SRI RAMACHANDRA
INSTITUTE OF HIGHER EDUCATION AND RESEARCH
(Category - I Deemed to be University) Porur, Chennai

SRMC PHARMVIGIL

A Passion for Better Medicine

Pharmacovigilance Newsletter

Department of Pharmacology

SRMC & RI
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Message from Editor

Dear Readers,

Warm Greetings to each one of you

I am glad to release "**SRMC PHARMVIGIL" newsletter** Volume 3 Issue 1 January 2024 for the index period of July 2023 - Dec 2023 on behalf of SRMC-AMC, department of Pharmacology, SRMC & RI, SRIHER. This issue offers informative sections and recent relevant updates regarding drug safety information. It highlights SRMC ADR reporting statistics, Good Pharmacovigilance Practice (GPP), Periodic Drug Safety Update Report (PSUR), Artificial intelligence in Pharmacovigilance (PV), Eco pharmacovigilance, Responsibilities of sponsors in PV, case report, DRESS syndrome, materiovigilance road map and drug safety alerts. In addition to this it includes riddles, comic, crossword and unscramble to keep the readers engaged similar to our previous issues.

Sri Ramachandra Medical College –Adverse drug Monitoring Centre (SRMC-AMC) regularly sensitize the Healthcare Professionals (HCPs) of various disciplines about the importance of ADR reporting. It instils consistent effort to support PvPI and WHO-UMC in enhancing patient safety through providing valid Individual Case Safety Reports (ICSRs).

We thank Department of General Surgery, SRMC & RI, SRIHER for reporting maximum number of ADRs during July-December 2023. I believe that all HCPs will continue to work as a team for improving patient safety by contributing ceaseless efforts in strengthening PV system in SRMCH.

Happy learning and stay safe!

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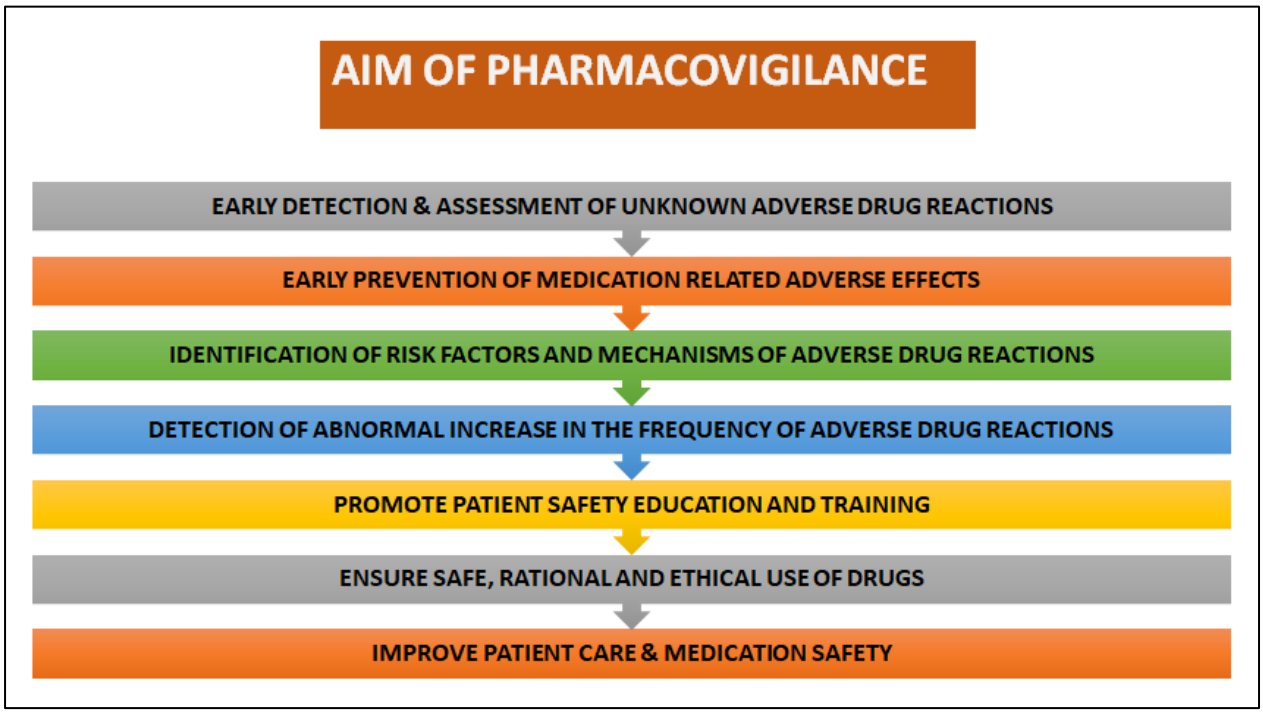
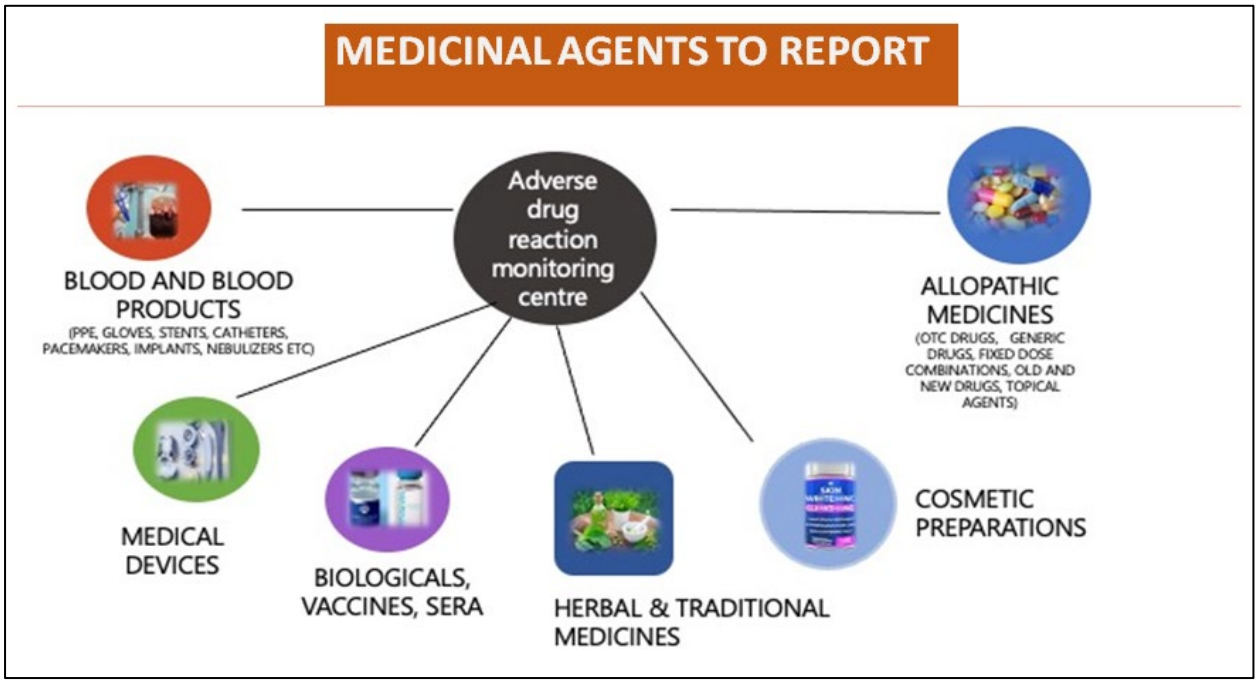
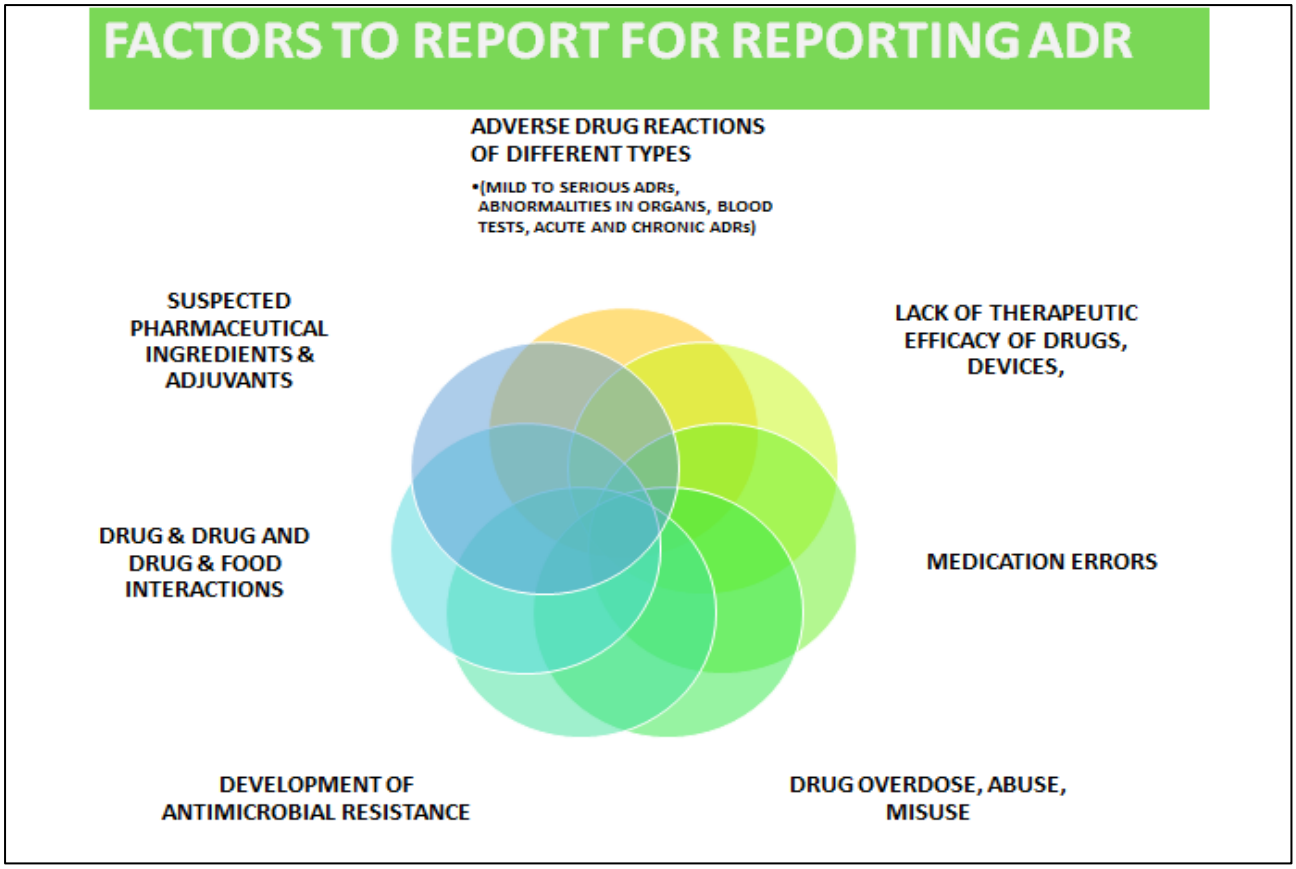
Reiterating all about Pharmacovigilance







Cutting Edge

DRESS Syndrome: Is still remaining a challenge to Treat or Prevent??

