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contents

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on the cover: update in oncology

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Editorial

Jane Lochrie, MD

Jane Lochrie, MD

While medicine has changed dramatically over the past century, I think that the changes since I finished my residency in 1986 have been most striking. Looking back, there were no hospitalists, electronic medical records, laparoscopic surgery or palliative care. Pharmaceuticals and research have exploded in cancer therapy, rheumatology and other subspecialties. We have seen the Human Genome Project and the changes that brought to medicine; imaging techniques have improved our diagnostic ability; and we have all been affected by the rise of corporate health care and the business of medicine.

I am very grateful for Dr. Herbert Dean, with whom I have worked for many years, first as a mentor when I was a resident, then as a colleague at Fallon clinic. Dr. Dean gave me his article that enumerates the advances in oncology and asked if it was something that *Worcester Medicine* would like to publish. This gave me the idea that we should look at other disciplines and how innovations have changed the way we practice medicine. I will be looking for authors and ideas for our future issues. Please contact me with your thoughts.

In the first article, Dr. Dean states that the goal of cancer treatment is to cure the cancer or turn it into a chronic and manageable disorder. We are now in the era of treating the patient based on genomic information and identification of driver mutations. The challenge is to identify the specific (driver) mutation that is causing the cancer. He describes the improvements in radiology, both diagnostic and interventional, as well as therapeutic options. He explains the new drug therapies and how they function and identifies the major challenges as drug resistance, minimizing side effects and the cost of the new drugs.

Elizabeth Keating, MS, APRN-BC, describes how nursing continues to provide safe, competent, holistic care in a nonjudgmental manner and advocates for patients, as nurses have done for many years. In addition, nurses must be prepared to educate their patients about side effects, both long-term and short-term, as well as about lifestyle modification and wellness promotion. They must be able to articulate the principles of genetics in their treatment program while tailoring their discussions to meet the needs of the patient.

MaryAnn Cooper, PharmD, BCOP, defines the advances in the treatment of non-small cell lung cancer (NSCLC) with the new immune checkpoint inhibitors, specifically the programmed death 1 (PD-1) inhibitors. Tumors that overexpress this ligand allow tumors to evade T-cell immune surveillance. These inhibitors stop the blockade of the immune system, thus eliminating the cancer cells. She opines that more studies are needed to optimize the usage of these drugs.

The patient perspective is provided by Anne E. Wright. She explains the anguish of being diagnosed with HER2-positive breast cancer and the difficult decision to undergo a bilateral mastectomy. In addition to the pain of surgery, she describes the complications with infection and the side effects of toxic chemotherapy.

Jonathan Gerber, MD, discusses the groundbreaking research in this field at the University of Massachusetts Medical School. Molecular medicine is now routine clinical practice. Unfortunately, despite the treatments' effectiveness and favorable side effect profile, they are not curative and relapse is often inevitable. Immunotherapy, including bone marrow transplant, has a tremendous potential but comes with major complications. He goes on to explain the theory of cancer stem cells and why the elimination of these cells could provide a cure for cancer. Dr. Gerber's research is targeting cancer stem cells, and he is hopeful that this new era will be the paradigm-shifting one for cancer care.

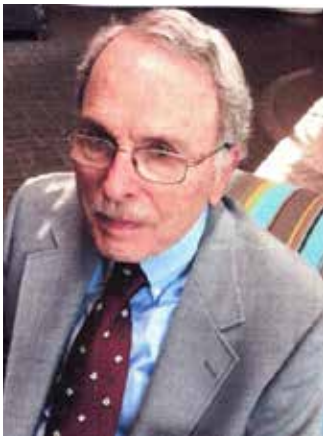
Our amazing student representative to *Worcester Medicine*, Alex Newbury, never ceases to surprise me with his talents. Alex is an accomplished songwriter and musician. In fact, one of his undergraduate degrees is in music. He plays classical piano, guitar, saxophone, and he continues to write music. He describes the music therapy division at the UMass Memorial Department of Pediatrics. The program is spearheaded by Trish Jonason, a board-certified music therapist. She promotes improvisation, encourages lyric composition and offers guitar and ukulele lessons to the pediatric patients. Music therapy addresses the psychological and cognitive components of a patient's care and is especially helpful in providing useful coping skills and a positive distraction during painful or long-duration procedures such as chemotherapy. Studies show that patients who participated in music therapy had a higher frequency of positive coping behavior compared to controls.

