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INSIDE

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Special Report: A Day in the Life of a Clinical Pharmacist

Up close and personal: Is this the face of pharmacy's future?

Nearly three hours into this day's post-op patient clinic — following early morning review of lab work, then inpatient rounds and a quick stop in the research department he directs — noon is nearing. So far, **Greg Smallwood**, RPh, has sneaked a cup of coffee, a glass of cider, and a piece of chocolate. And lunch is still an hour away.

As the lone clinical pharmacy specialist with the liver transplant surgical team at Emory University Hospital in Atlanta, the only facility undertaking liver transplants in Georgia, Smallwood is much in demand by patients and other team members.

Today, 40 patients are in the clinic. Some underwent a transplant as many as five years ago; others just several months ago. Together, a team made up of Smallwood, two surgeon-physicians, a chief and junior resident, and a transplant team nurse coordinator divide up the patients, though there is much overlapping. Every patient sees a physician. Nearly every one sees Smallwood, either alone, with or without a physician, or before or after a physician visit.

Several times, he is pulled away from his tasks by physicians seeking medication advice. Alternately offering medical and personal counseling or just small talk to patients he has come to know fairly well, Smallwood is clearly in his element. Seeing the relative success stories in the clinic, he says, outweighs his other duties of medication research and seeing patients hospitalized and in need of a transplant. "Otherwise, you'd just get depressed. You'd get a real skewed view of what you're doing."

A profession in flux

Emory hospital averages more than 80 liver transplants a year and reports a success rate of about 80%. The average patient age is 47, and the average length of stay after transplant is 18 days. Part of a 600-bed teaching hospital within the university's web of health care facilities, the hospital's pharmacy, like many around the country, is going through some changes.

Having followed the trend of establishing a decentralized pharmacy system (some five satellite pharmacies have been set up throughout the

hospital), plans are under way to return to a centralized setup, based in part on new automation being brought in. This spring, a McKesson Robot-Rx system is scheduled for installation for daily medication dose dispensing.

Staff reorganization is under way and includes placing pharmacy managers over specific pharmacy services. An assistant director of clinical services, for example, will oversee all of the clinical pharmacists, for example, who in turn will report to the director of pharmacy.

Currently, staff pharmacists rotate between clinical and dispensing duties, a basic structure that reorganization won't change. Lead pharmacists are matched with different disease states, and they must oversee the pharmacokinetics involved while working in a pharmacy satellite. Before joining the liver transplant team, for example, Smallwood served as lead pharmacist with the hematology oncology satellite.

On the down side, Emory's pharmacy department, again like many others, is suffering staff cuts by attrition. Positions are not being refilled, and new ones are not forthcoming, which is playing a role in the reorganization effort.

An indispensable pharmacist

In his role as liver transplant specialist, Smallwood, 43, is largely above the reorganization fray and far removed from the constant dispensing coming out of the satellites.

One key to the financial survival of his position at Emory is his role as director of research for the hospital's liver transplant program. Secured largely through drug company-sponsored research, grants coming into the hospital account for 40% of Smallwood's salary. "That really does help by freeing up the FTE for the hospital to use somewhere else, and the hospital is only paying for six-tenths of the FTE to have a clinical pharmacist, so it makes it affordable," he explains. "There's always a big question in the profession: If you have clinical services, who's going to pay for it? At least in part, we're answering that in innovative ways such as using research grants to subsidize my salary."

Since joining the transplant team in 1994, Smallwood has written or co-written numerous papers published in journals, including *Transplantation, Liver Transplantation and Surgery,* the *American Journal of Gastroenterology,* and *Hepatology,* among others. He has addressed conferences from Chicago to New Orleans to Rome, Italy, hosted by the International Transplant Nurses Association, the American Society of Transplant Physicians, and the American Society of Health-System Pharmacists.

When *Drug Utilization Review* visited Smallwood, he was involved in several ongoing clinical trials at Emory Hospital. The subject matter ranged from hepatitis C recurrence and steroid withdrawal to an investigation of the indications of daclizumab (Zenapax), an anti-rejection monoclonal antibody that hit the market in January 1998.