Dr. R. Kavitha
Professor & Head,
Department of Pharmacology

Drug reaction with eosinophilia and systemic symptoms syndrome (DRESS) is also known as drug induced hypersensitivity syndrome (DIHS). It is one of serious cutaneous adverse drug reactions and can be potentially life threatening condition. Earlier it was most frequently linked with phenytoin and hence initially described as phenytoin hypersensitivity syndrome. However, it was later found to be caused by various other medications such as anticonvulsants, sulphonamides, beta lactam antibiotics, anti-tuberculosis agents and non-steroidal anti-inflammatory agents (NSAIDs) (Table-1). Though the actual incidence of DRESS syndrome is unknown, it has been estimated that the overall population risk is between 1 in 1000 and 1 in 10,000 drug exposures. The diagnosis of DRESS syndrome is frequently overlooked in clinical practice because of unfamiliarity with the syndrome and its criteria. In most patients the reaction occurs 2 to 6 weeks after starting the drug, this latency period is longer than in most drug eruptions. The diagnosis of DRESS is often delayed and can be challenging, due to its variety of clinical presentations and long latency period in HSS/DRESS

The patients diagnosed with DRESS, commonly present with the clinical manifestation of fever, facial edema, lymphadenopathy, a morbilliform rash, and organ involvement. Laboratory investigations may reveal leukocytosis, atypical lymphocytes, eosinophilia, and abnormal liver and kidney function tests. It may have significant multisystem involvement, including haematologic, hepatic, renal, pulmonary, cardiac, neurologic, gastrointestinal, and endocrine abnormalities. The drugs associated with specific organ involvement risk in DRESS are depicted in Table -2. The mortality rate in DRESS has a range of 3.8% to 10%, most commonly from fulminant hepatitis with

hepatic necrosis. The pathophysiology of DRESS syndrome has not been exactly determined. However 3 key mechanisms have been considered; (i) deficiency or abnormality of the epoxide hydroxylase enzyme that detoxifies the metabolites of aromatic amine anticonvulsants; (ii) associated sequential reactivation of herpes virus family and (iii) ethnic predisposition with certain human leukocyte antigen (HLA) alleles (FIG-1).

Determination of the offending drug is often very difficult in cases of polypharmacy or when the sign and symptoms begin after a long latency period. Few clinical investigations have been established in determining the causative agent in DRESS syndrome, but they are often unreliable. Most commonly used investigations include skin patch test and lymphocyte transformation test (LTTs). However, information obtained from these tests may be helpful for physician in preventing future episodes. The most important challenge in DRESS syndrome is early recognition of the condition and immediate withdrawal of the offending drug. Failing to do so often proves crucial, leading to unwarranted morbidity and mortality. All patients should be given adequate supportive therapy to stabilise haemodynamics, antipyretics to reduce fever, and emollient and topical steroids to decrease the cutaneous symptoms. Empiric antibiotics should be avoided because it may exacerbate the condition further because of the cross-reactivity between drugs.

Systemic corticosteroids are the gold standard treatment for DRESS. Rapid resolution of rashes and fever occurs within days after initiating corticosteroids. Systemic steroid therapy should begin with a minimum dose of 1.0 mg/kg/day of prednisone or equivalent. Steroids need to be tapered slowly over 6–8 weeks, even upon clinical resolution, to prevent relapse. A multidisciplinary approach is often required for the proper management of DRESS. Long-term follow-up with laboratory testing is important to monitor relapse. Descamps et al from the consensus group of the French Society of Dermatology suggested a step-wise treatment of DRESS which is represented in FIG-2

Thus the diagnosis and management of DRESS syndrome are still remaining challenge to the physicians. Proper patient history, selection of appropriate drugs, close monitoring and early diagnosis and intervention can reduce the morbidity and mortality of the patients. Recently the Indian Pharmacopoeia commission (IPC) issued a drug safety alert for the commonly used NSAIDS, mefenamic acid which is found to cause DRESS syndrome as ADR. However, sufficient data in DRESS is not available from the Indian database regarding the causative drug and prognosis. Further studies and robust ADR reporting systems are needed in India to form a consensus statement applicable for this part of the world to overcome challenges in the prevention and management of DRESS.

Table: 1 Drugs most commonly associated with DRESS syndrome

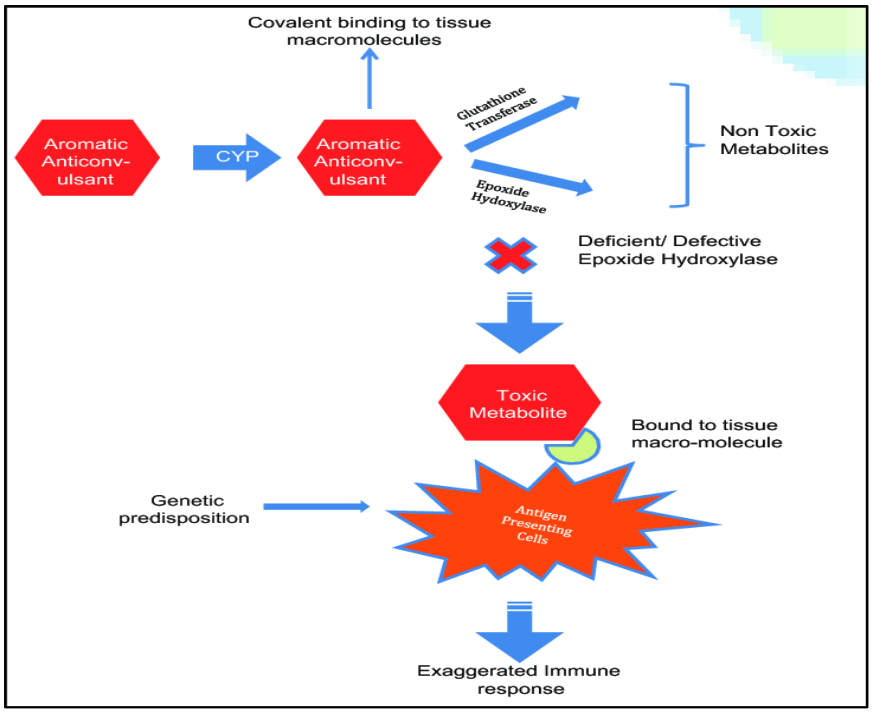
Groups	Drugs
Anti-epileptics	Aromatic antiepileptic drugs (Carbamazepine, lamotrigine phenobarbital, phenytoin, oxcarbazepine)
Antibiotics	Amoxicillin, ampicillin, azithromycin, levofloxacin, minocycline, sulfamethoxazole- trimethoprim, vancomycin
Anti-tuberculosis agents	Ethambutol, isoniazid, pyrazinamide, rifampin
NSAIDS	Aspirin, celecoxib, diclofenac, ibuprofen, piroxicam, MEFENAMIC ACID - Recent drug safety alert by IPC dated NOV 30 2023
Others	Allopurinol, amitriptyline, dapsone, hydroxychloroquine, imatinib, nevirapine, omeprazole, sulfasalazine

Table-2

Drugs associated with specific organ involvement risk in DRESS syndrome

Drugs	Organ involvement
Ampicillin	Cardiac
Dapsone	Hepatic and Renal
Carbamazepine	Renal
Phenytoin	Hepatic
Allopurinol	Renal
Minocycline	Hepatic, Pulmonary and Cardiac

FIGURE.1 –Mechanisms of aromatic anticonvulsants in Dress Syndrome.

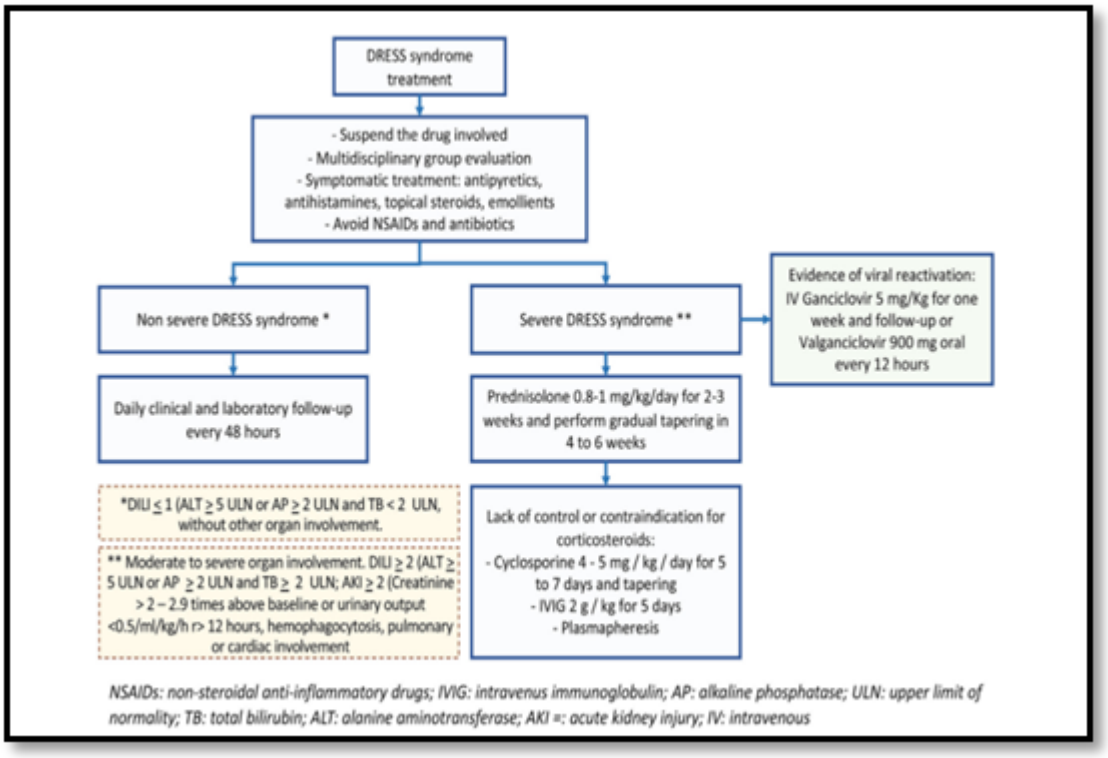


Epoxide hydrolase deficiency leads to reactive oxide arenes accumulation, causing immune response.

(CYP = cytochrome P450)

FIGURE-2

Recommended treatment algorithm for DRESS syndrome



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Pharmacovigilance responsibilities of sponsor

Dr. Ramya.S
Associate Professor

Introduction

In regard to investigational new drugs (INDs), sponsors have two key duties: safety assessment and safety reporting. This entails assessing aggregate data in conjunction with continuing safety reviews and determination of causality. A multidisciplinary team may be required for this, as well as an electronic system for storing, retrieving, and querying serious adverse event (SAE) reports and terms, as well as a fully operational drug safety unit and clinical research database. Blinded studies that do aggregate analyses and drug safety assessments should include methods for planned unblinding of safety data and its implications on trial integrity.

