As most of our readers are aware, the health sciences campus of Amrita University at Kochi is very dynamic with highly talented and internationally-recognized faculty. Amrita School of Pharmacy plays a distinctive and essential leadership role in the academic and professional evolution of the Pharmaceutical profession. Amrita Institute of Medical Sciences and Research centre (AIMS), a 1250 bedded multispecialty hospital provides all the facilities necessary for the clinical activities of the students. Students gain exposure to a variety of practice models, settings, and in-depth experiences to enhance and expand their knowledge, practice skills, judgment, and sense of responsibility necessary to support independent and collaborative practice. I am happy that our School of Pharmacy is publishing this newsletter and I am sure that our readers will find it to be Informative and Timely for those pursuing a profession of pharmacy and also for pharmacy education.

Dr. Prem Nair, Medical Director, AIMS

It is a matter of great happiness that our clinical pharmacy news letter AMRITA DRUG INTELLIGENCE is ready to start its journey with the first issue being released during Pharmacy week celebrations 2014. The clinical pharmacy activities of our Pharmacy Practice department has gained momentum in the last couple of years with the start of Pharm D programme and our faculty and students are involved in patient medication management and associated activities in about 18 clinical departments of AIMS, a tertiary care super specialty hospital. It is indeed a matter of great pride and pleasure to share some of our experiences in patient care with everyone of you! The faculty and student editorial team deserve special appreciations and I offer this news letter at the lotus feet of our beloved AMMA!

Dr. Sabitha M M.Pharm, Ph. D
CHEMOTHERAPY IV ADMIXTURE IN AIMS

Ameer Shajahan

Medical oncology center at AIMS provides expertise in the treatment of solid tumours & haematological neoplasms in adults & children. Facilities are available to undertake outpatient chemotherapies in specialised day care units. Methods of administering chemotherapy include the use of indwelling catheters and chemo ports and a biosafety cabinet for the intravenous admixture of chemotherapeutic agents.

All the Pharm.D 5th year students are trained to handle cytotoxic medications, operate biosafety cabinets, do dosage calculations and dilutions, manage spillage, document in chemotherapy log register, prepare IV admixtures of pre-medications & chemo-medications and check the appropriateness of prescriptions based on individual patient characteristics. Vertical laminar air flow hood provided facilitates aseptic technique to maintain sterility of the admixtures and at the same time protects the personnel handling the chemo drugs.

RECENT PUBLICATIONS FROM THE DEPARTMENT OF PHARMACY PRACTICE

11. Emmanuel James, Jissa Maria Cyriac. Impact of educational interventions on the physicians for early switchover of parenteral drugs to oral therapy. Eur J Hosp Pharm. Published Online First: 4 September 2014 doi:10.1136/ejhpharm-2014-000474
NEW DRUG APPROVALS

On 10th October 2014 US FDA approved the first combination pill (Harvoni® by Gilead) to treat HCV genotype 1 infection. Harvoni®, a fixed dose combination of Ledipasvir 90mg and Sofosbuvir 400mg, represents the first approved interferon and ribavirin free regimen for treatment of HCV. It should be taken orally once daily with or without food. Ledipasvir is an inhibitor of HCV NS5A protein essential for viral replication whereas sofosbuvir is a prodrug which after conversion to its active metabolite in the liver inhibits NS5B RNA polymerase essential for viral replication. Patients without cirrhosis who have a baseline RNA < 6 million IU/ml should take the combination tablet for 8 weeks where as treatment experienced patients with cirrhosis should take it for 24 weeks. Harvoni® can achieve sustained viral response in > 95% patients and may become the standard of care for treatment of HCV genotype 1 infection. Headache, fatigue, nausea, diarrhea and insomnia were the adverse effects reported.

The absorption of ledipasvir is pH dependent and hence avoid coadministration of antacids within 4 hours. Ledipasvir and sofosbuvir are substrates for the drug transporters P-glycoprotein (Pgp) and breast cancer resistance protein (BCRP), but Ledipasvir is also an inhibitor of Pgp and BCRP. Co-administration with Pgp inducers like Rifampicin or Carbamazepine can decrease the serum concentrations of the drug. Harvoni® may also markedly increase serum concentrations of Rosuvastatin, a BCRP substrate, and may lead to an increased risk of myopathy and rhabdomyolysis. The cost of Harvoni® is $1 125/tablet or $63,000 for an 8 week course.

