementation was associated with significantly increased risks of AFib compared with a placebo.

Source: https://www.sciencedaily.com/releases/2021/04/210428192710.htm

## NEW MOLECULE ENTITY & NEW THERAPEUTIC BIOLOGICAL PRODUCT

**MARGENZA (margetuximab-cmkb) approved on December 2020-**

The U.S. Food and Drug Administration (FDA) has approved MARGENZA, a HER2/neu receptor antagonist in combination with chemotherapy, for the treatment of adult patients with metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease. MARGENZA is administered as an intravenous infusion at 15 mg/kg over 120 minutes for the initial dose, then over a minimum of 30 minutes every 3 weeks for all subsequent doses. On days when both MARGENZA and chemotherapy are to be administered, MARGENZA may be administered immediately after chemotherapy completion. The drug works by inhibiting tumor cell proliferation and reducing shedding of HER2 extracellular domain. The most common adverse drug reactions with MARGENZA in combination with chemotherapy are fatigue/asthenia, nausea, diarrhea, vomiting, constipation, headache, pyrexia, alopecia, abdominal pain, peripheral neuropathy, arthralgia/myalgia, cough, decreased appetite, dyspnea, infusion-related reactions, palmar-plantar erythrodysesthesia, and extremity pain.

Source: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761150s000lbl.pdf

**INMAZEB(atoltivimab, maftivimab, and odesivimab-ebgn) ) approved on October 2020-**

The U.S. Food and Drug Administration approved Inmazeb (atoltivimab, maftivimab, and odesivimab-ebgn), a mixture of three monoclonal antibodies, as the first FDA-approved treatment for Zaire ebolavirus (Ebola virus) infection in adult and pediatric patients. The recommended dosage of INMAZEB is 50 mg of atoltivimab, 50 mg of maftivimab, and 50 mg of odesivimab per kg diluted and administered as a single intravenous infusion. The efficacy of INMAZEB however has not been established for other species of the Ebolavirus and Marburgvirus genera. The most common adverse events were pyrexia, chills, tachycardia, tachypnea, and vomiting.

Source: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761169s000lbl.pdf

## WORLD PHARMACIST DAY

Department of Pharmacy in collaboration with Student council celebrated World Pharmacist Day 2020 by organizing various interactive institutional competition through online mode on 25 september,2020. Theme of world pharmacist day-2020 was "Transforming Global Health". Event was organized to impart the role of pharmacist in global health crisis of COVID-19 and aware the students how to interact with population in COVID-19 condition.


## WORLD HEART DAY

Event was celebrated by organizing Health check up camp for staff members of Department of Pharmacy and online webinar on 29 September,2020. Theme of World Heart Day-2020 was "Use Heart … for society, your loved ones and you". Guest speaker for Webinar was Dr. Joseph Vinod, Liverpool John Moores University, UK. Objective was to drive action to educate people that by controlling risk factors such as tobacco use, unhealthy diet and physical inactivity, at least 80% of premature deaths from heart disease and stroke could be avoided.


## WORLD CHILDREN'S DAY

It was celebrated by exploring Community Awareness Programme related to management of burn injuries on 11 November,2020. Aim of event was to improve knowledge among children's regarding precautions measures and management of Burn injuries. Students of Shree G.N Patel Vidyalaya, District: Vadodara were informed about corrections management of burns related injuries and awareness regarding misconception and related practices. Due to current pandemic situation, programme was conducted through virtual platform.


## WORLD DIABETES DAY

Department of Pharmacy organized World Diabetes Day on 11th November, 2020 by arranging Community Awareness Programme at Patient Counselling Center, Near Dhiraj General Hospital. Students of Pharmacy had prepared handmade posters for general health awareness regarding diabetes. They also explained Do's and Dont's for diabetes by circulating leaflets. Patients were satisfied with the counselling of students.

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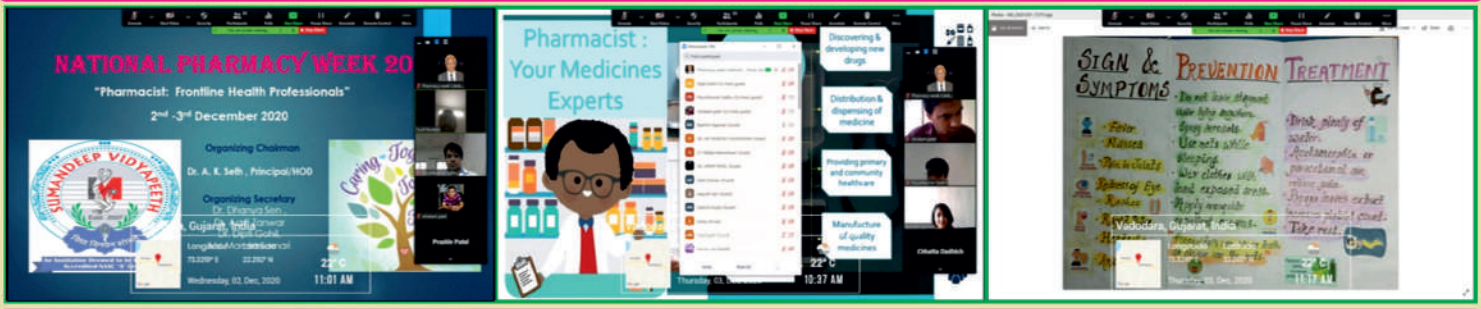
## NATIONAL PHARMACY WEEK

