The American Heart Association (AHA) reports that 200,000 patients out of 700,000 with stroke or transient ischemic attacks experience recurrent stroke in the United States. AHA guidelines for stroke prophylaxis in atrial fibrillation recommend treatment options, such as warfarin (Coumadin) and newer anticoagulation therapies such as rivaroxaban (Xarelto), dabigatran (Pradaxa), and apixaban (Eliquis). Safety concerns with these agents are common and thus, healthcare professionals at The Valley Hospital contribute to conducting a thorough review of patient medications in order to select the appropriate agent for optimal care. Drug-drug interactions with CYP3A4 and P-gp inhibitors may potentiate the drug levels of anticoagulants and the most common adverse effect is increased risk of bleeding. Examples of strong CYP3A4 inhibitors are voriconazole, ketoconazole, and clarithromycin; while examples of common moderate CYP3A4 inhibitors are verapamil, diltiazem, and erythromycin. P-gp inhibitors include dronedarone, ranolazine, amiodarone, and clarithromycin.

### Package insert (PI) suggestions for use of CYP3A4 and P-gp inhibitors are as follows:

<table>
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<tr>
<th>Drug</th>
<th>Interactions/Recommendations</th>
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| Warfarin | - CYP3A4 inhibitors have potential to increase exposure of warfarin and increase INR readings.  
- Dose adjustments and routine monitoring are recommended due to increased risk of bleeding associated with concurrent use.  
- P-gp interactions with warfarin are not addressed in PI. |
| Dabigatran | - Not a substrate, inhibitor, or inducer of CYP450 enzymes.  
- There is increased exposure of dabigatran when used concurrently with P-gp inhibitors, which may cause increased risk of bleeding in patients with renal impairment.  
- Use dabigatran at a reduced dose: 75 mg twice daily (normal dosing is 150 mg twice daily) in patients with moderate renal impairment (creatinine clearance [CrCl] 30-50 mL/min) with dronedarone or oral ketonazole.  
- Not necessary to adjust dose with verapamil, amiodarone, quinidine, clarithromycin, ticagrelor.  
- With P-gp inhibitors, information for one agent should not be extrapolated for use with other P-gp inhibitors. |
| Rivaroxaban | - Concomitant use with strong CYP3A4 and P-gp inhibitors increases exposure of rivaroxaban, which may result in bleeding risk.  
- Should not be used in patients with CrCl <80 mL/min receiving simultaneous P-gp and moderate CYP3A4 inhibitors in combination unless the potential benefits outweigh the risks.  
- However, ROCKET-AF trial analysis did not show increased bleeding in patients taking concomitant P-gp and weak/moderate CYP3A4 inhibitors having a CrCl 30-50 mL/min. |
| Apixaban | - A 50% dose reduction of apixaban 5 mg or 10 mg twice daily is recommended when used in combination with strong CYP3A4 and P-gp inhibitors.  
- In patients already taking 2.5 mg twice daily, coadministration should be avoided. |

For more information, see package inserts of the individual products.

**References:**
Pharmacy Department Participates in TVH’s Teddy Bear Clinic
By Marian Gergis, PharmD

This past October, The Valley Hospital Emergency Department hosted its 3rd annual Teddy Bear clinic. Parents from local neighborhoods are invited to bring their children (ages 2-10 years) and their teddy bear to come learn and play with ED doctors, nurses, and staff, including a pharmacist. The pharmacist’s role in the clinic is to emphasize the importance of common household poisonous products. Parent, child, and teddy bear friend are shown pictures of what to stay away from, or what to do if a poisonous product is encountered. Stickers, magnets, and coloring books are handed out by the pharmacist encouraging participants to use the poison control hotline and resources when such an event is encountered. The pharmacist is also there to answer any questions participants may have.

For more information on poison prevention, please visit the NJ Poison Information and Education System (NJPIES) website:

www.njpies.org

National Poison Control Hotline 1-800-222-1222

Parents are encouraged to post the number in their home and program it into their cellphones.

Pictured is Pharmacist Marian discussing medication safety with 5 year old Michaela and her Knuffle Bunny.

Question: Can risperidone be used for obsessive-compulsive disorder?

Response:
Risperidone is an atypical antipsychotic drug and is a selective mono-aminergic antagonist with a strong affinity for cortical serotonin type 2 (5-HT2) receptors and weaker affinity for dopamine type 2 (D2) receptors. A literature search of primary and tertiary literature resulted in publications documenting risperidone use in selective serotonin reuptake inhibitors (SSRIs) refractory obsessive-compulsive disorder (OCD).

