Dear colleagues:

I would like to share with you the fall 2010 edition of the Academic Physician Quarterly (APQ). In this issue, we have a Focus topic by Dr. Adil Shujaat on the utility of pleuroscopy in the diagnosis and treatment of pleural disorders. This endoscopic examination, unlike Video-Assisted Thoracoscopic Surgery (VATS) which is performed under general anesthesia, is performed under conscious sedation. The availability of this new technology will help our patients achieve quicker recovery and may reduce their length of stay in the hospital.

Our faculty members continue to be recognized nationally and internationally for their expertise. We are especially proud that Dr. Ted Bass, Chief of the Cardiology Division and the medical director of the Cardiovascular Center, has been appointed by the American Board of Internal Medicine (ABIM) as the next chair of the ABIM Interventional Cardiology Test Committee.

On a more personal note, I am delighted to announce that on September 10, 2010 Drs. Malcolm and Patricia Foster celebrated their 50th wedding anniversary. Malcolm and Pat had been the pillars of the Department for many years. Through their efforts the Department and the University of Florida COM Jacksonville have achieved important milestones in its quest for excellence in patient care, education and scholarly productivity. On behalf of the Department of Medicine, I would like to congratulate them on achieving a remarkable milestone in their marital life and wish them many more happy years in matrimony.

The exceptional performance of our residents and faculty members has increased the visibility of the Department nationally. The recruitment of new talented faculty has added to the array of technologies we now offer to our patients. As we welcome the season of “thanksgiving”, I am happy to say that we in the Department of Medicine have a lot to give thanks for. We hope that our fortunes will only grow over the years to come.

Arshag D. Mooradian, M.D.
Professor of Medicine
Chairman, Department of Medicine
Pleuroscopy – indications in contemporary times

Pleuroscopy is endoscopic examination of the pleural cavity for the diagnosis and/or treatment of pleural disorders. It is performed under conscious sedation in the endoscopy suite through a single entry site. It is also called Medical Thoracoscopy to distinguish it from Video-Assisted Thoracoscopic Surgery (VATS) which is performed under general anesthesia with single-lung ventilation in the operating room through three entry sites.

Pleuroscopy was introduced by Jacobaeus a century ago and was widely used mainly in the pneumothorax treatment of tuberculosis to break down adhesions that prevented the diseased lung from collapsing. It lost its use when streptomycin was discovered in 1945 and antibiotics became the standard treatment of tuberculosis. The advent of laparoscopic surgery in the 1980s led to an interest in improvising the technique of pleuroscopy and paved the path for the development of VATS. VATS is now a well-established procedure for performing lung biopsy, wedge resection, lobectomy and even pneumonectomy, and much more. Although it is also used for diagnosing and treating pleural disorders, it is too invasive and expensive for such purposes. Moreover, some patients may not be able to tolerate general anesthesia and single lung ventilation. Lastly, the recent availability of a flex-rigid pleroscope (Olympus LTF 160) has revived an interest in pleuroscopy among pulmonologists across the world. This pleroscope is similar in design and handling to a bronchoscope, and is compatible with the light source and video processor set-up used for bronchoscopy.

It is against this background that I will now go over the well established indications for pleuroscopy:

1) Evaluation of Undiagnosed Pleural Effusions:
   a) Malignancy  b) Tuberculosis
2) Staging of Malignancy:
   a) Lung Cancer  b) Metastatic Cancer  c) Mesothelioma
3) Treatment of Pleural Effusions:
   a) Malignant  b) Recurrent Non-Malignant
4) Treatment of Early Empyema
5) Treatment of Spontaneous Pneumothorax
6) “Gold Standard” in research on pleural effusions

1. Evaluation of Undiagnosed Pleural Effusions: Approximately 25% of pleural effusions remain undiagnosed after repeated pleural fluid analysis and closed needle pleural biopsy (1). The reported diagnostic accuracy of pleuroscopy in this setting varies from 69 to 96 per cent depending upon the methodology of the study (2-5). The most commonly diagnosed causes are malignancy and tuberculosis.