59th National Pharmacy week 2020 was celebrated by Department of Pharmacy on the theme "Pharmacists: Frontline Health Professionals" from 2nd – 3rd December, 2020 on virtual platform. Dr. D M Patel, Associate Professor at Graduate School of Pharmacy, Ahmedabad and Head, Establishment section of GTU was invited as a chief guest on 2nd December, 2020. Followed by the elocution competition and essay competition in which student actively participated and proposed their view on how pharmacist can help the society as the healthcare professional. On Second day 3rd December, 2020, students prepared the patient information leaflet covid 19, gastroenteritis, tuberculosis, malaria, dengue and chikungunya. In e-poster making competition students presented their creativity in a wonderful manner for casting the Pharmacist importance in Healthcare sector.




## Publications

1. Munde MK, Kulkarni NS, Rukhe NB, Sen DB. A Comprehensive Review on Analytical Method Development and Validation for SGLT-2 Inhibitors by HPLC in It's API and Dosage Form. Research Journal of Pharmacy and Technology. 2020;13(7):3472-9.
2. Munde MK, Kulkarni NS, Sen AK, Sen DB. A Novel Validated Stability Indicating Analytical Method for Simultaneous Quantification of Metformin Hydrochloride and Empagliflozin in Bulk and Marketed Formulation by HPTLC using Box-Wilson Experimental Design Approach. Indian Journal of Pharmaceutical Education and Research. 2020;54:644-56.
3. Maheshwari RA, Parmar GR, Hinsu D, Seth AK, Balaraman R. Novel therapeutic intervention of coenzyme Q10 and its combination with pioglitazone on the mRNA expression level of adipocytokines in diabetic rats. Life Sciences. 2020;258:118155.
4. Zanwar AS, Sen DB, Maheshwari RA, Chandrakar VR, Seth AK, Sen AK. Simultaneous analysis of mometasone furoate, miconazole nitrate, and nadifloxacin in cream formulation by HPTLC. Journal of Applied Pharmaceutical Science. 2020 Jul;10(07):108-15.
5. Sen AK, Sen DB, Zanwar AS, Maheshwari RA, Balaraman R. Simultaneous assessment of aliskiren hemifumarate and valsartan from it's pharmaceutical dosage form by three simple UV spectrophotometric methods. International Journal of Pharmaceutical Research. 2020;12(4):3617-24.
6. Sen DB, Sen AK, Balaraman R, Maheshwari RA, Zanwar AS. Simultaneous Assessment of Alogliptin Benzoate and Pioglitazone Hydrochloride in Combined Tablet Dosage Form by UV Spectrophotometric Methods. International Journal of Pharmaceutical Research. 2020;12(4):3625-31.
7. Zanwar AS, Sen DB, Shah MK, Kuber B, Patel KR, Patel P, Sen AK, Seth AK. Application of UV Spectrophotometric Methods in the Simultaneous Analysis of Amlodipine besylate and Celecoxib International Journal of Pharmaceutical Research. 2020;12(4):3591-98.
8. Rajput HS, Pandya H, Shah NV. Clinical Pharmacist involvement in Evaluation and Management of Drug Interactions at Critical Care Unit. International Journal of Pharmaceutical Research. 2020;12(4):3599-3605.
9. Parmar GR, Baile SB, Gohel K, Shah A, Patel S,Seth AK. An Ethno-botanical and Pharmacological Review on Phyla nodiflora. International Journal of Pharmaceutical Research. 2020;12(4):3667-73.
10. Balaraman R, Parmar G, Maheshwari RA, Dwivedi A. A Review on the Biological Effects of some Natural Products. Journal of natural remedies. 2020;20(3): 117-27.
11. Parmar G. A Paradigm Shift of Herbal Remedies in SARS-COVID-19 Pandemic. Journal of Intergrated Health Sciences. 2020;8(2):55-56.
12. Dhote V, Balaraman R, Raja MKMM. Cardioprotective Effect of Banaba on Myocardial Ischemia/Reperfusion Injury in Rats. Journal of natural remedies. 2020;20(3):140-48.

## Awards / Recognition / Achievements

1. Dr. Rajesh A Maheshwari was recognized as Judge and Moderator in a National Seminar e-Pharmavision 2020.
2. Dr. Nirmal Shah was recognized as Judge and Moderator in a National Seminar e-Pharmavision 2020.
3. Dr. Rajesh Maheshwari was recognized as reviewer in Archives of Physiology and Biochemistry an International Journal by Taylor & Francis.
4. Dr. Ashim Kumar Sen was recognized as reviewer in Plos One, an International Journal by Elsevier.
5. Dr. Kushal H Gohelwas recognized as reviewer in Plos One, an International Journal by Elsevier.
6. Dr. Ghanshyam Parmar was recognized as reviewer in Journal of Applied pharmaceutical science, an International Journal.
7. Dr. Dipti Gohil was recognized as reviewer in Journal of drug delivery science and Technology, an International Journal by Elsevier..

**Book-Post**

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