MEDICATION THERAPY MANAGEMENT (MTM)

Dr Johnson George, Faculty of Pharmacy and Pharmaceutical Sciences, Centre for Medicine Use and Safety, Monash University, Australia

The term MTM was first coined as part of the US Medicare Modernization Act of 2003 to provide services to selected beneficiaries, with the goals of providing education, improving adherence, or detecting adverse drug events and medication misuse. Various terms such as clinical pharmacy service, medication management, medication therapy management (MTM) and medication review have been described as pharmaceutical care. The modern definition of pharmaceutical care is "a patient-centred practice in which the practitioner assumes responsibility for a patient's drug-related needs and is held accountable for this commitment". Pharmaceutical care can encompass various models, activities and definitions, and be delivered across a range of healthcare settings. Pharmaceutical care interventions generally include: a one-to-one consultation between a patient and a pharmacist with a focus on managing health or resolving medication-related problems, development of a care plan, and follow-up. Such interventions are patient-centred and are targeted towards those at high risk of medication misadventure.

MTM services aim to reduce medication-related problems and related outcomes. It is different from patient counselling because it is delivered independent of dispensing and involves collaboration with patients and providers. MTM services involve collaboration between pharmacists and other health professionals to deliver patient-centred care that optimises medication use and improves patient health outcomes. There is no consensus on the recommended mode of delivery (i.e. face-to-face or by telephone) for MTM. Specific intervention components of each MTM program may vary based on the scope and setting.

MTM consists of five standard core elements:
1. Medication therapy review (MTR) (the systematic process of collecting patient-specific information, assessing medication therapies to identify MRPs, developing a prioritised list of MRPs, and creating a plan to resolve them);
2. Personal medication record (PMR) (a comprehensive record of the patient’s medications (prescription and non-prescription medications, herbal products, and other dietary supplements);
3. Medication-related action plan (MAP) (a patient-centric document containing a list of actions for the patient to use in tracking progress for self-management);
4. Intervention and/or referral to other health professionals; and
5. Documentation and follow-up.

MTM service-level expectations include an assessment of drug-related needs, identification of drug therapy problems, and care planning and follow-up.
FROM DOCTOR’S DESK...

CLINICAL PHARMACIST - AN INTEGRAL PART OF PATIENT CARE

Dr. S Sudhindran

Around the fifteenth century period, pharmacists were not merely dispensing medicines; they in fact almost had the status of the current day physicians. Pharmacist was the point of contact for patients, even used to diagnose the disease and prescribe the appropriate medicine and then formulate it. However, by the end of the 19th century, the medical profession had taken on the current institutional form, with defined roles for physicians and surgeons and the task of pharmacist was narrowly conceived as that of a “dispenser of drugs”.

In the scenario following transplantation, clinical pharmacist once again has a much bigger function. As the immunosuppressive medications have a narrow therapeutic window, maintaining the appropriate dose to prevent rejection and at the same time avoid toxicity becomes an art. The interaction between various other medications makes this more tedious. An in-depth knowledge of the kinetics and dynamics of all these drugs is vital. More importantly, a continuous lifelong rapport with the patients is the foundation of a successful transplant programme where the clinical pharmacist is the keystone!

Dr. S Sudhindran, MS, FRCS(Eng), FRCS(Gen), is the consultant vascular & transplant surgeon at AIMS, who did the first liver transplant surgery in Kerala.

ORAL ANTICOAGULATION SERVICE MANAGED BY PHARM.D INTERNS

Warfarin and other vitamin K antagonists are used to prevent blood clot formation in patients with atrial fibrillation, post prosthetic heart valve insertion, venous thromboembolism etc. Even though warfarin is an effective and cheap drug, narrow therapeutic range, propensity to cause interaction with co-administered drugs, diet and the genetic variability in the metabolism makes its use very challenging. It can cause adverse effects like bleeding, skin necrosis, purple toe syndrome etc. Intake of vitamin K containing foods during therapy with warfarin should be limited and INR monitored regularly to maintain a target value for ensuring maximum effectiveness and minimum toxicity. Hence the clinical pharmacist has a definite role in providing adequate counselling on warfarin use, adverse effects, foods to be limited/avoided, and the importance of regular INR monitoring.