   a) Malignancy: The sensitivity of pleural fluid cytology depends on the extent and nature of the primary malignancy and varies from 62% in patients with metastatic disease (6) to <20% in mesothelioma (7). Repeated thoracentesis improves the sensitivity by 27% at second aspiration (8). Addition of closed needle pleural biopsy increases the sensitivity by a mere 12% (9). On the other hand, the sensitivity of pleuroscopy in the diagnosis of malignant pleural effusion is high (95%) (9), and is similar for all types of malignant pleural effusions—lung cancer, extrathoracic primary malignancy, or mesothelioma (10). Pleuroscopy also allows biopsies of the diaphragmatic pleura which is not possible with the percutaneous closed needle. Pleuroscopy can provide enough tissue for accurate identification of the primary malignancy and for distinguishing metastatic adenocarcinoma and mesothelioma. This is especially important for the patient with mesothelioma who can claim financial compensation (11). Moreover, pleuroscopy can provide enough tissue for determination of hormone receptors in breast cancer, and for better characterization of lymphoma (10).

   b) Tuberculosis: Although the combined sensitivity of pleural fluid TB culture and closed needle biopsy is high (80%) in areas with a high prevalence of tuberculosis (12), the same is not true in areas with a low prevalence where the combined sensitivity is low (61%) and the sensitivity of closed needle biopsy histology alone is even lower (38%) (10). The sensitivity of pleuroscopy, on the other hand, is extremely high (94%-100%) regardless of the prevalence and high even for histology alone (94%) (10, 12). Thus, pleuroscopy can provide an immediate diagnosis of tuberculosis and avoid delays in starting anti-tuberculous therapy. Moreover, the sensitivity of positive TB cultures is twice as high (76%) (10), allowing susceptibility testing which may be of clinical importance especially in the HIV patients and immigrants from countries with high prevalence of tuberculosis and therefore also a high prevalence of multi-drug resistant tuberculosis.

   c) Other Pleural Effusions: Pleuroscopy can also provide clues to the cause of the pleural effusion. Whitish hyaline plaques indicate exposure to asbestos and suggest a diagnosis of benign asbestos pleural effusion. White fibrin deposits suggest rheumatoid pleuritis. Tortuous distended veins on the diaphragm indicate collateral vessels in cirrhosis (13).

2. Staging of Malignancy: Most patients with lung cancer and a negative pleural fluid
cytology turn out to have unresectable disease at thoracotomy (19), and pleuroscopy can help to avoid a thoracotomy in such patients (15, 16).

In patients with mesothelioma, pleuroscopy can not only provide an earlier diagnosis and better histologic classification but also more accurate staging (17,18). This is important because much better responses to local immunotherapy or chemotherapy have been reported in the early stages (I and II) (19-21).

3. Treatment of Pleural Effusions:

The pleural space can be obliterated to prevent reaccumulation of pleural fluid. This is called pleurodesis and can be achieved by the instillation of talc, doxycycline, povidone or another agent into the pleural space which causes inflammation followed by fibrosis and symphysis of the two pleural layers. Talc is the most commonly used agent for pleurodesis. It can be made into a slurry and instilled through a chest tube or it can be sprayed onto the pleural surface through a pleuroscope, a procedure called talc poudrage.

In malignant pleural effusions, talc poudrage is associated with success rates of more than 80% and is more successful than talc slurry (20) probably because it results in a more even distribution of the talc to all parts of the pleura. Early pleurodesis is preferred in malignant pleural effusions for two reasons: one— repeated thoracentesis can lead to a loculated pleural effusion and the adhesions may preclude the patient from undergoing pleuroscopy and talc poudrage, and two— delaying pleurodesis can result in a trapped lung.

In some cases of non-malignant recurrent pleural effusions that are refractory to conventional medical therapy or for which no adequate therapy exists, talc poudrage can be employed to achieve pleurodesis. Cirrhosis and chylothorax are the most common examples reported in the literature (22, 23).

4. Treatment of Early Empyema:

Pleuroscopy can be used in the treatment of early multiloculated empyema before the adhesions become too fibrous. During pleuroscopy the septations can be broken down, the pleural space completely drained, the chest tube optimally placed and the pleural surface inspected to determine if there is a need for decortication. In a retrospective study of 127 such patients identified by ultrasonography 94% were treated successfully with pleuroscopy and only 6% went on to require surgery (25).