Safety Surveillance Plans (SSPs)

Essentially, a written, continuous Safety Surveillance Plan must be created as a methodical way to analyse medication safety information. The methods and procedures for evaluating SAEs and other crucial safety data should be outlined in this strategy. A multidisciplinary approach should be used in the strategy, and the staff members in charge of examining, evaluating, and making decisions about IND safety reporting should have clearly defined roles and duties. It is imperative to conduct frequent reviews of SAEs and other pertinent safety information to guarantee their accuracy as outlined in the plan. Clear guidelines for when unblinding may be deemed required to correctly interpret the data should be included in blinded studies, along with procedures for upholding trial integrity, which may be carried out by an unblinded review of certain events by individuals separate from study personnel or with involvement of an Independent Data Monitoring Committee. The strategy should include when the regularly planned data reviews will take place, and it should be evaluated and revised on a regular basis if needed to ensure that they accurately reflect current practice.

Causality assessment

A suspected adverse reaction (SAR) is defined as one for which there is a reasonable possibility that the drug caused the adverse event (AE). A plausible possibility, as used in IND safety reporting, denotes the presence of evidence pointing to a possible causative link between the medication and the adverse event. The sponsor bears the vital responsibility of ascertaining the cause of an adverse medication event. Reporting results from ongoing or completed studies that point to a significant risk, pooled data from several studies, epidemiological studies, published and unpublished literature, and results from in vitro or animal testing that may indicate teratology, carcinogenicity, mutagenicity, or significant organ toxicity at or near the expected human exposure are among the other duties that sponsors

Reporting serious and unexpected suspected adverse reactions (SUSARs) is also required by drug regulations. In addition, the sponsor of each such report must include any IND safety reports that have already been filed with the regulatory body regarding a comparable significant adverse response and evaluate the new event's importance in relation to similar reports from the past as well as other pertinent data. Not just the research in which the present occurrence happened, but all studies and post-marketing experiences with the drug should be included in this analysis. When assessing the significance of the current and related event, it is crucial to take into account the magnitude of the increase in rate of recurrence as well as the consistency of occurrence across research.

In conclusion, carrying out the sponsor's obligations to disclose significant drug safety incidents and possible issues is a complex process involving several employees with various levels of specialised knowledge. It is imperative that each of these professionals familiarise themselves with the regulatory requirements necessary to carry out this crucial work by means of effective and robust training for the same.

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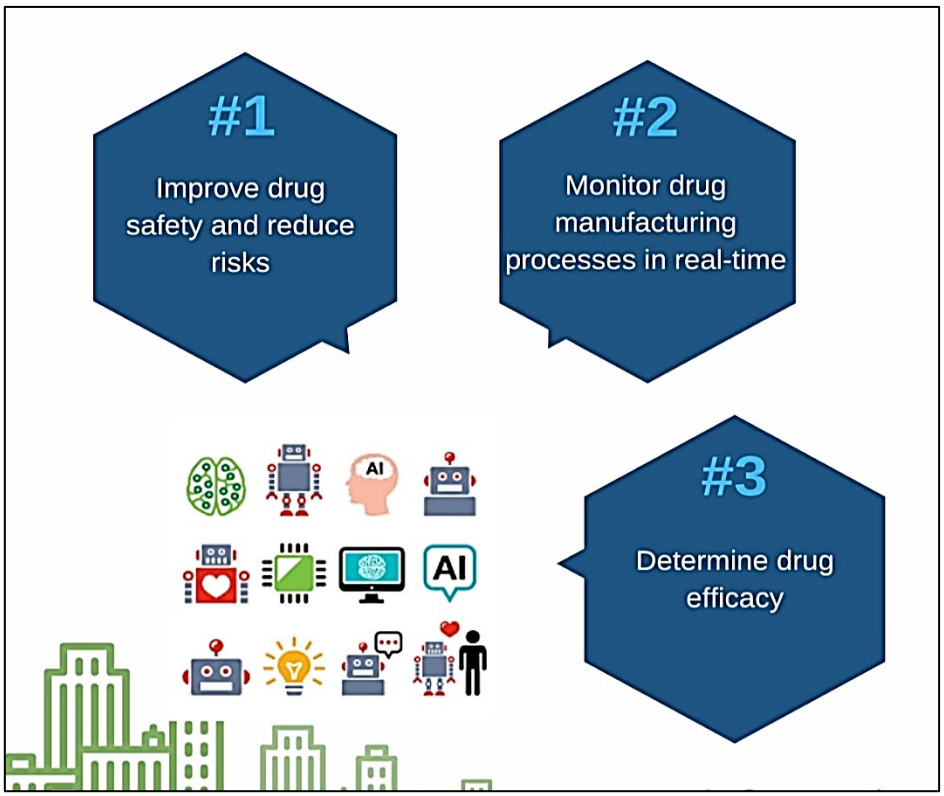
Artificial Intelligence In Pharmacovigilance

Dr.V.P.Karthik
Associate Professor

Artificial intelligence (AI) is a rapidly growing field of technology that has a lot of potential in pharmacovigilance. As AI continues to develop, it will play an even bigger role in drug safety

monitoring and adverse event detection. Some of the benefits of using AI in pharmacovigilance include faster detection of adverse events, more accurate dosing recommendations, and better prioritization of clinical trials. AI is being used increasingly to help with pharmacovigilance – the area of drug safety monitoring. The use of machine learning algorithms that are trained on large data sets from real-world experiments is a good example of how AI is being used to improve pharmacovigilance.



Need of Artificial Intelligence in Pharmacovigilance:

Artificial intelligence (AI) is a technology that has been widely used in several industries and has proven to be a valuable tool in several fields. One such field is pharmacovigilance. In pharmacovigilance, AI offers considerable advantages over human experts when it comes to data mining and regulatory compliance. AI can also play an important role in the detection and classification of adverse drug reactions (ADRs). With the growing demand for AI-enabled pharmacovigilance, organisations should consider implementing it to obtain the most out of its potential.

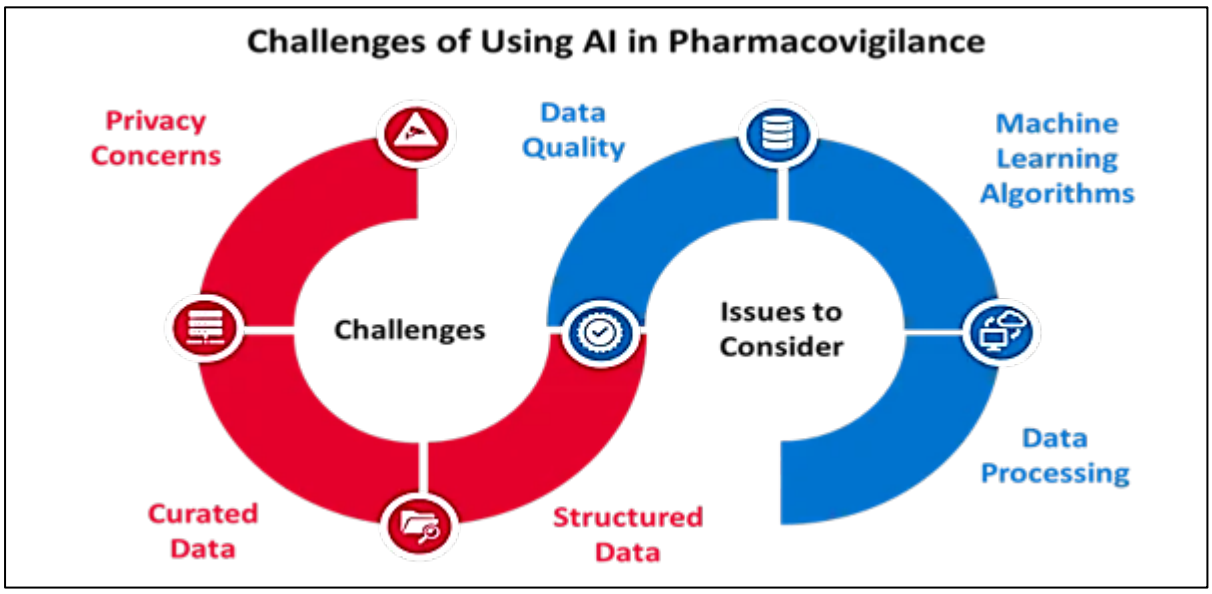
Opportunities for Artificial Intelligence in Pharmacovigilance:

Artificial intelligence (AI) is making a significant impact in pharmacovigilance. Advances in natural language understanding and image recognition allow AI to improve the quality of data received from drug studies, leading to improved decision making when it comes to drug safety. Further developments in big data analytics and cloud-based pharmacovigilance platforms will enable more sophisticated analysis of large datasets. The use of artificial intelligence can help reduce human error and speed up the process of risk assessment. AI can analyse large amounts of data to identify patterns and trends, which can help humans make better decisions more quickly. With the rapid expansion of AI and machine learning, there are many opportunities to apply these technologies in

Pharmacovigilance. Industry is looking for integrated solution that allows them to manage end-to-end pharmacovigilance tapping into hidden data and using automation for efficiency.

Challenges of Using AI in Pharmacovigilance:

Pharmacovigilance is a critical and essential function in healthcare. However, the use of artificial intelligence (AI) in this field is still a relatively new and developing field. One of the main challenges in adopting to AI is availability of structured and curated data for training the software to identify potential drug safety issues. Additionally, there are privacy concerns with using AI for pharmacovigilance, as data could potentially be used for other purposes without consent from individuals involved.



Some other issues that need to be considered when deploying AI in drug safety monitoring are data quality, machine learning algorithms and data processing. Data quality can be improved by Oversight of data management and data quality assurance processes. Machine learning algorithms can be improved by incorporating a human intelligence module into the system. Data processing can be improved by using a machine learning algorithm that is robust to missing data.

With the continued development of AI and the advancement of data-driven algorithms, it is likely that pharmacovigilance will overcome increasingly rely on AI in the coming years.

Case Report

A case of Tuberculosis in Rheumatoid arthritis patient following therapy with a Biologic agent

Dr. Sowmya. P
Assistant Professor

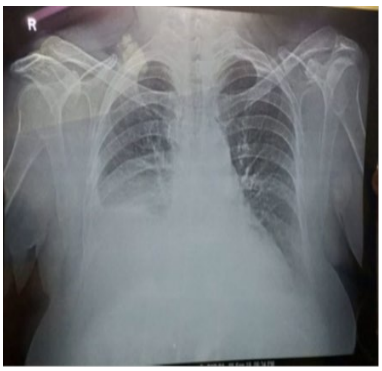
Introduction

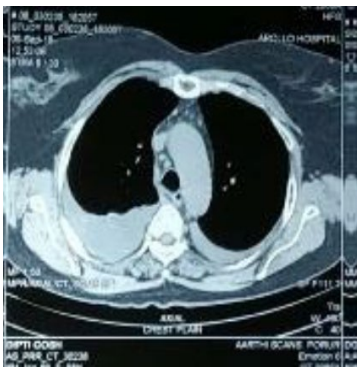
Biologic DMARDs like TNF blockers have revolutionized the treatment of Rheumatoid arthritis. These drugs are highly effective but also need stringent screening before initiation to minimize the risk of adverse effects.