As always, please don't close this issue of *Worcester Medicine* without reading Legal Consult and Society Snippets.

Finally, I would like to welcome our new managing editor, Martha Wright, MBA, to *Worcester Medicine*. If you see her at one of the upcoming events, please take a moment to introduce yourself to her. She will be the executive director of the Worcester District Medical Society when Joyce Cariglia retires. Martha has worked in the Worcester medical community for the past 25 years, including 15 years at St. Vincent Hospital and 10 years at the University of Massachusetts.

Oncology Landscape - The Next Few Years

Herbert Dean, MD, FACP



Herbert Dean, MD, FACP

Goal of therapies

To cure cancer or turn it into a chronic and manageable disorder.

The era of personalized precision medicine is upon us – treating a patient's cancer based on genomic information and identification of the driver mutation. Next-generation sequencing technology will increasingly be utilized from cancer tissue, allowing rapid and inexpensive identification of mutations within cancer cells. Cancers have mutations ranging from several to more than a hundred.

The challenge remains to identify the specific (driver) mutation causing the cancer versus passenger mutations (not playing a role in carcinogenesis) and developing actionable therapies aimed at the specific mutation.

Classification and treatment of cancers will include identifying cancers anatomically – based on tissue/organ of origin – as well as employing the driver mutations, i.e. BRAF mutation, ALK mutation, EGFR, etc.

The detection of cancer in blood at an earlier stage through circulating free DNA derived from cancer cells offers promise for screening for cancers, especially those with no effective early detection, such as pancreas or ovary cancer, and to monitor and detect for relapse in patients with previously treated cancers.

Changes/Improvements in Technology

There is continued improvement in radiological technology/equipment including CT, PET and MRI scans. Monoclonal antibody alone or combined with radioactive isotopes directed at tumor antigens has improved staging and can be employed as a delivery system for effective therapeutic agents.

Improvements in photon radiation delivery to the cancer field through Intensity Modulated Radiation Therapy (IMRT) reduces radiation to adjacent normal tissue, causing fewer side effects. Proton beam systems offer similar advantages.

Stereotactic radiation, the ability to deliver pinpoint radiation to the tumor while sparing normal tissue, has proven useful in a variety of cancers, including metastatic brain cancers that would otherwise receive whole brain radiation or require surgical intervention. Patients with resectable lung cancer who cannot undergo surgical resection due to comorbid conditions have also been successfully treated with this modality, avoiding radiation to a larger field and damage to uninvolved tissue.

Interventional radiologists play an increasingly important role in the diagnosis and management of cancer patients through their ability to place catheters and obtain biopsies from all areas of the body.
Destroying cancers through other methods such as radiofrequency ablation (RFA, similar to microwaves) of liver metastases; cryoablation, a freezing technique for treating prostate cancer with more rapid recovery and reduced side effects; and intra-arterial infusion of chemotherapeutic drugs or radioactive isotopes (beads) that can be infused directly into the arterial bed of liver cancer, hyperthermic limb infusions for sarcomas, or embedded into material and placed directly into the resected bed of brain cancers are procedures that are used.

Changes in Drug Therapies

Moving away from cytotoxicity therapy (chemical poisons that destroy cancer cells but also can damage normal tissue and cells) to targeted therapies directed at specific cell surface antigens or mutations in pathways driving carcinogenesis and drugs called checkpoint inhibitors, which boost or increase the host defensive responses, including T-cells, by overcoming the ability of cancer cells to suppress or turn off immune cellular defenses, have changed the practice of medical oncology.

In the past, the FDA approved three to five new cancer drugs per year. In 2017, 51 new cancer drugs were introduced, creating increasing challenges for clinicians to keep abreast of new developments and therapeutic options, the off-label use of these agents and how to select the optimal therapies. These include new cytotoxic agents with different mechanisms of action, targeted agents and monoclonal antibodies aimed at specific antigens or intracellular pathways, sometimes combined with radioactive agents, vaccines and checkpoint inhibitors, PD-1 and PDL-1, agents that effect the program cell death pathways, which are normally present but can be selectively turned off by cancer cells (pembrolizumab/Keytruda, nivolumab/Opdivo, two of several drugs now in use). In October, the Nobel Prize in Medicine went to Dr. James Ellison, of the United States, and Dr. Tasuka Honjo, of Japan, for their groundbreaking research that led to the development and introduction into clinical practice of checkpoint inhibitors that have dramatically altered the therapy and outcome for many types of cancer.