5. Treatment of Spontaneous Pneumothorax:

Although patients with recurrent primary spontaneous pneumothorax or secondary pneumothorax have traditionally been treated surgically with bullectomy and pleural abrasion to prevent recurrence, they can be treated with pleuroscopy and talc poudrage particularly when respiratory insufficiency precludes them from undergoing surgery.

In the randomized multi-center European Study on Medical Video-Assisted Thoracoscopy (ESMEVAT) of 108 patients with primary spontaneous pneumothorax, most of which were recurrent, talc poudrage was compared to chest tube drainage and found to be more effective in preventing pneumothorax (recurrence rate 5% versus 34%) (26).

Lee et al. employed talc poudrage in the recurrence prevention of spontaneous pneumothorax in 41 patients with severe COPD who were at high risk for general anesthesia and VATS (mean age 70.7 years, mean FEV1 0.88L). The 30-day mortality was 10% and the recurrence rate in the survivors was 5.4% (27).

REFERENCES:
24. Mares CC, Mathur PN. Thoracoscopic talc pleurodesis for lymphoma induced chylothorax, a case series of twenty two treated hemithoracaces in eighteen patients. Am J Respir Crit Care Med 1997; 155:S181
A CLINICAL CASE

Frederic N. Nguyen MD, Internal Medicine Resident
Karishma Ramsubeik, MD, Internal Medicine Resident
San K Chang, M.D., Internal Medicine Resident
James M. Phillips, MD., Assistant Professor of Medicine

Angel’s trumpet associated anticholingeric delirium in the setting of alcohol intoxication: a case report.

CASE PRESENTATION

A 58 year old Caucasian gentleman with history of polysubstance abuse was brought to emergency room with new onset disorientation and visual hallucinations five hours after ingestion of a hallucinogenic drug. During an evening of alcohol intake of four beers without hard liquor, the patient ingested approximately 300 ml of a tea brewed from two large flowers of Angel’s trumpet heated in 1 liter of hot water.

On initial presentation his vital signs were temperature 97.4, pulse rate 90 beats/min, respiratory rate 16 breaths/min, blood pressure 174/99 mmHg and oxygen saturation 99% on room air.

The patient was agitated and alert, but only oriented to person (not time or place). Both pupils were dilated to 10 mm and were mildly reactive. The patient had dry mucous membranes and the skin of his face, arms, and trunk was noticeably flushed. His lungs were clear and cardiac examination revealed a systolic ejection murmur. Abdominal examination was benign with hypactive bowel sounds. During a repeat examination, mydriasis was confirmed and horizontal nystagmus was also noted.

The patient demonstrated flight of ideas, with inappropriate responses, and was not oriented to place, believing that...
he was in a garage. He had visual hallucinations of uniformed police and military officers. Although the patient had an extensive history of poly-substance abuse (including lysergic acid diethylamide LSD, diacetylmorphine, benzoylmethylecgonine, and cannabis), there was no history of street drug use within four weeks of the Angel’s trumpet ingestion. There was no history of amphetamine use. He also has a forty-pack-year history of smoking and reports drinking four beers a day for several years. The patient had no known history of other mental health problems, and there were no suicidal or homicidal ideations.

The electrocardiogram revealed sinus tachycardia with normal axis and intervals. Results of routine chemistry studies (including complete blood count, electrolytes, liver function tests, and urinalysis) were normal.

The patient was admitted to the general medicine floor and given intravenous fluids. He was also provided 2 mg intravenous lorazepam every four hours as needed for agitation. Within the subsequent forty-eight hours, the patient’s autonomic and somatic symptoms had resolved and he was discharged home with self-care.