In AIMS, anticoagulation service is provided by properly trained Pharm.D interns/M.PharmPharmacy Practice students since 2011 with the approval of concerned doctors. The administration has provided an ‘on call’ mobile and the contact number (9400998746) is given to all patients on warfarin therapy. The clinical pharmacists make warfarin dose adjustments based on INR values and also clarify patient’s doubts about the therapy. The ‘on call’ service is provided 7 days a week from 10 a.m to 7 p.m and an average of 5-6 calls are received daily. 103 patients are on follow-up including 60 males and 43 females. Among the 103 patients, 30 patients were newly started on warfarin therapy, 53/73 of the old patients are maintained within the therapeutic INR range in the reporting period. Patient counselling, supplemented by booklets on oral anticoagulation, is provided to all discharged and OP patients on warfarin. We are currently handling patients from the stroke unit and are planning to extend our services to other departments too.

Report by Giby Susan and Emmanuel James
ADVERSE DRUG REACTIONS (ADRs) DETECTED DURING AUGUST - NOVEMBER 2014

ORGAN SYSTEMS AFFECTED BY ADRs (n=106)

THERAPEUTIC GROUPS IMPLICATED IN ADRs (n=106)

ADR causality assessment by Naranjo scale showed 80% as probable, 19% possible and 1% as definite ADRs

DRUG INFORMATION QUERIES ADDRESSED

A total of 211 drug information queries were received during August-November 2014. Majority (94.3%) of the queries were from physicians and the remaining from nurses and others. 41.7% of the queries were regarding therapeutic use, 28.4% were related to administration and dosage, 11.8% related to side effects/ADRs and 9.1% were regarding mechanisms of action.

ADR BULLETIN: FOCUS ON RITUXIMAB

Alice Neetha, Naveen Kumar, Neeraj Sidharthan*

In the context of adverse drug events associated with the use of rituximab in patients for treatment of malignant & nonmalignant hematological disorders, a retrospective study was conducted in the medical oncology and hematology department of AIMS. ADRs of 23 patients who had immediate and infusion related adverse events attributed to cytokine release were analyzed.

*consultant medical oncologist

PATIENT COUNSELLING CENTRE AT AIMS

All the discharged patients are given medication counselling at the annam patient counselling centre by clinical pharmacy students [Pharm. D interns/ Pharm. D 5th year/ M. Pharm. 2nd year/ Pharm. D (PB) 2nd year] of Amrita School of Pharmacy routinely as a part of the discharge process. The discharge process is completed only after the signature of the counselling pharmacist on the discharge sheet. A total of 5336 discharged patients were counselled during August – November 2014. Besides counselling on medications, patients are also given advice regarding their diseases and the required lifestyle modifications. During the counselling process some dispensing and prescribing errors could be intercepted and resolved and the data are given below. Majority of the patients expressed satisfaction with the services even though some delay occurs at peak hours.

Medication Errors Detected During Patient Counselling of Discharged Patients

<table>
<thead>
<tr>
<th>DISPENSING ERRORS</th>
<th>No. of ADRs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong strength</td>
<td>4</td>
</tr>
<tr>
<td>Drug omission</td>
<td>14</td>
</tr>
<tr>
<td>Wrong drug</td>
<td>1</td>
</tr>
<tr>
<td>Wrong label</td>
<td>12</td>
</tr>
<tr>
<td>Failed to label</td>
<td>9</td>
</tr>
<tr>
<td>Duplication of therapy</td>
<td>2</td>
</tr>
<tr>
<td>Omission of drug therapy</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PRESCRIBING ERRORS</th>
<th>No. of ADRs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong instructions for administration</td>
<td>7</td>
</tr>
<tr>
<td>Wrong strength prescribed</td>
<td>1</td>
</tr>
</tbody>
</table>
NEW GUIDELINES FOR TREATMENT OF HYPERLIPIDEMIA