Tumor Treating Fields (TTF), technology employing electrical fields of specific frequencies aimed at disrupting tumor cellular growth, has already shown to be effective in treating brain cancer and is under investigation for other tumor types, including lung, ovary and pancreas.

CAR-T (Chimeric Antigen Receptor) cells, adoptive cell transfer, collecting and using patient's own re-engineered T cells, have been employed effectively in hematological malignancies, including lymphoblastic leukemia and lymphoma, in relapsed and refractory cases and is now being used in multiple myeloma and is under investigation for use in solid tumors.

Mutations that have effective drugs leading to durable remissions include BCR-ABL, HER-2, MET, EGFR, ALK, ROS1, BCR-ABL, BRAF, PD-L1, and PD-1. Cancers that have treatable mutations include chronic myelogenous leukemia, nearly 100%; breast cancer, 20-25%; and melanoma, > than 50%. For most other cancer types, the number with an actionable mutation is < than 10%.

As of May 2018, 10 cancer types have received approval for use of checkpoint inhibitor drugs, of which there are now several. For cancers with the microsatellite instability mutation (MSI-H), present in many cancers but highest in colon cancer, checkpoint inhibitors have been shown to be effective.

Increased use of oral agents, as well as new formulations that allow administering chemotherapy subcutaneously rather than via IV, has simplified administering chemotherapy.

Challenges

The ability to identify driver mutations in cancers, as well as identifying effective drugs, remains a challenge. Even when actionable therapy is available, back-up drugs are needed to counter new mutations that develop, causing resistance to drugs that were initially effective (example include BCR-ABL, ALK and EGFR mutations).

How to effectively combine the various classes of drugs with different mechanisms of action to achieve synergy while minimizing side effects and maintain toxicities at an acceptable level. The second major challenge is when to incorporate new agents shown to be effective in recurrent/refractory cancers and move them into first-line therapy.

Clinicians need to incorporate the expanding knowledge into clinical practice, develop experience with the new drugs, either as single agents or in combination, and manage the side effects and toxicities. The checkpoint inhibitors can cause autoimmune diseases affecting the lung, gastrointestinal tract and endocrine organs. Target-directed therapies have less cytotoxicity and fewer effects on bone marrow but present diverse side effects involving the skin, gastrointestinal tract, fatigue/stamina issues, atrial fibrillation and hypertension. For many malignancies in complete remission, the duration of any maintenance treatment and criteria for stopping treatment is often unclear.

The obesity epidemic is leading to an increased risk of cancer occurring in younger people. Obesity-related cancers include breast, colon, renal, endometrial and thyroid, with evidence from animal models that obesity accelerates the rate of cancer growth. Breast cancer patients who are obese have a greater likelihood of recurrence post treatment.

The cost and affordability of drugs – many now cost more than $100,000 per treatment course – issues with co-payments and out-of-pocket expenses, which can be barriers to care, and health care costs are one of the leading causes of personal bankruptcy. The cost/charge for manufacturing CAR T cells is in the range of $375,000 to $475, 000, not including ancillary costs of hospitalization and medical care, and if associated with the cytokine release syndrome, increase the cost to around a $1 million.

The era of precision and personalized medicine for cancer patients has generated very high expectations, thus we need to separate the hope (promise) from the hype. Fewer than 10% of cancer patients have identifiable mutations with a specific drug to utilize. Cancers that harbor higher numbers of mutations appear more responsive to checkpoint inhibitors. Overall, when present, genomic-informed therapies have response rates of up to 50%, with median response rates of close to 30 months.

Specific Cancers, The Big Three

Breast Cancer

Reduced morbidity and side effects resulting from the treatment of breast cancer have been achieved though earlier diagnosis and lower stage of disease at diagnosis through screening and mammography combined with ultrasound and MRI, especially with dense breast tissue. Lumpectomy with post-operative radiation versus mastectomy is now an acceptable and preferred choice for many women. The staging of the axilla with sentinel node biopsies, which, if negative, avoids carrying out axillary node dissection, and improved radiation delivery, along with reduced surgery in many cases, has decreased the incidence of lymphedema, chest wall/shoulder/arm pain and range of motion issues. Physical therapy has also improved the functional capacity of the involved limb.