On top of that, Smallwood and his colleagues collaborate on a bimonthly in-house newsletter, and he teaches the hospital's pharmacokinetics certification to staff pharmacists.

In addition, he is pursuing his PharmD degree through a home-study Internet program offered by the University of Georgia College of Pharmacy, an undertaking he says is becoming more vital for aspiring clinical pharmacists. "When I graduated [BS in pharmacy, University of Georgia, 1979] I thought the PharmD was not going to be the practice degree; it was going to be the graduate degree, which is not the way it has turned out to be," he says.

The course offers exams, discussion, and bulletin boards over the Internet, with actual classroom time held once a month on weekends at the

COMING IN FUTURE MONTHS

- The debate over beta blockers
- Pharmacy and the Human Genome Project
- Should fast-tracking be derailed?
- NTIs and liability
- Preventing errors with antineoplastic agents

Athens, GA, campus. "Now if you're coming from an accredited school of pharmacy, you have to have the PharmD," he says, "and I think the schools are recognizing the problem so they are going to the nontraditional PharmD program."

Making the rounds

By 8:30 in the morning, Smallwood begins "clinic day" by scanning the IntelliHealth Online Web site, looking for new drug approvals and related medication topics relevant to liver function. "You must be ready to answer questions," he says, from patients who really keep up with their care.

Then he reviews the most recent lab reports of the transplant patients currently admitted. For this, he uses his own Palm Pilot, which he constantly keeps with him. Plugged in is a database on each patient, including his or her medications, assigned physician, and demographics. Here, Smallwood is looking for trends and red flags concerning platelet counts or liver enzyme levels to note prior to inpatient rounds, set to begin at 9 a.m. Among the patients is a woman in her early '50s being treated for thrombosis of the liver, who, he says, is unfortunately "not a candidate for another transplant."

Another patient is being treated for an abscess and is receiving gentamicin and the third-generation cephalosporin ceftazidime (Fortaz), along with antifungals and steroids. Fortaz is used to counter any pseudomonas coverage, which can complicate liver transplants. Therapy with gentamicin, a nephrotoxic aminoglycoside, is watched closely for reactions in patients being given other nephrotoxins such as Prograf or Cyclosporin. And, Smallwood notes, the drug is cleared less than normal in liver transplant patients due to hepatorenal syndrome, which translates into a risk of overdose.

Another patient is suffering from hepatic disease and lung disorders, admitted for a second transplant because rejection occurred after the first surgery.

During the inpatient rounds, Smallwood consults with the physician on one patient's need for a permanent catheter to replace the line currently being run. Based on the patient's lab results, Smallwood recommends no change, and the physician agrees. The consultation is not one of testing, like that between a doctor and residents, but is a genuine consultation, one of several to come.

Other brief consults include whether a patient should receive a solid or oral medication, and for another patient suffering from hepatitis C and cirrhosis, a discussion centers on the right dosage of the commonly used infection-fighting prophylaxis ciprofloxacin.

In the case of another patient, who is in his third day of post-op, medication-use guidelines come into play after the team notices low albumin levels on the chart. They suspect albumin is leaking into the patient's stomach and discuss whether to replace it with the diuretic furosemide (Lasix) as the guidelines suggest.

The team completes inpatient rounds in about 40 minutes, and Smallwood briefly stops in the research office before joining the team in clinic. Here, another problem awaits. His assistant recently left the position, and on top of his clinical duties and his studies, Smallwood is taking resumes and conducting a search for a new research assistant.

He notes that there are several entrees for pharmacists looking to get involved in sponsored research. "Pharmacists in general have not become involved enough with case report forms. Pharmacists are well-versed in the protocols, but you need to either be in good with a surgeon or pursue pharmacokinetics or outcome studies," he offers. And with that, it's off to the outpatient clinic, stopping briefly along the way to return a page from the team's nurse coordinator concerning a prescription. It's a question Smallwood easily handles by reviewing patient records stored in his Palm Pilot.