Case Description

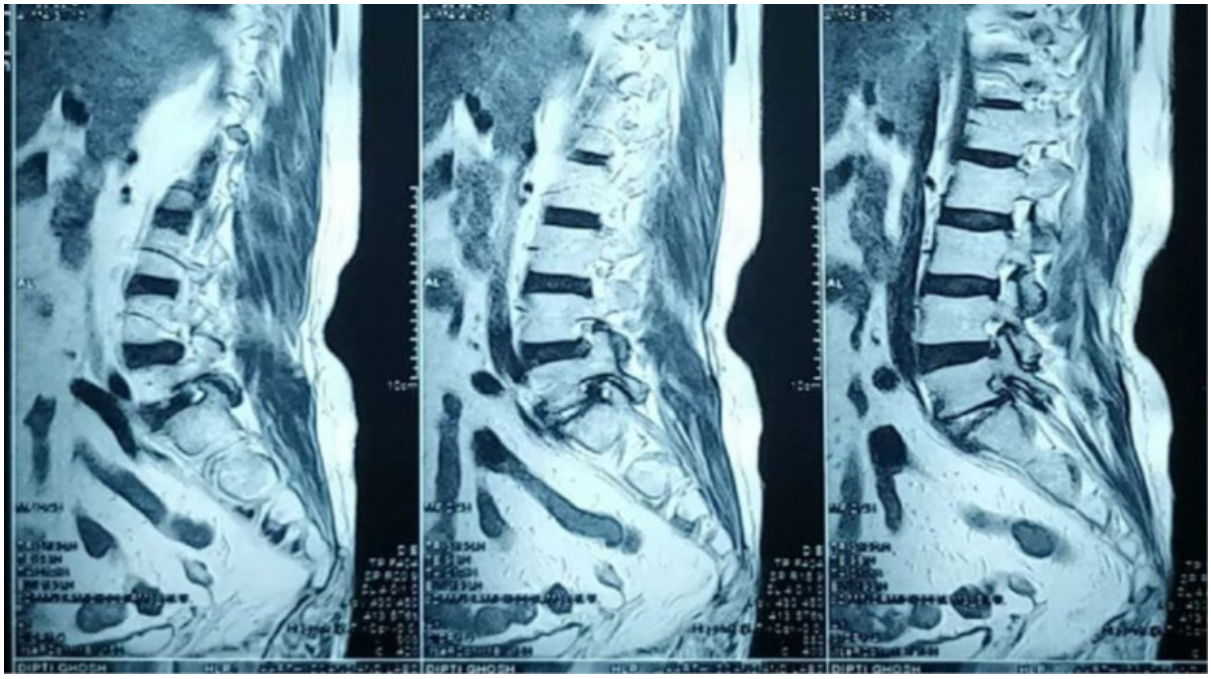
This case report documents a 54 year female patient with Rheumatoid arthritis with high disease activity, with minimal response to conventional DMARDs. She was started on injection Adalimumab 40 mg fortnightly by a doctor elsewhere. After receiving six doses of Adalimumab she presented to Rheumatology department with fever, breathlessness and abdominal discomfort. After preliminary evaluation patient was found to have bilateral pleural effusion, multiple splenic abscesses. Mantoux test was negative and IGRA was strongly positive. Pleural fluid ADA levels were elevated, and AFB was positive. Patient was started on anti-tuberculosis therapy and discharged after her symptoms improved. Patient presented again 10 days after discharge with severe back pain. MRI spine showed thin prevertebral collection. A diagnosis of disseminated tuberculosis after receiving a short course of Adalimumab was made

Chest x ray **CT chest**





Bilateral Pleural Effusion Causing Collapse Of Right Lower Lobe



MRI SPINE

Mild T2, hyperintensity in L5/S1intervertebral disc with mild erosion and minimal marrow edema in adjacent endplates at L5, S1 levels, thin pre-vertebral, pre-sacral collection L4 to S3

Discussion

Before initiation of Adalimumab, LTBI screening was not done in this patient. Chest x ray was done which was unremarkable. There is wide variability in clinical practice among doctors in optimisation of screening strategies before initiation of biologics. This patient is on immunosuppression for more than 6 years. Before initiation of strong immunosuppressive like Anti TNF, LTBI testing is mandatory which was missed in this patient. If she was screened and found to be LTBI positive, LTBI prophylaxis could have averted a serious problem like disseminated tuberculosis

Conclusion

TST, IGRA and chest x ray should be done as a part of LTBI screening for all patients being planned for anti TNF therapy

KEYWORDS

DMARD – Disease modifying anti Rheumatic drugs , ADA- Adenosine Deaminase , AFB – Acid fast Bacilli, TNF – Tumour necrosis factor , TST – Tuberculin skin test , IGRA – Interferon gamma release assay , LTBI – Latent tuberculosis infection

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Eco Pharmacology and One health perspective - Countering Anti microbial Resistance

Dr. Yazhini PM
2nd year PG

Eco pharmacology is a field that focuses on the ecological and environmental effects of pharmaceuticals. It involves studying the fate and behaviour of pharmaceuticals in the environment, their impact on non-target organisms, and the development of sustainable pharmaceuticals and drug management strategies. As we know, Pharmacovigilance is the practice of monitoring and assessing the safety and effectiveness of drugs. By incorporating eco pharmacology into pharmacovigilance, we can better understand the potential risks and harms that drugs may pose to the environment. This includes the pollution of water, soil, and animals, as well as the development of antibiotic resistance in bacteria.

In the past, many chemicals and drugs were introduced into the market without considering their consequences on the environment and human health. Considering the environmental impact of drugs is crucial for sustainable and responsible drug use. By studying eco pharmacology, we can identify potential risks, develop strategies to mitigate them, and promote more rational drug use that is beneficial for both patients and the ecosystem.

Antibiotic Resistance and One-Health Approach

Antimicrobial resistance (AMR) is one of the top ten global health threats facing us according to WHO, with rising worldwide rates driven by the misuse of antibiotics in healthcare and agriculture. Factors such as inadequate infection control, poor hygiene, and limited access to clean water exacerbate the issue. AMR leads to increased morbidity, mortality, healthcare costs, and diminished treatment effectiveness. Infections from drug-resistant microorganisms are harder to treat, resulting in longer hospital stays and higher rates of complications and death. The economic impact includes rising healthcare expenses, productivity loss, and reduced agricultural output, with estimates projecting global economic damage comparable to the 2008 financial crisis by 2050.

Efforts to combat AMR include the World Health Organization's Global Antimicrobial Resistance Surveillance System (GLASS), but challenges persist, especially in resource-limited settings.

The One-Health approach, recognizing the interconnectedness of human, animal, and environmental health, addresses antibiotic resistance through coordinated efforts in human and veterinary medicine, agriculture, and environmental science. It emphasizes understanding and addressing factors contributing to resistance, monitoring antibiotic use, and implementing strategies to prevent spread, fostering a collaborative, multidisciplinary effort for sustainable solutions.

Wastewater Treatment Plants as observatories for Antimicrobial resistance

With increasing construction of wastewater treatment plants in urban areas of India, these engineered ecosystems are emerging as potential “observatories” for monitoring the antibiotic residues and presence of Antibiotic Resistant Genes in bacteria present in sewage. Close monitoring of wastewater treatment plants (WWTPs) can help track antimicrobial resistance (AR) in a community in several ways:

- Surveillance of Antibiotic Resistant Bacteria (ARB) and Genes (ARGs): By monitoring both incoming and treated wastewater, WWTPs offer valuable data on AR prevalence and trends

in the community. This aids in pinpointing AR hotspots and guiding targeted interventions. WWTPs act as reservoirs for antibiotic resistance genes, providing insights into resistance mechanisms present in the community. Analysing wastewater samples helps identify and quantify ARGs, guiding interventions against antibiotic resistance.

- Identification of emerging resistance: WWTPs serve as early warning systems for emerging resistance patterns. By monitoring the wastewater for novel resistance genes or unusual patterns of resistance, public health authorities can detect and respond to emerging threats promptly.
- Long-term monitoring at WWTPs enables tracking resistance trends. Analysing data over time assesses intervention effectiveness, evaluates policy impact, and identifies areas of increasing or decreasing resistance, informing public health strategies.
- WWTP monitoring can help identify the sources of AR in the community. By comparing the resistance profiles of bacteria and ARGs in wastewater with those from specific sectors (e.g., hospitals, farms), researchers can determine the contribution of different sources to the overall resistance burden. This knowledge can guide targeted interventions and promote responsible antimicrobial use.

WWTPs and Antimicrobial resistance

In addition to the possibility of serving as an early warning system for changing resistance patterns, the WWTPs can provide AR data at the community level without involving individuals, therefore, provides more representative data without ethical challenges, with the minimum infrastructure-demanding.

Having said that, WWTPs can function as hotspots for horizontal gene transfer, enabling the spread of ARGs between different bacterial species, as WWTPs are not originally designed for elimination of either antibiotics residuals or ARB and ARGs. There is a strong need for effective communication among environmentalists, scientists, engineers and clinicians to evolve a one-health approach towards tackling AR and use WWTPs not only as observatories of Antimicrobial resistance but also evolve treatment methods to eliminate antibiotic residuals, ARBs and ARGs.

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Novel Drug Approvals For 2023: FDA's Centre For Drug Evaluation And Research CDER's New Molecular Entities And New Therapeutic Biological Products

Dr. K. Karthika
Assistant Professor

S.No	Drug name and date of Approval	Mechanism of action	Indications	Dosage and administration	Common adverse effects
1.	Lecanemab-irmb 1/6/2023	Amyloid beta-directed antibody	Alzheimer's disease	10 mg/kg - Intravenous infusion over approximately one hour, once every two weeks	Infusion-related reactions, headache and ARIA-edema.
2.	Bexagliflozin 1/20/2023	Sodium-glucose co-transporter 2 inhibitor	Type 2 diabetes mellitus as an adjunct to diet and exercise	20 mg once daily, taken in the morning orally	Female genital mycotic infections, urinary tract infection and increased urination
3.	Pirtobrutinib 1/27/2023	Selective, non-covalent BTK inhibitor, designed to block both normal and mutated forms of BTK	Relapsed or refractory mantle cell lymphoma in adults who have had at least two lines of systemic therapy	200 mg orally once daily	Fatigue, musculoskeletal pain, diarrhea, edema, dyspnea, pneumonia and bruising.
4.	Daprodustat 2/1/2023	Hypoxia-inducible factor prolyl hydroxylase inhibitor	Anemia caused by chronic kidney disease for adults on dialysis for at least four months	4 mg administered orally once daily	Hypertension, thrombotic vascular events and abdominal pain.
5.	Sparsentan 2/17/2023	Endothelin and angiotensin II receptor antagonist	To reduce proteinuria in adults with primary immunoglobulin A nephropathy at risk of rapid disease progression	400 mg once daily orally	Hepatotoxicity, peripheral edema, hypotension, dizziness, hyperkalemia and anemia