**DISCUSSION**

We report a case of delirium following recreational use of hallucinogenic herbal toxin in the setting of alcohol abuse. This diagnosis was based on the history of voluntary use of Angel’s trumpet in conjunction with clinical findings of anti-cholinergic syndrome. Consistent with previous reports of Angel’s trumpet ingestion (1-4), the anti-cholinergic and somatic effects seen in this patient include mydriasis, visual hallucinations, incoherent thoughts and disturbances of orientation. Our patient was sufficiently treated with intravenous benzodiazepines and direct observation over forty-eight hours (2).

The name Angel’s trumpet generally refers to plants of the genus Datura or Brugmansia, both of which are common ornamental plants seen throughout the southeastern United States (5). The genus Brugmansia are woody shrubs or small trees and have pendulous flowers, while the genus Datura have more erect flowers. More commonly, Angel’s trumpet refers specifically to the large, pendulous, trumpet-shaped flowers with ornate colors and scents. Intoxication can result from ingestion of any part of the plant, which is known to contain atropine and scopolamine (4).

Medical literature on Angel’s trumpet intoxication mainly reflects prospective data review and case reports. In a prospective Australian study, Isbister et al. found thirty-three cases of moderate intoxication requiring only sedation with benzodiazepines (2). Although Greene GS et al. noted a ten-fold increase in the number of reported ingestions throughout the state of Florida in 1994 (3), there has been no significant increase in reported cases in the past decade. Additionally, there have been reports of Angel’s trumpet use associated with high risk behaviors. Marneros reported Angel’s trumpet use associated with self-amputation of the penis and tongue (3). Wiebe et al. also reported four uncomplicated cases of adolescent usage of Angel’s Trumpet associated with substance abuse (3).

This case report adds to the literature and suggests that health care providers should consider anti-cholinergic plant ingestion in the differential diagnosis of abrupt onset delirium.

**REFERENCES**


**RX UPDATES**

Kathryn DeSimone Pharm.D., PGY1 Pharmacy Resident, Russell McKelvey Pharm.D., Drug Information Specialist.

**Management of Intravascular Catheter-Related Infections**

Reprinted with some editing from Drug Update, April/May 2010 with permission.

Intravascular catheters are an integral part of modern-day medical practice; especially in an intensive care unit (ICU). Healthcare institutions use more than 150 million intravascular catheters annually. (1) Although such catheters provide necessary vascular access for administration of intravenous fluids, blood products, medications, total parenteral nutrition (TPN) therapy, and for hemodialysis, their use is not without complications. Infectious complications can include local site infection, catheter-related blood-stream infection (CRBSI), septic thrombophlebitis, abscess formation, endocarditis, and osteomyelitis. Intravascular catheter complications are associated with increased mortality, prolonged hospitalization, and higher medical costs (1).

A study published by Warren and colleagues in 2006 demonstrated that ICU patients who developed a CRBSI, after controlling for other factors, had a $12,000 increase in medical costs and a 7.5-day longer hospital length of stay (LOS) compared to those who did not. Total medical costs and hospital LOS for the ICU patients with CRBSI averaged $83,500 and 45 days, respectively (2). A 1994 study from JAMA by Pittet and colleagues put the cost increase due to CRBSI even higher at $40,000 (3).

In 2009, The Infectious Disease Society of America (IDSA) published updated guidelines for the diagnosis and management of intravascular catheter-related infections. These guidelines serve as an update to the previous guidelines published in 2001. Updates in this publication include specific criteria for diagnosis of intravascular catheter-related infections, new recommendations for antibiotic therapy, and information on catheter salvage therapy for those patients with a need for long-term intravascular catheterization (4).

Continued on Page 6
The incidence of CRBSI varies considerably by type of catheter, frequency of catheter manipulation, and patient-related factors. Peripheral venous catheters are the devices most frequently used for vascular access. Although the incidence of local or bloodstream infections associated with peripheral venous catheters is usually low, serious infectious complications produce considerable annual morbidity because of the high frequency with which such catheters are used.\(^1\)

The recent IDSA guidelines detail specific criteria for the diagnosis of intravascular catheter-related infections. These infections should not be diagnosed purely on clinical findings, as these finding can lack specificity (i.e., positive cases are correctly identified) and specificity (i.e., negative cases are correctly identified). Febrile episodes may be sensitive for CRBSI, but also have many other possible causes. Local site reactions, such as inflammation and purulence around the insertion site, have a high specificity, but lack sensitivity. Therefore, it is recommended to obtain both blood cultures and catheter cultures (if the catheter is removed) in patients with suspected CRBSI.\(^1\) The catheter tip should be cultured, as opposed to the subcutaneous section. Growth of greater than 15 colony-forming units (CFU) by a semi-quantitative (roll-plate) method reflects colonization (i.e., microbial growth within the catheter).