Clinic 101

Patients in Emory Hospital's liver transplant outpatient clinic are seen once a week for the first month after discharge, then every two weeks for three months, then once a month for six months. After that, patients come about once every three months, depending how they are faring medically.

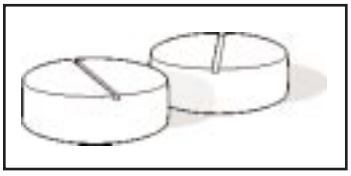
With patients coming from as far away as North Carolina, Florida, or Louisiana, Emory sets up communication with each patient's

hometown, Department of Veterans Affairs, insurance plan doctor, or hepatologist to get blood samples regularly sent to the hospital.

Smallwood and the team conduct clinics two days a week. On clinic days, patients arrive at 8 a.m. for a blood draw, then meet in group therapy while the lab results are documented. The team sees patients beginning about 10 a.m.

This day, there are 40 patients for the five-member team, and the atmosphere is largely one of grab a chart and hit a room, though Smallwood makes sure to visit patients with whom he has struck up a relationship.

For one such patient, who is on a regimen of eight drugs, Smallwood begins by asking if he's suffered any recent chills, fever, diarrhea, or pain that either shoots through or travels around the patient's trunk. He goes on to discuss any problems the patient may be having based on possible interactions specifically from the use of ciprofloxacin and tacrolimus (Prograf). The combination is commonly given to liver transplant patients, showing good results in staving off Candida infection or when patients show biliary problems.



He tells the patient he will talk to the doctor about stopping a magnesium supplement because related lab work shows positive levels. The patient asks Smallwood about an over-the-counter sinus medicine he's taking, which Smallwood says he also will clear with the doctor.

Getting to the next patient room takes some time. First, a physician stops Smallwood to discuss whether an antihypertensive a patient is taking is safe for transplant patients. Then a nurse stops by to talk about blood draw records she's pulling for a clinical study within the hospital. Smallwood remembers that the doctor conducting the study is no longer with the hospital, and he directs her to halt the protocol.

The next patient, whom a physician has just visited, goes over everything he and the doctor talked about, eager to hear Smallwood's opinions on his blood pressure and an OTC cough medicine he's taking. The pharmacist is worried about the effects of an antihistamine on the patient's post-op regimen. He prescribes lots of water and an immediate call if any fever or itching occurs. Later, he says, "Interactions are one of the most important things I do, and that's part of the educational process we give [patients] to make sure they tell us all the medications they are taking from all over the place. Because of their immunosuppression, a lot of interactions can occur. A lot of the drugs we use are nephrotoxic, and if their immunosuppression goes too high, they could wind up with a lot of side effects or their kidneys could shut down. Likewise, if they are taking medications that induce enzymes, they may clear immunosuppression quicker so they wouldn't have enough in their body to prevent rejection," he explains.

Working with doctors long-distance

It's a fine medication line many of the patients walk, made more difficult by the long-distance medicine often practiced, though Smallwood says for the most part the patients' local doctors will consult before prescribing. "The point is, maybe there's some better choices than what [a physician] is accustomed to giving their general population."

The size of the second patient's belly causes Smallwood to speak to a team surgeon about scheduling a biopsy. Smallwood is worried about post-op fibrosis and about conducting serology tests based on a low white-cell count. The physician agrees.

Heading back to the main clinic area, he is stopped twice by team doctors, once to consult on a particular patient's diet and then on a question of interactions.

On the way to see another patient, Smallwood remarks that he asks patients to take their own blood pressure at home before coming to the clinic, which he believes counters the "white-coat" effect that blood pressure readings could take on if done in the clinic environment.

In a third patient room, Smallwood begins with basic questions of itching or pain. When

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told itching has been occurring, he reacts by observing the patient's surgery scar, which runs from sternum to waist and around the entire stomach. The patient says he's been experiencing some heartburn and offers a look at a heart medicine prescription he was given. Smallwood doesn't recognize the medication, so he takes one pill from the bottle so he can research it. Noting that the patient works in construction and wears heavy clothes, Smallwood suggests baby powder, though he'll bring in the physician to talk about it.