Neoadjuvant chemotherapy has led to complete remission of cancers in up to 40% of patients and led to improved disease-free and overall survival, especially in triple negative and HER2-positive cancer. A question yet to be answered: Can this achievement offer the prospect of not requiring additional treatment?

Hormonal therapy for pre- and post-menopausal women with tamoxifen and aromatase inhibitors has led to an increase in disease-free and overall survival, although introducing some side effects that are manageable in most cases.

Genomic testing by several available tests, including the most frequently used one, Oncotype Dx, a 21-specific gene analysis, has led to stratifying women who are at low risk of recurrence and do not need chemotherapy while identifying those who have a high likelihood of recurrence and therefore will benefit from adjuvant chemotherapy.

BRCA1 and BRCA2 are genes that produce tumor suppressor proteins. Mutations in these genes, which occur in about 10% of women, increase the likelihood of developing breast and ovarian cancer at an early age, as well as several other cancers.

Breast reconstructive procedures have improved self-image and acceptance of breast cancer treatment. Physical and occupational therapy have improved functional recovery. Integrating post-operative breast radiation with breast reconstruction for optimal cosmesis remains a challenge.

Lung Cancer

Preventive health measures aimed at reducing the number of adult smokers in the United States have proven to be successful. The United States Preventive Services Task Force recommends annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30-year smoking history.

Currently 75% of lung cancer patients present with symptoms of advanced local or metastatic disease that result in a poor prognosis. Patients diagnosed through screening have earlier stage disease, with a five-year survival rate for non-small cell lung cancer (which represents 80-85% of lung cancers) of 77%, versus 15-20% for those who are unscreened and are diagnosed with advanced stage disease. Annual low-dose CT scanning will allow detection of lung cancer at an earlier stage, leading to an increased cure rate and a reduction in the need for aggressive adjuvant chemotherapy/radiation.

Combining a checkpoint inhibitor (pembrolizumab) along with standard chemotherapy has proven to increase survival in newly diagnosed metastatic non-small cell lung cancer and already offers promise for use in adjuvant setting for earlier stage disease.

Colon Cancer

Screening measures have led to an increase in cure rates for cancer diagnosed at an earlier stage. The American Cancer Society recommends cancer screening beginning at age 45 rather than 50, since the disease is occurring more frequently in younger individuals.

It is not possible or practical to screen everyone through colonoscopy, which remains the gold standard of detecting colon cancer, and removal of pre-cancerous polyps. Cologuard, a DNA stool test, easy to utilize for mass screening has a sensitivity (identifying disease if present in the 92-93% range), with a specificity of 85% (a positive finding results in a confirmed diagnosis – about 1/8 false positives). High-sensitivity fecal occult blood tests (FOBT) are also effective as a screening for colon cancer with a lower sensitivity/specificity compared to Cologuard.

Differences in mutations and response to therapy between lesions arising in the right colon from those more distally located have recently been noted. Adjuvant combination chemotherapy has led to improved disease-free and overall survival in locally advanced disease (Stage 111), improving overall survival from around 50% to 70%. Platinum-induced peripheral neuropathy remains a chronic problem for 15-20% of patients who receive adjuvant chemotherapy.

In metastatic disease, combination chemotherapy has improved median survival to greater than two years. Patients who present or develop hepatic metastases can be cured with surgical resection, ablative procedures and chemotherapy in about 25% of cases.

A Few other Cancers

Ovary Cancer

Improved disease-free survival now approaching four years has been achieved with combination chemotherapy, including dense dose chemotherapy (administering the calculated dose at more frequent intervals, thus shortening the total time while increasing the dose intensity), and incorporating intraperitoneal (IP) chemotherapy into the treatment. More recently, employing hyperthermic IP chemotherapy at the time of debulking surgery has reduced the otherwise complex nature of this procedure, usually done in an adjuvant setting.

Women who have genetic mutations of BRCA1 and BRCA2 who are platinum-resistant are responsive to a class of oral drugs, PARP inhibitors.