In regards to blood cultures, it is recommended to obtain two samples from different collection sites (one peripheral) before the initiation of antibiotic therapy. To prevent contamination when obtaining a blood sample, it is essential to disinfect the skin where the sample is to be drawn. Alcohol, tincture of iodine, or alcoholic chlorhexidine can be used. Also, when a catheter-related infection is suspected, the exit site exudates should be swabbed and cultured.\(^1\)

The updated guidelines also focus on the importance of appropriate antibiotic therapy for intravascular catheter-related infections.\(^2\) Vancomycin is recommended for empiric therapy of suspected CRBSI in healthcare settings with an elevated prevalence of methicillin-resistant Staphylococcus aureus (MRSA). Approximately two-thirds of Staph isolates at Shands Jacksonville are MRSA. The use of linezolid (Zyvox\(^\text{®}\)) for empiric coverage is NOT recommended. If a catheterized patient has a SINGLE positive blood culture that grows coagulase-negative Staph, additional cultures of blood samples obtained through the suspected catheter and from a peripheral vein should be performed BEFORE the initiation of antimicrobial therapy and/or catheter removal. Coagulase-negative Staph is part of normal skin flora and is a common possible contaminant of blood cultures; however, it can be a true pathogen causing bacteremia, or other potential complications such as endocarditis.

Empiric coverage for gram-negative bacilli should be based on local antimicrobial susceptibility data and severity of disease. Treatment options include: a fourth-generation cephalosporin, carbapenem, or beta-lactam/beta-lactamase combination, with or without an aminoglycoside. Empiric combination antibiotic coverage for multi-drug resistant (MDR) gram-negative bacilli (e.g., P. aeruginosa) should be used when CRBSI is suspected among: (1) neutropenic patients (2), severely ill patients with sepsis, or patients known to be colonized with such pathogens (3); until culture and susceptibility data are available and deescalation of antibiotic therapy can be performed.

Empiric therapy for suspected catheter-related candidemia should be used in septic patients with any of the following risk factors: (1) receiving TPN (2), prolonged use of broad-spectrum antibiotics (3), hematologic malignancy, (4) receipt of bone marrow or solid-organ transplant (5), femoral catheterization, or colonization with Candida species at multiple sites (6). Fluconazole (Diflucan\(^\text{®}\)) can be used for patients without azole exposure in the previous 3 months and in healthcare settings where the risk of C. kruerii or C. glabrata infection is very low. Otherwise, an echinocandin (e.g., caspofungin) should be used.

Once culture and susceptibility data are available, de-escalation of antimicrobial therapy should be conducted. Four to 6 weeks of antimicrobial therapy should be administered to patients with persistent infection after catheter removal (i.e., occurring more than 72 hours after catheter removal).

The necessity for catheter salvage therapy in patients who require long-term vascular access (e.g., hemodialysis, extended TPN therapy, chemotherapy infusion) is discussed in detail within the guidelines. Long-term catheters should be removed from patients with CRBSI associated with any of the following conditions: (1) severe sepsis; (2) suppurative thrombophlebitis; (3) endocarditis; (4) bloodstream infection that continues despite more than 72 hours of antimicrobial therapy to which the infecting microbes are susceptible; or (5) infections due to S. aureus, P. aeruginosa, fungi, or mycobacteria. For uncomplicated CRBSI involving long-term catheters due to pathogens other than S. aureus, P. aeruginosa, Bacillus species, Micrococcus species, Propionibacteria, fungi, or mycobacteria, treatment can be attempted without catheter removal, using both systemic and antimicrobial lock therapy.