OCD is a neuropsychiatric disorder characterized by frequent, obsessive thoughts and extensive, compulsive rituals performed to reduce anxiety. Patients cannot control their thoughts nor activities for more than a short period of time. According to American Psychiatric Association guidelines for OCD, first line treatment is SSRIs such as fluvoxamine, fluoxetine, paroxetine, and sertraline, as well as tricyclic antidepressants such as clomipramine. The guidelines also recommend specific cognitive-behavioral therapy with the pharmacotherapy to treat OCD.

However, some patients’ conditions and symptoms are not well controlled on SSRIs. Maher et al. published three pooled studies comparing risperidone with placebo in OCD patients, where risperidone doses ranged from 0.5 mg to 2.25 mg by mouth per day. The study results indicated an approximately 4-fold increase in response to risperidone compared to placebo. The study also identified risperidone to be statistically significant in reducing overall mean score on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) to 3.89 points (95% CI=1.43-5.48). This indicates that risperidone may be beneficial in OCD.

In McDougle et al., 70 patients received 12 weeks of open label serotonin reuptake inhibitor (SRI). Thirty-six patients were refractory to SRI and randomized to either risperidone (n=20) or placebo (n=16) for six weeks. Patients were given risperidone 1mg/day by mouth for 7 days and then increased each week up to 6 mg per day as tolerated. Of the patients that completed the study, 14 patients in the risperidone group showed significant reduction in total Y-BOCS (24.8±4.5 to 18.3±6.2, P=0.007). Nine of eighteen risperidone treated patients responded to treatment compared with zero of fifteen in the placebo group (p=0.005). These results suggest that adding risperidone may be beneficial in reducing refractory OCD.

In conclusion, risperidone has a role in managing patients with refractory obsessive-compulsive disorder.

References:
Luckow Pharmacist receives prestigious award at the NJ Pharmacists Association Annual Convention

**Luckow pharmacist Lou Spinelli** received the Rosario J. Mannino Pharmacist of the Year Award at the NJ Pharmacists Association (NJPhA) Annual Convention in Atlantic City in October. This prestigious award honors NJPhA President Emeritus Rosario J. Mannino, RPh, and is given to a pharmacist for meritorious service to the profession of pharmacy and the NJPhA.

Lou is a graduate from St. John’s University College of Pharmacy & Health Sciences. He has practiced in community, hospital, and consulting pharmacy, and at the NJ Department of Health. Lou joined The Valley Hospital in 2002 as a staff pharmacist to initiate the program at the Blumenthal Cancer Center and is now Clinical Ambulatory Pharmacy Specialist at Luckow Pavilion Same Day Surgery Center. He is active in NJPhA where he held positions Regional President and State Trustee. In 2007, he was awarded the American Pharmacists Association “Bowl of Hygeia” award, the nation’s highest honor for a pharmacist. He is currently regional co-chair of NJPhA’s Continuing Education Committee.

Pictured is Lou Spinelli receiving the Pharmacist of the Year Award from NJPhA President, Ron Mannino.
N-acetyl-5-methoxytryptamine (Melatonin)

Melatonin is a natural medicine used for insomnia. It is an endogenous hormone secreted by the pineal gland and when administered exogenously, melatonin can normalize sleep patterns and facilitate sleep. Melatonin is available as an oral formulation and can be administered prior to bedtime. At TVH, melatonin will be available for use without restrictions.

Arformoterol tartrate (Brovana®)

Arformoterol is an inhaled beta 2 agonist indicated for patients with COPD. Arfomoterol is typically administered twice daily via nebulizer. Arformoterol has an onset of action of 7 to 20 minutes, therefore, it should only be used for maintenance treatment of COPD. At TVH, arformoterol is restricted to pulmonary and critical care medicine.

Talminogene laherparepvec (Imlygic®)

Talimogene Laherparepvec, (Imlygic) is a genetically modified live attenuated Herpes Simplex Virus Type 1 used to treat local unresectable melanoma on the skin (cutaneous and subcutaneous) and in lymph nodes after initial surgery. Its use is restricted to Luckow Infusion.

Correction: intravenous ibuprofen (Caldolor®)

The Spring 2016 issue of the newsletter incorrectly stated that IV ibuprofen (Caldolor) is restricted to pediatrics. IV ibuprofen is not restricted at TVH.

Ibuprofen injection is a NSAID indicated for the management of mild to moderate pain, and moderate to severe pain as an adjunct to opioid analgesics, and fever reduction. Ibuprofen injection is FDA-approved for adults and pediatrics 6 months of age and older.