Melanoma

The incidence of melanoma has been steadily increasing. Prognosis with metastatic disease has been dismal, but remarkable improvement in response rate and increased survival has been achieved with the identification of the BRAF V600 mutation and treatment with specific drugs used in combination directed against this mutation or with checkpoint inhibitors. Adjuvant chemotherapy in Stage 111 (nodal involvement), dabrafenib combined with metinib, has now received FDA approval based on > than 50% increase in survival.

Prostate Cancer

Even though the number of men diagnosed with prostate cancer has increased through screening using the PSA test, the death rate due to this disorder continues to decrease through earlier detection and improved treatment.

There is controversy regarding at what age to begin screening, frequency of testing and if continued screening beyond 70 is appropriate due to concern that many men are diagnosed with prostate cancer in whom the disease would not clinically impact their life even if detected. Prostate cancer is associated with aging, with autopsy studies showing about 20% of men at age 60 have evidence of microscopic prostate cancer, 40% at age 70, and up to 80% at age 80, with only 3-5% of men dying due to prostate cancer.

Advances in diagnosis include greater use of MRI for staging purposes, as well as a more focused biopsy of the gland, and information provided by genomic mutation profile, which indicate more aggressive disease. For men who have low-stage disease and low Gleason scores (measures grade 6 or lower), observation and regular surveillance (wait and watch) can be offered with intervention based on disease progression.

Robotic prostatectomy with nerve-sparing surgery has reduced erectile dysfunction, and improved radiation delivery through conformal radiation and IMRT has reduced morbidity and side effects resulting from rectal and bladder injury. The use of neoadjuvant and adjuvant hormonal therapy for more unfavorable prostate cancer (higher Gleason score, 7 or greater) has improved the disease-free and overall survival with radiation therapy. For appropriate patients, radioactive seed implants (brachytherapy), as well as cryotherapy, are effective in treating this disease.

The use of total hormonal androgen blockade for biochemical molecular relapse or metastatic disease has improved overall survival. More recently, total hormonal androgen blockade, even while achieving castrate testosterone levels, has not shut off this pathway leading to castrate-resistant disease. Newer agents (enzalutamide and abiraterone) that further block androgen synthesis and the androgen receptor are effective when faced with this situation. Incorporating these newer agents into treatment at the time of biochemical relapse, indicated by a rising PSA, appears promising.

A personalized vaccine for biochemical relapse, Provenge (sipuleucel-T), is now available, and Radium-223 is effective in treating bone-only disease.

Hematological Cancers

Multiple Myeloma

There are many new drugs available to treat this disorder, given as doublets or triplets as part of induction chemotherapy, often followed by an autologous stem cell transplant (sometimes done as an initial one followed by a second one after recovery, called tandem transplants), followed by maintenance therapy, turning this disorder into a chronic disease with median survival going from three years to up to 10 years.

Daratumumab, a monoclonal antibody to CD38, a surface protein expressed by multiple myeloma cells, has recently been shown to be effective in treating refractory and recurrent disease, and its place as front-line treatment in combination with other drugs is expected to be effective. Bone-modifying agents are effective in reducing bony-related complications such as fractures and recommended for up to two years and restarted as indicated.

Chronic Lymphocytic Leukemia (CLL)

Long-term remissions and disease control are regularly achieved in this disorder turning it into a chronic disease for many patients. Cytogenetics, along with other prognostic indicators, can identify high-risk patients and effective treatment exits for even those with previously unfavorable criteria with newer drugs.

In addition to older effective drugs, either given as single agents or in combinations, new drugs have led to disease control and durable remissions, including ibrutinib and acalabrutinib (BTK inhibitors), venetoclax (a BCL-2 inhibitor), zydleig (a P13k inhibitor) and rituximab and ofatumumab (monoclonal antibodies directed against the CD20 antigen on B-cells).

Lymphomas

Many new drugs are available for treating lymphomas and the various subtype of this disease, including combinations of drugs, as well as single agents. Follicular lymphoma, the most common type, with the use of drugs described under CLL, has survivals of up to 18 years, although there remains a subgroup of 20% with a more unfavorable prognosis.

Diffuse lymphoma comprises many subtypes and can be cured with aggressive chemotherapies combining several cytotoxic drugs along with monoclonal antibodies or by allogeneic stem cell transplant. Improved control of cGVHD (chronic graft vs. host disease) has improved outcomes in this group of patients. Overall, about two thirds of patients are cured. Refractory and recurrent diffuse lymphoma have been effectively treated with CAR-T (Chimeric Antigen Receptor) cells treatment.