"I'm looking toward survivability . . . and I'm not guaranteed we're going to have a liver transplant program for the rest of my working career."

The patient then asks him about the possibility of exposing his wife to hepatitis C via sex. (This patient needed a transplant after contracting hepatitis C.) Smallwood discusses some basic contraception with the patient and notes that his bilirubin levels have increased, which could mean a flare-up of hepatitis C. He tells the patient he also will bring the doctor in to talk about this.

The patient says the skin on his hands has become tender and shows Smallwood some cuts and scabs. That, Smallwood replies, is the likely result of the prednisone the patient is on. "We try to get people off it quickly," Smallwood tells him, because the drug also carries the risk of causing bones to become brittle.

Side effects to steroids cause concern

The patient also is concerned because he's been having difficulty controlling his temper, sleeping, and keeping his weight down. That information signals a possible problem with the steroids and furosemide the patient is taking.

"Now, steroids can get on your nerves, and you're also getting used to your new liver. You're a different person now, and you're not as dependent on [your wife] as when you were sick," he says, moving from medical to a little psychological counseling.

When the physician comes in, Smallwood suggests stopping the patient's Lasix. The physician agrees that eliminating drugs is an overall treatment goal; in this case, the Lasix and the prednisone. For now, the physician decides to lower the prednisone dosage and continue the Lasix because the patient also is experiencing shortness of breath. The physician ends by prescribing more vegetables in the patient's diet and scheduling a blood test in a month's time.

Smallwood takes the heart pill to the floor's computer station and looks the medication up on a MicroMedex database system. He finds the drug profile and determines it's not harmful for the patient to continue taking it.

The clinic continues for a little more than three hours before all of the patients are seen, and the team begins to disassemble for lunch. On the way, though, he is asked to confirm a prescription for a hepatitis B patient who is cramping.

Finally, he sits down to eat at about 2 p.m., only to be interrupted by several pages.

Research and career-building

The rest of Smallwood's day, he says, will be spent in research mode. Specifically, he has just received a FedEx package in the mail with questions and comments from a peer review panel that is evaluating some research papers Smallwood has submitted for publication. Answers need to go back as soon as possible.

Overall, it's a career path Smallwood says he's satisfied with, but he's not taking it for granted, evidenced by his pursuit of a PharmD. "I'm looking toward survivability. I want to practice 20 more years, and I'm not guaranteed we're going to have a liver transplant program for the rest of my working career."

He relates that when his predecessor on the transplant team left the hospital, he responded by voicing an interest. He was given a chance to test for the position and make a presentation, after which he was given the position.

"Even though I've got some publications and have done the work in the liver transplants, if you have someone to stack up against side by side, and they've done all that but one has a doctorate degree and a residency, who are you going to hire?" ■

GUEST COLUMN

Somatostatin or Sandostatin?

By **Linh P. Barclay**, PharmD
University of Florida College of Pharmacy
Shands Hospital AGH, Gainesville

The confusion between somatostatin and Sandostatin usually arises when somatostatin is prescribed, when in fact the drug that is actually being requested is the somatostatin analogue, octreotide. Adding to the problem, the brand name of octreotide (Sandostatin) sounds and looks similar to somatostatin.

Somatostatin was first identified in 1968 as a substance that inhibited the pituitary secretion of growth hormone (GH) in rats. Also, somatostatin inhibited the release of other pituitary hormones (i.e., thyrotropin, prolactin) and suppressed both exocrine and endocrine functions of the gastro-entero-pancreatic system. In humans, prolonged intravenous infusion of somatostatin inhibits GH, thyrotropin, insulin, glucagen, and basal and gastrin-stimulated gastric acid secretion.