6.	Trofinetide 3/10/2023	Analogue of the neuropeptide (1-3) IGF which reduces neuroinflammation and supporting synaptic function.	Rett syndrome	35 kg to <50 kg: 10,000 mg (50 mL) PO BID ≥50 kg: 12,000 mg (60 mL) PO BID	Diarrhea and vomiting
7.	Fezolinetant 5/12/2023	Neurokinin 3 receptor antagonist	Moderate to severe hot flashes caused by menopause	45 mg tablet orally once daily	Abdominal pain, diarrhea, insomnia, back pain, hot flush and hepatic transaminase elevation
8.	Nirmatrelvir, Ritonavir 5/25/2023	Coronavirus 2 main protease (Mpro) inhibitor	Mild-to-moderate COVID-19 in adults at high risk for progression to severe COVID-19	300 mg Nirmatrelvir with 100 mg Ritonavir taken orally together twice daily for 5 days.	Dysgeusia, diarrhea, anaphylaxis and hepatotoxicity
9.	Ritlecitinib 6/23/2023	An inhibitor of JAK3 and the TEC family	Severe alopecia areata	50 mg orally once daily	Urticaria, folliculitis, pyrexia, atopic dermatitis, dizziness, blood creatine phosphokinase increased and herpes zoster
10.	Zuranolone 8/4/2023	Neuroactive steroid GABAA receptor positive modulator	Postpartum depression	50 mg orally once daily in the evening for 14 days	Somnolence, dizziness, diarrhea, fatigue, nasopharyngitis and urinary tract infection.
11.	Palovarotene 8/16/2023	Retinoic acid receptor-gamma (RAR-γ) agonist that inactivates activin receptor-like kinase 2 (Alk2) receptors	To reduce the volume of new heterotopic ossification with fibrodysplasia ossificans progressiva	5 mg once daily orally	Arthralgia, pruritis, rash, alopecia, peripheral edema and fatigue

12.	Gepirone 9/22/2023	Partial agonist of the serotonin 5-HT1A receptor	Major depressive disorder	18.2 mg administered orally once daily	Dizziness, nausea, insomnia, abdominal pain, dyspepsia and increased risk of suicidal thinking and behavior in pediatric and young adult patients
13.	Nedosiran 9/29/2023	Small interfering RNA to inhibit hepatic lactate dehydrogenase	To lower urinary oxalate levels in patients 9 years and older with primary hyperoxaluria type 1 and relatively preserved kidney function	160 mg subcutaneous once monthly	Injection site reactions
14.	Etrasimod 10/12/2023	Sphingosine 1-phosphate receptor modulator	Moderately to severely active ulcerative colitis	2 mg orally once daily	Headache, elevated liver tests and dizziness.
15.	Zilucoplan 10/17/2023	Targeted C5 complement inhibitor	Generalized myasthenia gravis in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.	Subcutaneous, once a day administration <56 kg: 16.6 mg 56 to <77 kg: 23 mg ≥77 kg: 32.4 mg	Serious meningococcal infections, injection site reactions, upper respiratory tract infection and diarrhea.

References:

1.https://www.drugs.com/newdrugs.html

2.https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-newtherapeutic-biological-products/novel-drug-approvals-2023

FOOD – DRUG INTERACTION: CNS

Dr. K. Kranthi
Assistant Professor

Grape fruit

DIAZEPAM

Grapefruit juice contains furano-coumarins and certain flavonoids which inhibit the CYP3A4 isozyme➔ Increased sedation or other CNS effects

(Avoid taking oral Diazepam with grapefruit juice)

High-tyramine foods

MAOI and high-tyramine foods➔ tyramine can quickly reach dangerous levels➔ serious spike in blood pressure and require emergency treatment.

(Avoid consuming foods that are high in tyramine if you take an MAOI)

Caffine

Amphetamine and coffee are central nervous system stimulants. Taking the two together can enhance their effects, potentially causing adverse side effects

Alcohol

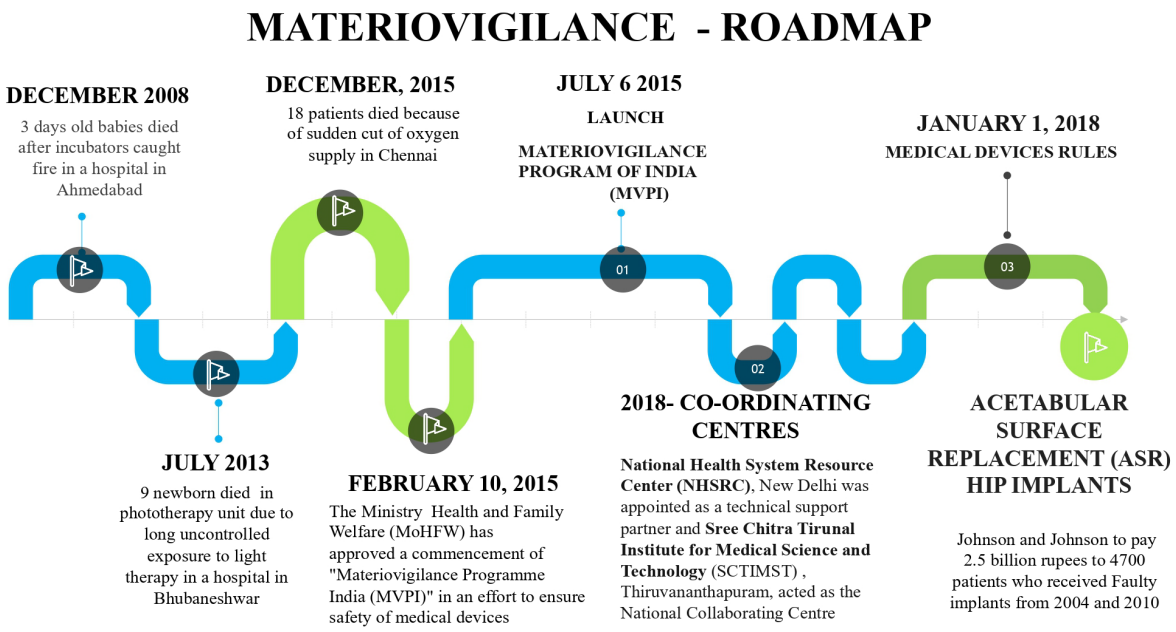
METRONIDAZOLE

Metronidazole can cause severe disulfiram-like reaction when taken with alcohol. The reaction includes flushing, headache, nausea, vomiting, sweating, and increased thirst. The reaction can last from 30 min to several hours

REFERENCE:
1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3191675/
2. https://www.hopkinsmedicine.org/health/conditions-and-diseases/fooddrug-interactions

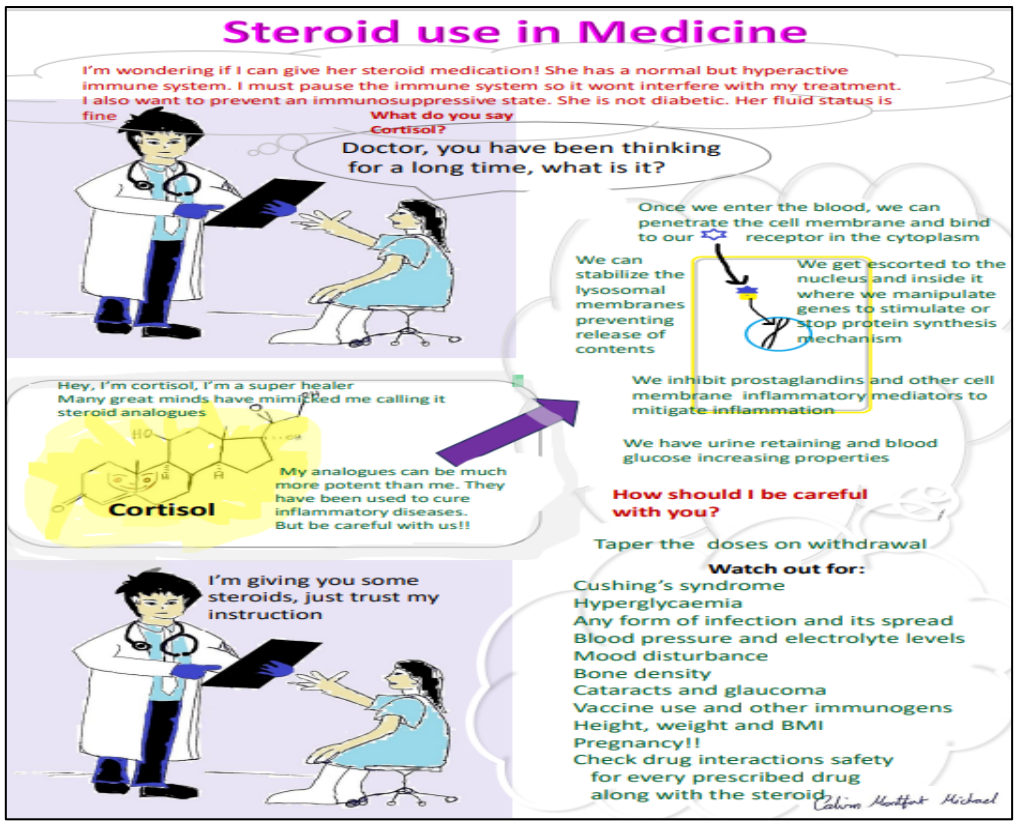
MATERIOVIGILANCE – ROAD MAP

Dr.Priya Gayathri K
Senior Resident



Comic – Steroid use in Medicine

Dr. Calvin Monfort Micheal
First year Post graduate



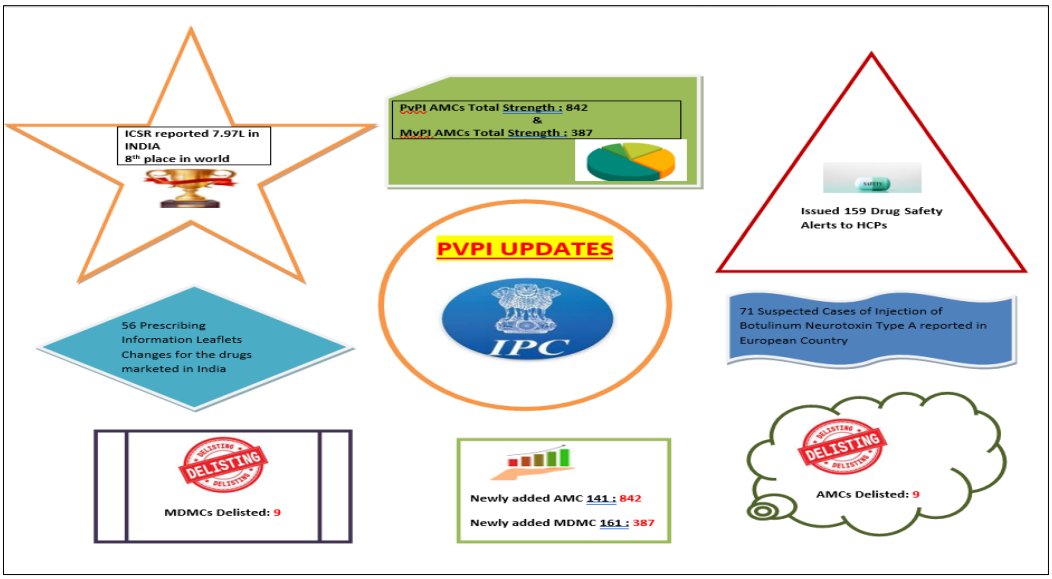
Drug safety alert – 2023

SI. No.	Suspected Drug	Indication	Adverse Drug Reaction
1	Colistimethate Sodium	For the treatment of some serious infections caused by Gram-negative bacteria, including those of the lower respiratory tract and urinary tract, when more commonly used systemic antibacterial agents may be contraindicated or may be ineffective because of bacterial resistance.	Bartter's like syndrome
2	Levonorgestrel	• Used as emergency Contraceptive. • For Control of Fertility. • For the treatment of Contraception, Menorrhagia & Endometrial Hyperplasia during Estrogen replacement therapy in women.	Deep Vein Thrombosis
3	Esomeprazole	• GERD, erosive reflux esophagitis, prevention of relapse of esophagitis & helps in eradication of H. Pylori associated peptic ulcer. • For the treatment of GERD, gastric and duodenal ulcer, Zollinger-Ellison syndrome.	Hyperprolactinaemia
4	Co-trimoxazole	Indicated in the treatment of respiratory tract infection, urogenital infections, G.I. tract infections etc.	Fixed Drug Eruption (FDE)
5	Mefenamic Acid	Treatment of rheumatoid arthritis, osteoarthritis, dysmenorrhoea, mild to moderate pain, inflammation, fever, dental pain.	DRESS Syndrome