Emmanuel James

The new lipid guidelines formulated jointly by the American College of Cardiology (ACC) and American Heart Association (AHA) represent substantial changes from the previous recommendations in the 2004 update of the Adult Treatment Panel (ATP)-III dyslipidemia guidelines. The new guidelines indicate that reducing the Low Density Lipoprotein (LDL-C) below a target level (i.e. ≤100mg/dl or ≤70mg/dl) is not evidence based and need not necessarily reduce the cardiovascular risk. Hence those days of focusing on laboratory number for cholesterol control are over. Randomized controlled trials have demonstrated cardiovascular risk reduction using specific statin doses and not based on LDL targets. Even titrating the statin doses to specific LDL targets is not recommended. Moreover, addition of non-statin lipid lowering agents has not been proven to reduce cardiovascular risk and hence not routinely recommended. A new risk calculator for estimation of 10 year cardiovascular risk was also introduced. (available at http://my.americanheart.org/cvriskcalculator).

The new guidelines recommend high intensity (≥ 50% reduction from base line LDL) or moderate intensity (30-49 % reduction from base line LDL) statin therapy. Moderate intensity statin therapy is advised for patients who cannot tolerate high intensity statin therapy. Atorvastatin 40-80 mg daily or rosuvastatin 20-40 mg daily is suggested for high intensity statin therapy. Moderate intensity lipid lowering can be achieved with low dose rosuvastatin 5-10 mg daily, atorvastatin 10-20 mg OD, simvastatin 10-40 mg OD, pitavastatin 2-4 mg OD, pravastatin 40-80 mg OD or fluvastatin 40 mg BD/80mg XL OD. The new policy may lead to reduced prescribing of cholesterol absorption inhibitors, bile acid sequestrants, fibrates, niacin containing products, omega-3 fatty acids, dietary supplements that contain plant stanols and sterols. It is unclear how much of the new guideline will change clinical practice as many physicians still strive for the old LDL targets at least for some of their high risk patients. An older man with low LDL level who smokes and who has moderately elevated blood pressure will qualify for statin therapy under the new guideline as his ten year cardiovascular risk will be> 7.5%. But what he really needs is to stop smoking and get his BP under control. As with any guideline the new recommendations of ACC/AHA are not fully perfect. But they are based on a multiyear review of best evidence available at present. (Circulation. 2014; 129: S1645). Recently updated NICE guidelines for hyperlipidemia also stress the role of statins in CVD risk reduction. (NICE guideline 181, Sept. 2014)

NEW GUIDELINES FOR TREATMENT OF HYPERLIPIDEMIA

Amrita PhamD Student Mr. Aneesh S A, presented a paper at 6th AASP (Asian Association of schools of Pharmacy) conference. The presentation was on “Development and Implementation of Amrita Pediatric Dosage Information Software & Preparation of Pediatric Formulary & Drug Therapy Guide in AIMS” under the guidance of Roshni P R, Senior Lecturer and Dr. P Sasidharan, HOD, Dept. of Pediatrics and Neonatology, AIMS. The event was hosted in Shah Foundation Alumini House by the GEA-NUS (Pharmaceutical Processing Laboratory, Department of Pharmacy, National University of Singapore.)

HARD FACTS

8 Cause 80%

Eight germs cause more than 80% of life-threatening blood stream infections, UTI, ventilator associated pneumonia and surgical site infections:

1. Staphylococcus aureus (38%) 
2. Enterococcus spp. (14%) 
3. Escherichia coli (12%) 
4. Coagulase-negative staphylococci (11%) 
5. Candida spp. (9%) 
6. Klebsiella pneumoniae and K. oxytoca (10%) 
7. Pseudomonas aeruginosa (8%) 
8. Enterobacter (5%)
CLINICALLY SIGNIFICANT INTERACTION BETWEEN MEROPENEM AND SODIUM VALPROATE - CASE REPORT
Giby Susan George, Emmanuel James, Soumya Alex*, Vidya Menon*