Somatostatin affects the absorption, motility, splanchnic blood flow, and trophic functions of the GI tract. In clinical studies, somatostatin inhibited peptide secretion and was shown to produce rapid symptomatic improvement in patients with acromegaly, insulinomas, glucagonomas, carcinoid tumors and vasoactive intestinal polypeptide-secreting tumors (VIPomas), nontumoral secretory diarrhea, and gastrointestinal bleeding.

However, the usefulness of somatostatin is limited by its short duration of action and lack of selectivity. Its use has lead to rebound hypersecretion of GH and other substances following cessation of somatostatin infusion. Also, long-term use of somatostatin may result in intestinal malabsorption and glucose intolerance.

Somatostatin is an orphan drug manufactured by Ferring Laboratories of Tarrytown, NY, under the trade name Reducin. Octreotide (Sandostatin) is a long-acting synthetic analogue of somatostatin. It has similar qualitative effects, but differs in potency and selectivity for target issues. Octreotide can suppress the secretion of serotonin, VIP, gastrin, insulin, glucagon, GH, secretin, motilin, and pancreatic polypeptide. Octreotide also exerts effects on GI function by prolonged intestinal transit time, regulating intestinal water and electrolyte transport, and decreasing splanchnic blood flow. In 1988, octreotide was approved by the FDA for use in the treatment of malignant carcinoid syndrome and VIP-secreting tumors. This, however, was considered by many to be only a "beachhead" indication. Based on its pharmacology, the anticipated use of octreotide is much more varied.

Preclinical studies comparing octreotide with somatostatin have indicated that octreotide is 70 times more potent in inhibiting the release of GH, 23 times more potent in glucagon inhibition, and three times more potent in insulin inhibition. In humans, octreotide is approximately 20 times more potent than somatostatin in the inhibition of GH secretion. Octreotide is highly selective for target cells, with less effect on insulin secretion compared with its effect on GH and glucagon.

Somatostatin given by continuous IV

One important drawback of the clinical application of somatostatin is its very short biological half-life of one to three minutes. This requires that somatostatin be given by continuous IV infusion. Octreotide is more resistant to tissue and serum peptidases. This, combined with higher receptor affinity, increases octreotide's elimination half-life to approximately one and one-half hours and prolongs the duration of action of six to 12 hours. Although somatostatin must be administered by continuous infusion, octreotide may be given by subcutaneous injection of IV bolus.

The most frequent adverse reactions associated with both agents involve the GI system. These include diarrhea, steatorrhea, abdominal pain, nausea, vomiting, hypochlorhydria, and mild malabsorption. Most cases are mild to moderate in severity and tend to decrease over time. There are reports of central nervous system effects such as dizziness, headache, weakness, fatigue, blurred vision, and anxiety with octreotide. Octreotide is associated with less rebound hypersecretion of hormones when its effect tapers off, but hypoglycemia may be seen following octreotide and somatostatin administration.

Compared with somatostatin, octreotide produces a less marked hypoglycemia, less inhibition of splanchnic glucose output, and a diminished rebound phenomenon after infusion. The duration

of insulin suppression is shorter following chronic therapy. No rebound hypersecretion of GH is seen following administration of octreotide in contrast to somatostatin withdrawal. In a prospective study, baseline thyroid hormone levels, thyroid-stimulating hormone, cortisol, and gonadotropins were not altered by octreotide.

However, there has been a report of hypothyroidism with octreotide. Several cases of cholelithiasis or cholecystitis associated with chronic octreotide administration have been reported. Somatostatin may transiently increase blood pressure and pulse slightly. Ventricular premature systoles have been seen in patients treated with somatostatin. However, no adverse cardiac effects have been reported with octreotide.

Dosages differ for the two drugs

Problems could occur when somatostatin is prescribed inadvertently instead of octreotide. Because of octreotide's greater potency and selectivity, lower dosages are required when this drug is used. For example, when used acutely to treat patients with bleeding esophageal varices, somatostatin is usually administered with a 250 µg bolus, followed by 250 µg / hr continuous IV infusion. Octreotide is generally infused at 5 µg to 100 µg / hr for this use.