Reference:

1. https://www.ipc.gov.in/~ajeet/ipc/mandates/pvpi/pvpi-updates/8-category-en/416-drug-safety-alerts.html

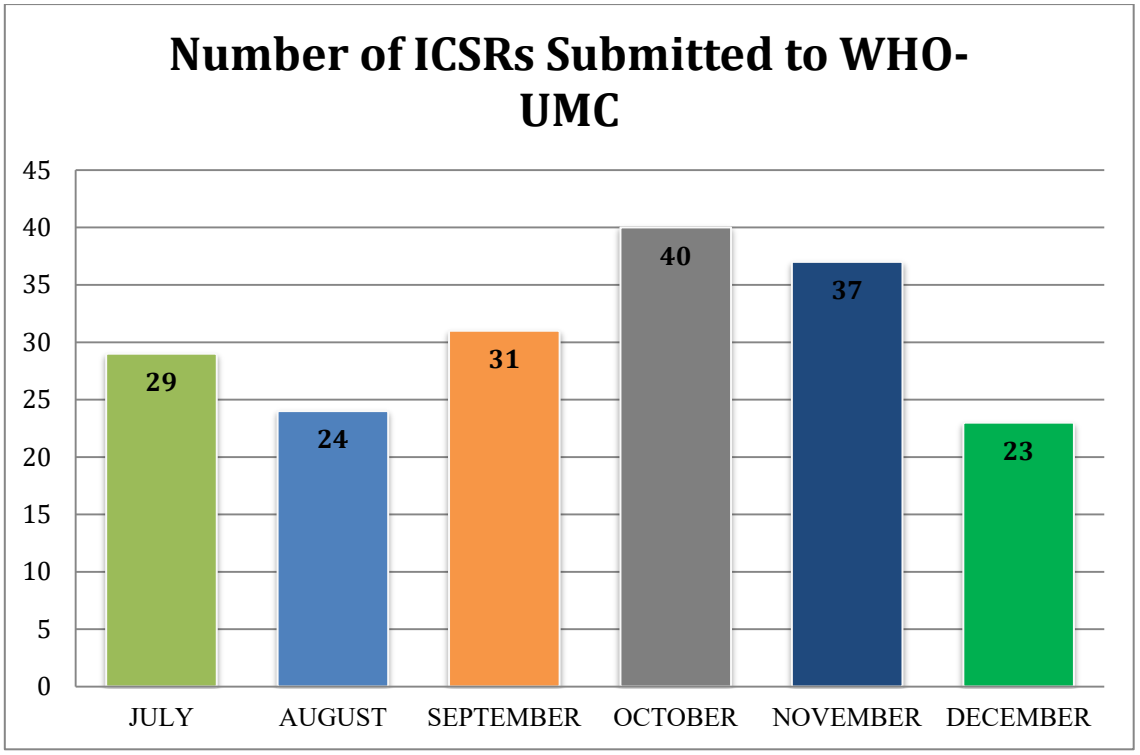
Recent PvPI Updates- 2023



Spotlight

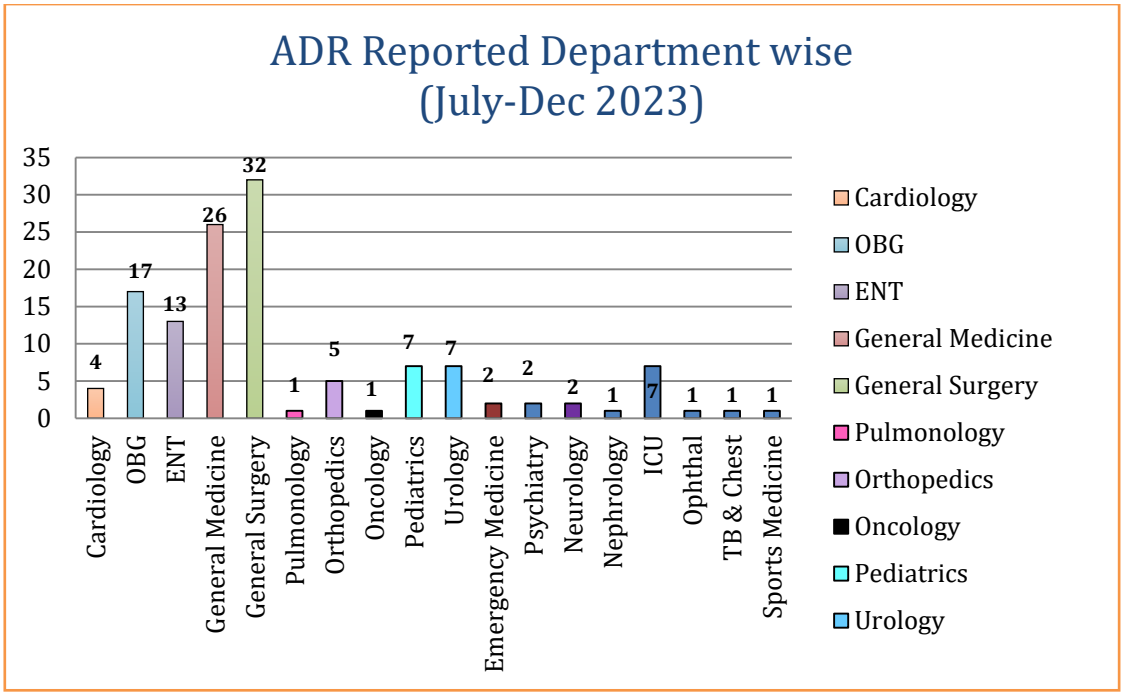
2023 (July-December) SRMC ADR Reporting Statistics

Faculties and PGs
Dept of Pharmacology



*ICSR - Individual Case Safety Report

ADRs reported by various departments of SRMC-AMC, Chennai



Departmental Happenings

PV- Sensitization Programmes (Conducted during July – December 2023)

S. No	Date of Training	Title of the Training	Department	No. of. Participants
1	04.07.2023	Materiovigilance, Importance of Materiovigilance, Roles & Responsibilities of SRMC-MDMC, Materiovigilance Case Scenario Discussion	Medication Safety Nurses and Staff Nurses	30
2	31.07.2023	Pharmacovigilance, Materiovigilance, Hemovigilance, Adverse Event Following Immunization, Roles and Responsibilities of SRMC-AMC	CRRI Students	38
3	31.07.2023	Materiovigilance, Importance of Materiovigilance, Roles & Responsibilities of SRMC-MDMC, Materiovigilance Case Scenario Discussion	Staff Nurses (ICU, OBG)	30
4	08.08.2023	Materiovigilance, Importance of Materiovigilance, Roles & Responsibilities of SRMC-MDMC, Materiovigilance Case Scenario Discussion	Medication Safety Nurses and Staff Nurses	157
5	10.08.2023	Materiovigilance, Importance of Materiovigilance, Roles & Responsibilities of SRMC-MDMC, Materiovigilance Case Scenario Discussion	Medication Safety Nurses and Staff Nurses	169
6	31.08.2023	Pharmacovigilance & Importance of ADR Reporting	Consumer/Patients	50
7	13.09.2023	MEDSAFE – A VIGIL ON MEDICAL DEVICES • Artistic e-poster competition	All Health Care Professionals	335
8	17.09.2023 – 23.09.2023	3rd National Pharmacovigilance Week	All Health Care Professionals	195

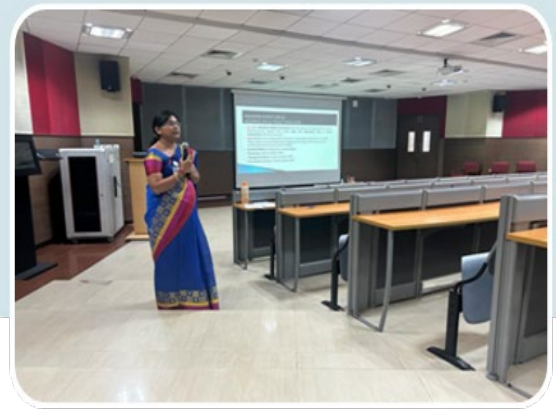
		Celebration 2023 • Walkathon • E-Poster Competition • Slogan Competition • Poem Writing Competition • Awareness Video Making • Awareness Skit • Pamphlet Distribution • Sensitizing the Urban & Rural Health Centre • Faculties participated in Pharmacovigilance Sensitization Programme in Other Colleges		
9	17.10.2023	Pharmacovigilance, Importance of ADR Reporting, Roles & Responsibilities of SRMC-AMC, Materiovigilance	Post Graduate Students	150
10	17.10.2023	Types of Vigilance, Pharmacovigilance, Importance of ADR Reporting, Roles & Responsibilities of SRMC-AMC, Materiovigilance, Importance of Materiovigilance, Roles & Responsibilities of SRMC-MDMC	BDS Students	60
11	14.11.2023	Pharmacovigilance, Importance of ADR Reporting, Roles & Responsibilities of SRMC-AMC, Materiovigilance	M.SC Clinical Research	20
12	18.11.2023	Materiovigilance, Importance of Materiovigilance, Roles & Responsibilities of SRMC-MDMC	Lab Medicine	15

13	30.11.2023	Pharmacovigilance, Importance of ADR Reporting, Roles & Responsibilities of SRMC-AMC, Materiovigilance, Importance of Materiovigilance, Roles & Responsibilities of SRMC-MDMC	MDS Students	35
14	15.12.2023	Pharmacovigilance, Importance of ADR Reporting, Roles & Responsibilities of SRMC-AMC, Materiovigilance, Importance of Materiovigilance, Roles & Responsibilities of SRMC-MDMC	Clinical Pharmacist	19