A 26 year old male was admitted in AIMS, Kochi for parieto-temporo-occipital disconnection surgery for refractory seizures. He had history of febrile convulsions since 2 years of age and later suffered multiple episodes of status epilepticus and developmental delay. He was on antiepileptic drugs since childhood and on five different anti-seizure medications (Tab. oxcarbazepine 300 mg BD; Tab. phenobarbitone 60 mg BD; Tab. sodium valproate 500 mg BD; Tab. clobazam 5 mg BD; and Tab. lacosamide 50mg OD) upon admission, in spite of which he had recurrent seizures. After the disconnection surgery, there was improvement in seizure control while on antiepileptic drugs. Later he developed acute renal failure and sepsis which were managed with haemodialysis and antibiotics respectively. During this phase he had persistent fever spikes despite negative blood, urine, and sputum cultures. But the results of a pus culture from the surgical site showed scanty growth of ESBL positive *Klebsiella pneumoniae* and Inj. *Meropenem* 500 mg BD and Inj. *Clindamycin* 600mg BD were started on 29/09/14. One day after the administration of *Meropenem*, the patient started developing recurrent seizures.

On reviewing the medication chart, clinical pharmacist identified a significant drug interaction between meropenem and sodium valproate. Based on a previous report in the literature the physician agreed to discontinue meropenem (after administration of 6 doses) and Inj. *Cefepime* 2g OD was substituted. Sodium valproate level drawn on 1/10/14 was reported to be sub-therapeutic (21.1 mcg/ml, normal range: 50-100 mcg/ml). But a repeat sodium valproate level checked after discontinuation of meropenem was found to be within the therapeutic range (95.7 mcg/ml). The patient became afebrile, symptoms improved and had seizure free period during the hospital stay thereafter.

Valproic acid (VPA) gets glucuronidated in the liver to form VPA-glucuronidate (VPA-glu), which is excreted by the kidneys. Hence one or a combination of the following mechanisms may be responsible for the reduction in valproate levels in the patient. Carbapenems may enhance the rate of glucuronidation of VPA in the liver or hasten the renal clearance of VPA-glu or inhibit the bacterial beta glucuronidase enzyme that hydrolyses VPA –glu to VPA resulting in the suppression of entero-hepatic circulation of VPA leading to decreased concentrations of VPA. Such an interaction can occur with other carbapenem antibiotics like imipenem, ertapenem and doripenem. Increasing the valproate dose does not always compensate for the reduction in serum valproate levels caused by the carbapenem. **Hence all carbapenem antibiotics should be avoided in patients receiving concurrent sodium valproate.**


*Medical ICU, AIMS (A detailed version of the article communicated to J Pharm Pharm Sci by Dr. Vidya Menon)*

THALIDOMIDE

Thalidomide was released in the market in 1957 in West Germany under the label of Contergan. Primarily prescribed as a sedative or hypnotic, thalidomide also claimed to cure "anxiety, insomnia, gastritis, and tension". Afterwards it was used for nausea and to alleviate morning sickness in pregnant women. Thalidomide became an over the counter drug in Germany around 1960, and could be bought without a prescription.

After the sale of the drug, in Germany alone, 5,000 to 7,000 infants were born with malformation of the limbs (phocomelia). Only 40% of these children survived. The drug is back in clinical use for multiple myeloma and AIDS related stomatitis.
**DEPARTMENTAL HIGHLIGHTS**

Medical camps attended by our students

Ms. Sagi Sashidharan of M. Pharm 2013 batch won 1st prize in inter-collegiate poster competition organized by Dept. of Endocrinology, AIMS, in connection with World Diabetes Day.

Ms. Sujisha Surendran of M. Pharm 2012 batch was sanctioned a research grant from Kerala State Council for Science, Technology and Environment for the project entitled “Evaluation of the effect of epidural analgesia on maternal and neonatal outcome - A prospective study” under the guidance of Roshni P R, Senior Lecturer and Dr. Nitu P V, Clinical Assistant Professor, Dept. of Anaesthesia, AIMS.

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**AMRITA DRUG INTELLIGENCE**

A NEWS LETTER FROM CLINICAL PHARMACY SERVICES
DEPARTMENT OF PHARMACY PRACTICE
AMRITA SCHOOL OF PHARMACY

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Emmanuel James

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