Chronic Myelogenous Leukemia

This disease is the prototype for precision medicine that evolved out of a series of discoveries – the Philadelphia chromosome, a transformation between chromosome 9 and 22 leading to the BCR-ABL mutation, causing an abnormal protein driving the proliferation of myeloid tissue. The discovery of the tyrosine kinase inhibitor, imatinib, has resulted in 85-90% patients achieving a complete hematological remission, including a molecular one in some. Additional second- and third-generation tyrosine kinase inhibitors have been developed that are even more effective and can be used when resistance develops from a new mutation. Recently, the drug nilotinib has a new FDA label that permits cessation of treatment for those who have achieved a sustained remission documented by a 4.5 log molecular reduction in detecting the mutation and felt to represent a potential cure.

Conclusion

Progress in cancer treatment by enhanced population screening and identifying the drivers of cancer through genomic testing, together with the discovery and employment of new classes of drugs to treat cancer with acceptable side effect profiles, will lead to improved, disease-free, overall survival and cure rates in lung, breast and colon cancer; other solid cancer types; and hematological malignancies. For many, cure is not achievable at this time, but the ability to control the disease for prolonged intervals by means of newer drugs and approaches will turn cancer into a chronic manageable disorder.

Coordination of care through multi-disciplinary tumor boards provides the most appropriate treatment plan for each patient. The importance of introducing, even during the active treatment phase of cancer, the benefits of a healthy lifestyle, including regular exercise, proper nutrition, weight control, etc., and maintaining them into the post-therapy observation phase needs to be incorporated into the management of all cancer patients

There are currently estimated to be 18 million cancer survivors, many of whom have returned to their baseline performance status. There are some who continue with chronic residual therapy-related side effects resulting from their cancer therapy, including peripheral neuropathy, cardiac, pulmonary, musculoskeletal, chronic fatigue and cognitive dysfunction.

Rehab efforts, including focused physical and occupational therapy, along with exercise programs, cognitive training, nutritional and dietary support (including measures aimed at reducing obesity), mind-body programs and psychosocial behavioral health intervention, when appropriate, can lead to improvement and ameliorating these residual side effects, enabling most to resume their pre-illness level of activity, including occupational pursuits in many cases.

Herbert Dean, MD, FACP, was involved with the Fallon Health Care System for more than 30 years, including the Fallon Clinic (now Reliant), serving in several administrative roles, as well as a hematologist/oncologist. He was also president of the Fallon Community Health Plan for five years. He is affiliated with Saint Vincent Hospital and UMass Medical School and is currently an oncology consultant at UNUM.

Oncology Nursing in the Age of Precision Medicine

Elizabeth Keating, MS, APRN-BC

Early in the spring of 1983, the program nurse coordinator, Kate, from the pediatric oncology clinic came to the inpatient unit to advise the nursing staff of a new patient diagnosed with a primary bone cancer in his left arm. This young man, Jack, age 20, would be admitted the following day to begin his treatments. Per her usual practice, Kate wanted to provide the patient and his family with the name of his primary nurse. Mary, a registered nurse on the unit, knew, as she heard the details of Jack's story, that she wanted to be an integral part of caring for him and his family. Over the ensuing weeks and months, Mary cared for Jack during his numerous inpatient stays. In those days, there were limited anti-emetic agents and patients were heavily sedated; blood counts were followed closely, as growth factors did not exist to limit nadirs. Symptoms had to managed in creative ways, as evidence-based practice had not yet emerged.

It was during these days and nights that Mary provided the essence of nursing care through her presence and expertise. She sat with Jack following his arm amputation to treat his pain – both physical and emotional. She heard about his fears, as well as his plans for the future. "Do I have a chance with a girl I like?" he asked one night at 2 a.m. As effective treatments were limited, Jack's cancer stopped responding over time. Mary called upon her skills in the palliation of symptoms and end-of-life care. She grieved with his family when Jack passed away one night and during the services which followed.

This story highlights what oncology nurses have been experts in since the creation of this specialty practice. This was the reality of our medical limitations in this evolving discipline of oncology. This was my experience in nursing in the early 1980s.