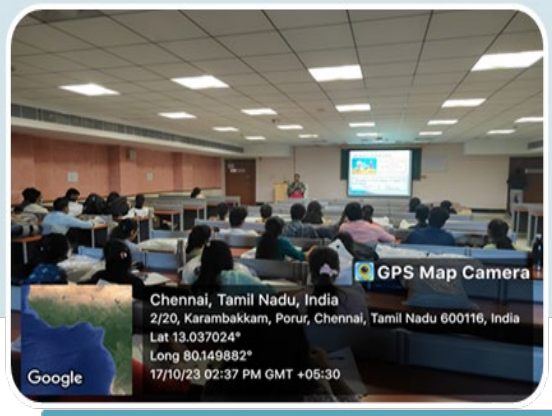
Departmental Happenings

Notable events conducted to create awareness regarding ADR reporting – July – December 2023

Glimpses from Departmental Happenings



PV Sensitization PG Students
17.10.2023



PV Sensitization BDS
17.10.2023

MEDSAFE – 2023
INAUGURATION CEREMONY

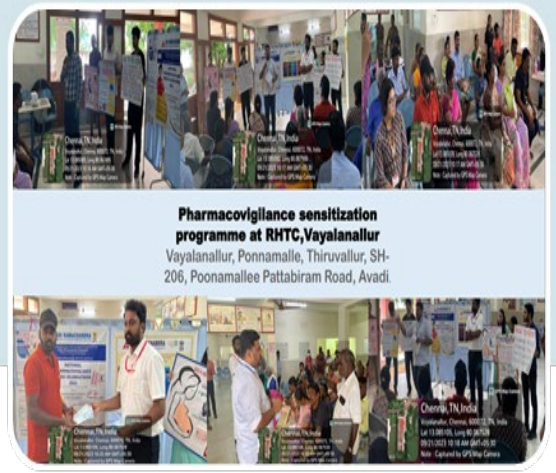
MEDSAFE – 2023
Valedictory Function

NPW 2023

Walkathon 19.09.2023

NPW 2023

PV Awareness Activity



NPW 2023

PV Awareness Activity

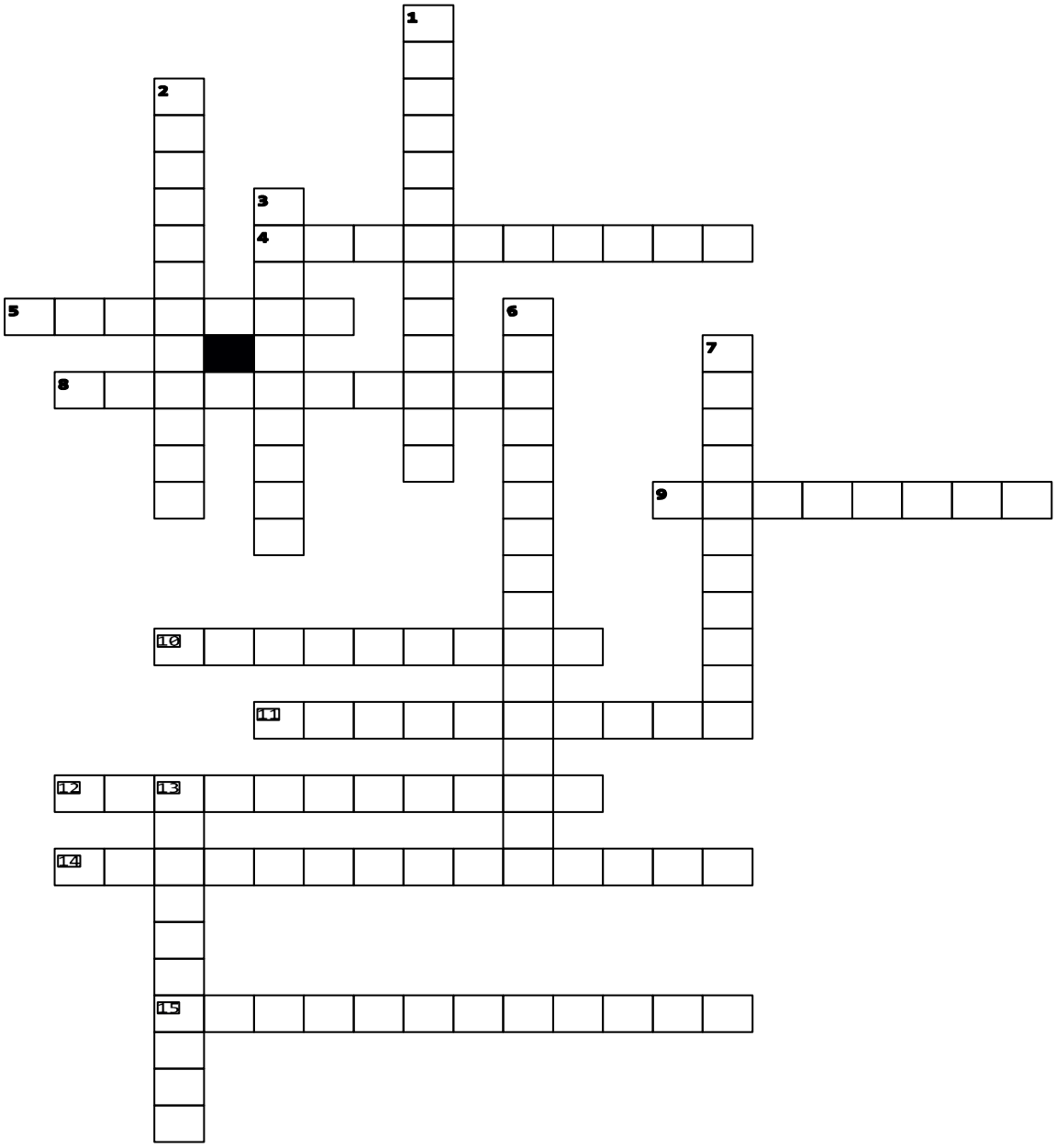
NPW 2023

Valedictory Function

Brain Storming

Crossword– Cardiovascular system and Diuretics

Dr. Jeffrey Pradeep Raj
Assistant Professor



Across:

4. Which is an antisense oligonucleotide that acts as an inhibitor of apo B 100 synthesis

5. Which antiarrhythmic has both class II and III activity

8. Blue vision in patient being treated with Paroxysmal Supraventricular Tachycardia

9. Antidote for digoxin toxicity

10. Drug of choice for termination of Paroxysmal Supraventricular Tachycardia

11. Microsomal triglyceride transfer protein inhibitor

12. Which hypolipidemic drug has highest myopathy risk

14. Patient working in a manufacturing unit gets headache and feels dizziness every Monday after his weekend off. Which compound is he exposed to?

15. Coronary steal phenomenon is seen in

Down:

1. Drug of choice for symptomatic relief for acute mountain sickness

2. Evolocumab a PCSK 9 inhibitor administered as

3. Which drug is contraindicated in interstitial lung disease

6. Drug of choice in pheochromocytoma

7. Which drug blocks L & N type Ca2+ channel

13. Which drug is preferred for chronic hypertension in pregnancy

Unscramble

Dr Deepan K, Dr Tejas M
1st Year PGs

1. Drug is the most commonly used loop diuretic - MDROEFEUSI
2. Drug utilized by athletes to eliminate steroids from their body -UTIMNEBDAE
3. Thiazide having the lowest bio availability - IRLCHOZDITAEOH
4. This drug leads to increase in plasma Ca levels- ZMLEOAOTNE
5. Most common side effect of K sparing diuretic - IYHLAAKPMREE
6. Drug of choice for patient having ventricular fibrillation - COIILADNE
7. Example of direct renin inhibitor – NRIEKSALI
8. Beta receptor antagonist - RAPOOPLNOL
9. Alpha blocker used in pheochromacytoma - XEMNIYZHAENEOBNP
10. Cardiac glycoside used as inotrope - GINXOD

Who am I?

Dr. Nidarsan Viswanathan
Senior Resident

1. I am an ingredient of Brazilian viper venom, I cause vasodilation of efferent glomerular arterioles, I will raise potassium and decrease vascular resistance.
2. I am a macrolide compound and native to Rapa Nui Island, initially used as antifungal but now I stem transplant rejection.
3. I am a polypeptide, sourced from saliva of Gila monster, I mimic the gut hormone in action, pancreatitis is my adverse drug reaction.
4. I was born in 19th century for gout, but later served a different bout, tiny in structure, tardy in action, hypothyroidism and tremor are my adverse reactions.
5. I once held a promise as a cure for morning sickness, tragedy struck and limbs were altered and a generation was scarred and I was banned, but I have my found my way back by immunomodulation.
6. I am structurally related to thyroxine and good at managing bad rhythms. I have a very long half-life and I get deposited in the eye.
7. I am an ally of serotonin, used to lift the blues and cure your obsession, but you lose sleep and I can bulk you up.
8. I am named after the Greek god of dreams .I bring relief with a calming touch and all pain is muted.
9. Within cancers battlefield, I win the battle by alkylating your DNA, but a bladder bleed is inevitable.
10. On October 16 in 1846,when I was first used in Massachusets General Hospital to remove a tumor from jaw, the doctor exclaimed" Gentlemen this is no humbug", Who am I?

ANSWERS

Crossword

Across

4. Mipomersin
5. Sotalol
8. Flecainide
9. Digiband
10. Adenosine
11. Lomitapide
12. Gemfibrozil
14. Nitroglycerine
15. Dipyridamole