Antibiotic lock therapy involves instillation of a highly concentrated antibiotic solution into the catheter lumen. In patients with long-term catheter placement, bacteria are likely to migrate into the catheter lumen, leading to a CRBSI that can be difficult to eradicate. Placement of supratherapeutic concentrations (i.e., 100 to 1000-times the therapeutic bloodstream concentrations with 2,500 to 5,000 units of heparin) allows for the killing of intraluminal bacteria. Several clinical trials have demonstrated the efficacy of antibiotic lock therapy. Two controlled clinical trials assessing the use of antibiotic lock therapy (n=92) demonstrated successful treatment in 75\% of patients treated with an antibiotic lock versus 58\% in control subjects.\(^6\) The likelihood of successful treatment varies with the site of infection and pathogen(s) involved. The duration of antibiotic lock therapy varies among studies from 3 to 30 days, but most studies use a 2-week duration.

In conclusion, the updated version of these guidelines provides needed information to supplement clinical judgment in the diagnosis and management of intravascular catheter infections.

References

Dr. Theodore Bass Selected as Chair of ABIM Interventional Cardiology Test Committee

Theodore A. Bass, M.D., Professor in the Department of Medicine, Division of Cardiology, with the University of Florida, College of Medicine-Jacksonville, has been appointed by the American Board of Internal Medicine (ABIM) as the next chair of the ABIM Interventional Cardiology Test Committee.

Dr. Bass, Chief of the Cardiology Division, Medical Director of the Cardiovascular Center and Program Director of the Interventional Cardiology Fellowship, will serve a four year term on the national committee beginning in 2011.

ABIM’s Test Committee members apply their individual and shared knowledge toward the development of the policies, standards and requirements for certification in their subspecialty, with a special focus on development of the certification exam.

ABIM is one of 24 medical specialty boards that make up the American Board of Medical Specialties (ABMS). Through ABMS, the boards work together to establish common standards for physicians to achieve and maintain board certification.

MEET YOUR COLLEAGUES

Ashwani Gupta, M.D., M.P.H., Assistant Professor of Medicine, Division of Nephrology & Hypertension

Dr. Gupta earned his medical degree from All India Institute of Medical Sciences in India. He completed his residency in Internal Medicine at Michigan State University and his fellowship in Nephrology at Henry Ford Hospital. He also earned a Masters in Public Health from Harvard University. Dr. Gupta’s clinical interests include hemodynamic monitoring and dialysis.

Leighton James, M.D., Associate Professor of Medicine, Division of Nephrology & Hypertension

Dr. James earned his medical degree at the University of Toronto and also completed both his residency in Internal Medicine and his fellowship in Nephrology at University of Toronto. His areas of clinical special interests include diabetic and hypertensive kidney disease, Glomerulonephritis (IgA, Immune and Pauci-Immune, other) and end stage kidney disease management. His areas of research interests include molecular pathogenesis of diabetic and hypersensitive kidney disease.

Hsiao-Yen Kuo, M.D., Assistant Professor, Division of General Internal Medicine

Dr. Kuo earned her medical degree at the Institute of Medicine in Myanmar. She completed her residency in Internal Medicine at Unity St. Mary’s and Wyckoff Heights Medical Center and her fellowship in Geriatric Medicine at the University of Florida, Gainesville. Dr. Kuo’s clinical interests include geriatric medicine.

Naeem Latif, M.D., Assistant Professor of Medicine, Division of Hematology & Medical Oncology

Dr. Latif earned his medical degree from Ayub Medical College in Pakistan. He completed his residency in Internal Medicine at the University of Pittsburgh and his fellowship in Medical Oncology from the University of Florida - Jacksonville. Dr. Latif’s research interests include medical oncology.
We have an app for that.

Our app?
The application of state-of-the-art medicine. University of Florida physicians at the Shands Jacksonville Neuroscience Institute are dedicated to diagnosing and treating disorders of the brain and nervous system – from the everyday to the very rare.

Emergency treatment for stroke. Specialized care for epilepsy, Parkinson's, sleep problems and other disorders. Advanced procedures for removing brain tumors so deep many other surgeons won't try.

Comprehensive, cutting-edge care at the Shands Jacksonville Neuroscience Institute.