A higher dose of octreotide may increase the chances of a patient experiencing significant adverse reactions, such as hypoglycemia. Though not as likely, somatostatin administered by the incorrect route (i.e., IV bolus or subQ) probably would not be effective. If octreotide is prescribed using somatostatin's dosage, it would be very expensive. For instance, if octreotide is given for esophageal varices at somatostatin dosages (i.e., 250 µg bolus and 250 µg / hr for six hours), the patient charge is $567, substantially more than that for conventional doses of octreotide ($214).

There is also a logistical problem. Somatostatin must be obtained through the Drug Orphan Program. When octreotide is prescribed, it is readily available. To minimize the confusion between somatostatin and octreotide, physicians should specify octreotide, rather than the trade name Sandostatin, and the two should not be used interchangeably. Likewise, when evaluating these agents in the literature, the drug being used, and the corresponding dose should be confirmed.

[For more information, call Barclay at (352) 372-4321.] ■

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Editor: **Greg Fulton**, (770) 980-1870, (gfulton@mindspring.com)
Drug Criteria & Outcomes Editor: **Barry A. Browne**, PharmD.
Publisher: **Brenda Mooney**, (404) 262-5403, (brenda.mooney@medec.com).
Executive Editor: **Susan Hasty**, (404) 262-5456, (susan.hasty@medec.com).
Managing Editor: **Paula Stephens**, (404) 262-5521. (paula.stephens@ahc.com)
Production Editor: **Terri McIntosh**.

Editorial Questions

Questions or comments?
Call **Greg Fulton** at (770) 980-1870.

NEWS BRIEFS

Medicare to cover capecitabine

Hoffman-La Roche's breast cancer treatment Xeloda (capecitabine) has become eligible for Medicare reimbursement by a recent decision from the Health Care Financing Administration. The ruling takes effect immediately, making the drug the first oral chemotherapeutic monotherapy for late-stage metastatic breast cancer to receive a reimbursement designation.

Since receiving accelerated approval by the FDA in April 1998, capecitabine has been largely indicated for patients with tumors resistant to traditional chemotherapy regimens such as paclitaxel and regimens containing anthracycline agents. Approval followed clinical trials showing tumor reduction of up to 50% in one of four patients, but the drug causes notable side effects in some patients, including gastrointestinal disorders, severe diarrhea, and bone marrow depression.

The Health Care Financing Administration based the ruling on clinical trials and FDA approval but notes that the drug has yet to show specific data on patient survival or the overall improvement of cancer symptoms, two areas Hoffman reports are being studied. ▼

Study promotes calcium for colorectal adenomas

A four-year, National Institutes of Health-sponsored study is promoting calcium supplements to reduce the risk of recurrence of colorectal adenomas (polyps), a known precursor to colorectal cancer. A total of 832 patients were enrolled in the placebo-controlled Calcium Polyp Prevention Study, using 1,200 mg doses of calcium carbonate supplements. Those receiving the supplement had a 19% decrease in the risk of adenoma recurrence, with a 24% decrease in the actual number of adenomas also reported. Patient average age was 61, with 72% being men. See the January 14 *New England Journal of Medicine.* ▼

H. pylori gene similarities to be target of new drugs

Researchers at Genome Therapeutics Corp. in Waltham, MA, and the Astra Research Center in Cambridge, MA, say they have found genetic sequencing similarities between two virulent strains of *Helicobacter pylori* that present new, specific targets for drug and vaccine development that could fight the disease on several fronts.

Comparing gastritis and duodenal ulcer strains in separate patients, researchers say the similarity in the binding and clustering of the bacteria "greatly simplifies" the science of producing gene-based treatments that could cover different strains.

Current treatments center on antibiotics and acid suppression to fight the bacteria, found in the stomach and muscosal lining of the gastric tract. Accordingly, both companies say research has begun on new treatments.

For details, visit Genome Therapeutics' Web site at: http://www.genomecorp.com. ■