Down

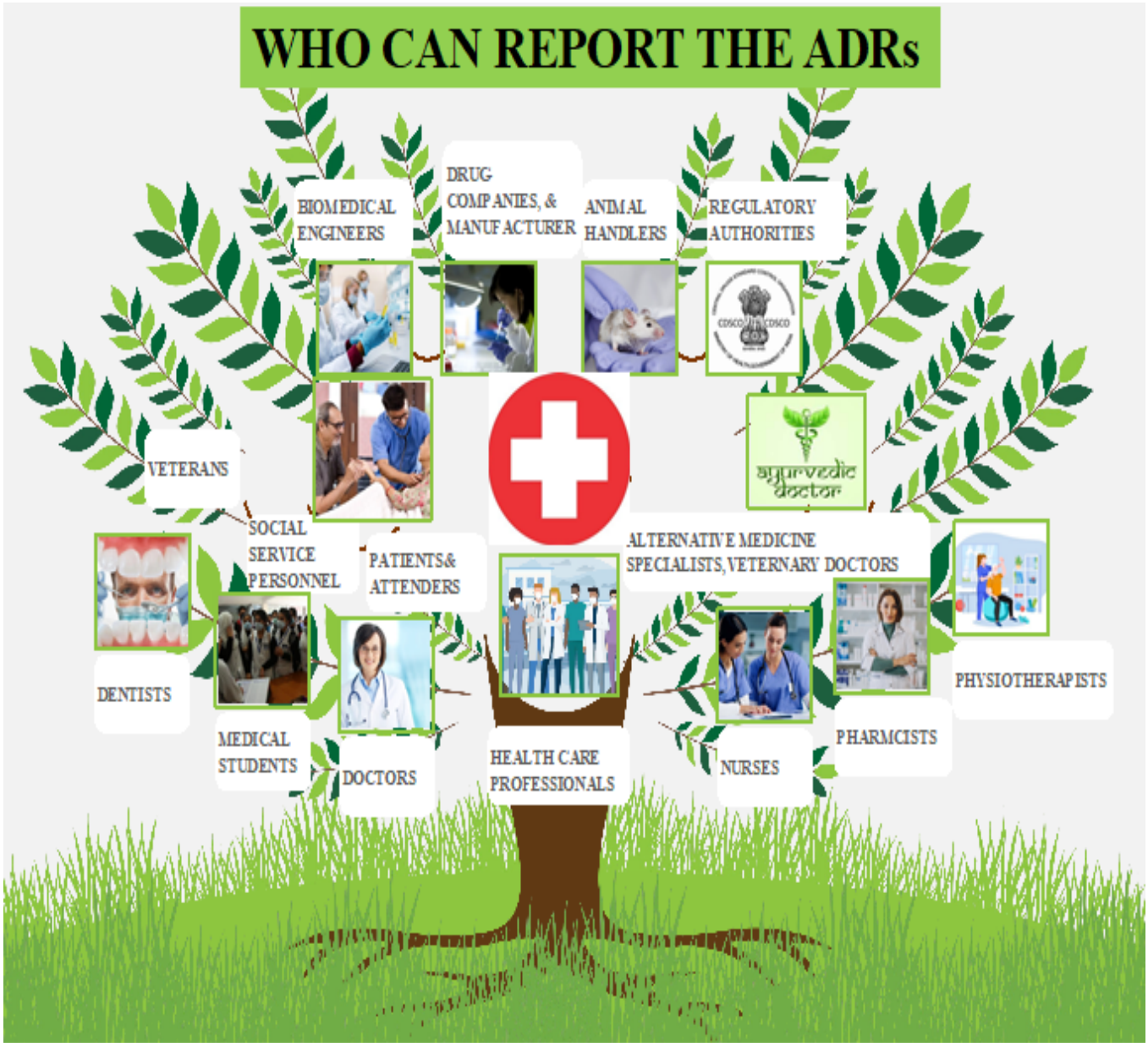
1. Acetazolamide
2. Subcutaneous
3. Amiodarone
6. Phenoxybenzamine
7. Cilnidipine
13. Methyldopa

Unscramble

1. Drug is the most commonly used loop diuretic - FUROSEMIDE
2. Drug utilized by athletes to eliminate steroids from their body - BUMETANIDE
3. Thiazide having the lowest bio availability - CHLOROTHIAZIDE
4. This drug leads to increase in plasma Ca levels- METOLAZONE
5. Most common side effect of K sparing diuretic -HYPERKALEMIA
6. Drug of choice for patient having ventricular fibrillation - LIDOCAINE
7. Example of direct renin inhibitor - ALISKIREN
8. Beta receptor antagonist - PROPANOLOL
9. Alpha blocker used in pheochromocytoma - PHENOXYBENZAMINE
10. 10.Cardiac glycoside used as inotrope – DIGOXIN

Who am I

1. CAPTOPRIL
2. SIROLIMUS
3. EXENATIDE
4. LITHIUM
5. THALIDOMIDE
6. AMIODARONE
7. FLUOXETINE
8. MORPHINE
9. CYCLOPHOSPHOMIDE
10. ETHER


WHO CAN REPORT THE ADRs
BIOMEDICAL ENGINEERS
DRUG COMPANIES, & MANUFACTURER
ANIMAL HANDLERS
REGULATORY AUTHORITIES
VETERANS
SOCIAL SERVICE PERSONNEL
PATIENTS& ATTENDERS
ALTERNATIVE MEDICINE SPECIALISTS, VETERNARY DOCTORS
DENTISTS
MEDICAL STUDENTS
DOCTORS
HEALTH CARE PROFESSIONALS
NURSES
PHARMCISTS
PHYSIOTHERAPISTS

For any suggestions/comments kindly mail to hod.pharmacology@sriramachandra.edu.in

Annexure

Version 1.4

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For **VOLUNTARY** reporting of ADRs by Healthcare Professionals

INDIAN PHARMACOPOEIA COMMISSION (National Coordination Centre-Pharmacovigilance Programme of India)

Ministry of Health & Family Welfare, Government of India, Sector-23, Raj Nagar, Ghaziabad-201002

PvPI Helpline (Toll Free) :1800-180-3024 (9:00 AM to 5:30 PM, Monday-Friday)

Initial Case ☐ Follow-up Case ☐

FOR AMC / NCC USE ONLY

Reg. No. / IPD No. / OPD No. / CR No. :

AMC Report No. :

Worldwide Unique No. :

A. PATIENT INFORMATION *

1. Patient Initials:

2. Age or date of birth:

3. Gender: M ☐ F ☐ Other ☐

4. Weight (in Kg.)

B. SUSPECTED ADVERSE REACTION *

5. Event / Reaction start date (dd/mm/yyyy)

6. Event / Reaction stop date (dd/mm/yyyy)

7. Describe Event/Reaction management with details , if any

12. Relevant investigations with dates :

13. Relevant medical / medication history (e.g. allergies, pregnancy, addiction, hepatic, renal dysfunction etc.)

14. Seriousness of the reaction : No ☐ if Yes ☐ (*please tick anyone*)

☐ Death (dd/mm/yyyy) ☐ Congenital-anomaly
☐ Life threatening ☐ Disability
☐ Hospitalization-Initial/Prolonged ☐ Other Medically important

15. Outcome:

☐ Recovered ☐ Recovering ☐ Not Recovered
☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S) *

S. No.	8. Name (Brand/ Generic)	Manufacturer (if known)	Batch No. / Lot No.	Expiry Date (if known)	Dose	Route	Frequency	Therapy Dates		Indication	Causality Assessment
								Date Started	Date Stopped		
i											
ii											
iii											
iv#											

9. Action taken after reaction (*please tick*)

S. No. as per C	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown
i						
ii						
iii						
iv						

10. Reaction reappeared after reintroduction of suspected medication (*please tick*)

Yes	No	Effect unknown	Dose (if re-introduced)

11. Concomitant medical product including self-medication add herbal remedies with therapy dates (Exclude those used to treat reaction)

S. No.	Name (Brand / Generic)	Dose	Route	Frequency (OD, BD, etc.)	Therapy Dates		Indication
					Date Started	Date Stopped	
i							
ii							
iii#							

Additional Information :

D. REPORTER DETAILS *

16. Name & Address : _____

_____

Pin : _____ Email : _____

Contact No- : _____

Occupation : _____ Signature : _____

17. Date of this report (dd/mm/yyyy) :

Signature and Name of Receiving Personnel :

Confidentiality : The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

Use separate page for more information

* Mandatory Fields for suspected ADR Reporting Form

Annexure

ADVICE ABOUT REPORTING

A. What to report?

All adverse events should be reported

Report non-serious, known or unknown, frequent or rare adverse drug reactions due to Medicines, Vaccines & Herbal Products.

Report every serious adverse drug reactions. A reaction is serious when the patient outcome is :

- Death
- Life-threatening
- Hospitalization (initial or prolonged)
- Disability (significant, persistent or permanent)
- Congenital anomaly
- Report intervention to prevent permanent impairment or damage

NOTE : Serious/Adverse Event following immunization can also be reported in Serious AEFI case Notification Form available on http://www.ipc.gov.in

B. Who can report?

All healthcare professionals (Clinicians, Dentists, Pharmacists and Nurse etc.) can report adverse drug reactions

C. Where to report?

Duly filled in Suspected Adverse Drug Reaction Reporting Form can be sent to the nearest Adverse Drug Reaction Monitoring Centre (AMC) or directly to the National Coordination Centre (NCC) for PvPI.

Call on Helpline (Toll Free) 1800 180 3024 to report ADRs or directly mail this filled form to pvpi.ipc@gov.in

A list of nationwide AMCs is available at : http://www.ipc.gov.in, http://www.ipc.gov.in/PvPI/pv_home.html

D.What happens to the submitted information?

- Information provided in this form is handled in strict confidence. The causality assessment is carried out at AMCs by using WHO-UMC scale. The analyzed forms are forwarded to the NCC-PvPI through ADR database. Finally the data is analyzed and forwarded to the Global Pharmacovigilance Database managed by WHO Uppsala Monitoring Centre in Sweden.
- The reports are periodically reviewed by the NCC-PvPI. The information generated on the basis of these reports helps in continuous assessment of the benefit-risk ratio of medicines.
- The Signal Review Panel of PvPI reviews the data and suggests any interventions that may be required.

E. Mandatory fields for suspected ADR Reporting Form (*)

Patient initials, age at onset of reaction, reaction term(s), date of onset of reaction, suspected medication(s) & reporter information.

For Adverse Drug Reaction Reporting Tools

- **E-mail : pvpi.ipc@gov.in**
- **PvPI Helpline (Toll Free) : 1800 180 3024** (9:00 AM to 5:30 PM, Monday-Friday)
- **ADR Mobile App : "ADRPvPI"**

NOTIFICATION SLIP FOR SUSPECTED ADVERSE DRUG REACTIONFROM SRIRAMACHANDRAMEDICALCOLLEGEHOSPITAL

SRI RAMACHANDRA HOSPITAL

ADVERSE DRUG REACTION MONITORING CENTRE

DEPARTMENT OF PHARMACOLOGY, SRI RAMACHANDRA MEDICAL COLLEGE & RESEARCH INSTITUTE
SRI RAMACHANDRA UNIVERSITY, PORUR, CHENNAI - 600 116. Email : adrsrmc@gmail.com

NOTIFICATION OF SUSPECTED ADVERSE DRUG REACTION FORM **CONFIDENTIAL**
(As per CDSCO, Ministry of Health & Family Welfare, Govt. of India)

Patient Name : Age: Sex: I.P/O.P No: Unit/Dept:

Suspected drugs/vaccines Generic name: Trade name: Batch No:

Concomitant drugs:

Diagnosis for use:

Outcomes: Fatal ☐ Recovering ☐ Recovered ☐ Continuing ☐ Unknown ☐ Others(specify) ☐

Drug started on: Drug stopped on: Date of reaction:

Brief description of reaction:

Name of the Doctor/Reporter: Signature: Date:

Please drop it in ADR drop box at DMS office (OP building) or DNS office (IP building)

SRI RAMACHANDRA PHARMACOVIGILANCE CENTRE

ADVERSE DRUG REACTIONS MONITORING CENTRE OF PvPI

PLEASE REPORT

Adverse Drug reactions

(Known or unknown, Serious or Non-Serious, Frequent or Rare)

Associated with Medicines, Medical Device, Blood Products, Vaccine and Herbal

To

Adverse Drug Reaction Monitoring Centre,
Sri Ramachandra Medical College, Porur, Chennai.

Dr. R. Kavitha M.D., HOD & Coordinator SRMC-AMC Ph No: 9444551410 Email: hod.pharmacology@sriramachandra.edu.in	Dr. D. Anusha M.D., Deputy Coordinator SRMC-AMC Ph No: 9884313112 Email: pvpisrmc@gmail.com	Dr. B. Prasath Kumar Pharm.D., Pharmacovigilance associate SRMC-AMC Ph No: 8056738396 Email: pvpisrmc@gmail.com

DEPT OF PHARMACOLOGY

CONTACT NUMBER - 044 2476 8027 : EXTENSION NUMBER – 226/223