As we experience this current paradigm shift in cancer care, we have to contemplate the role of nursing in this age of precision medicine. Over the past 30 years, the discipline of oncology has become increasingly specialized. The profession of oncology nursing has recognized this and has continued to keep pace by providing nurses with evidence-based practice research, journal publications, topic programs and conferences to address their knowledge needs. Academic nursing programs have created subspecialties in oncology for advanced-practice nurses.

As precision medicine continues to emerge, are the roles and responsibilities of the professional nurse changing? When we explore traditional nursing roles, we continue to highlight providing holistic care and addressing the human response to illness and treatments. What does this mean to our daily practice? Nurses continue to provide care coordination and advocacy, assisting patients from the time of their diagnosis. Other elements of care include patient and family education, symptom management, working as part of an inter-professional team and providing palliative and end-of-life care.

How is this changing? As individuals respond to targeted therapies, they are surviving cancers which were previously considered to be lethal. This has led to the concept of cancer survivorship. Nurses need to be prepared to educate patients about potential long-term treatment side effects, as well as lifestyle modification interventions and the promotion of wellness. Nurses must continue to be experts in managing symptoms associated with the cancer, as well as the new cancer therapies. Many of these agents have a unique constellation of toxicities. Patients and caregivers need to be appropriately informed about early signs of these side effects, which often cluster.

Personalized medicine requires nurses to be able to articulate the principles of genetics and genomics in the design of a patient's treatment plan. Helping patients access and understand health information is challenging, as their health literacy ranges from highly adequate to very limited. Some patients are highly sophisticated about their diagnosis and care. Conversely, many patients may have a lower level of health literacy and require a different style of education in order to achieve an adequate level of understanding. Nurses need to tailor their approach to meet the patient's needs. Oncology nurses work to navigate patients through these treatment regimens, which can be rigorous and financially costly. In addition, they may need to advocate for their patients facing ethical dilemmas such as those associated with ending treatment.

Despite these changes, the essentials of providing care to patients have remained much the same in oncology nursing over the past 30 years. Providing safe, competent, holistic care in a nonjudgmental manner and advocating for patients and families by serving as their voice continues to be the mission of oncology nursing.

Elizabeth Keating, MS, APRN, is an instructor at the UMass Medical School's Graduate School of Nursing. She serves as faculty in the Graduate Entry Pathway Program and teaches in the Oncology Subspecialty Program. She has worked as an oncology nurse practitioner, specializing in breast oncology, for more than 20 years.

My Breast Cancer Experience

Anne E. Wright

Anne E. Wright

I'll never forget the afternoon when the first sign of cancer reared its ugly head. I was sitting at my desk, one month into a new job that I was truly enjoying, when I felt a sharp, throbbing pain in my right breast. I asked my co-worker if she had any ibuprofen. She did, but the pain didn't go away.

At first, I had no thoughts of cancer. I had done regular self-exams, had followed the guidelines regarding mammograms and had never found a lump. Besides, I had always heard that breast cancer didn't cause pain (. . . but this one did.)

After two weeks, when the pain did not subside, I went to see my GP. She didn't find anything suspicious either, but sent me for a mammogram. It was a Friday. I knew when I got a message to call her early the next week that it wasn't a good sign.

She sent me to what I call the "super smasher." I'm sure there is a more technical term for it, but it's a machine that flattens your breasts to mere pancake dimensions. Immediately after, I was sent to the radiologist for an ultrasound. My previous and current mammograms were pinned to the wall, and you didn't need to be a medical professional to see that something was amiss. The earlier mammogram was clear as a bell. In the current one, my breast seemed to be littered with white rice.

Then, the radiologist did the ultrasound, and she didn't mince words. "See this," she said, pointing to an ominous looking area. "This is cancer. It's fast-moving, and it has to come out right away. And this," she said, pointing to another spot, "is most likely cancer as well."

The next few weeks were a blur of doctor visits, tests and decisions. I decided to have a double mastectomy with reconstructive surgery opting for saline implants. Initially, the surgery appeared to have gone well, but then I developed an infection on my left side, which required emergency surgery to remove the tissue expander that had been implanted during the mastectomy to make room for the eventual implants.

Pathology results for my right breast weren't great either. The primary tumor was HER2-positive (a fast-spreading cancer) that was "high risk" (which meant it had a greater risk of recurrence) and was invasive – meaning it had spread past the ducts with the potential to spread to other parts of the body. The treatment – a year of chemotherapy.

I was crushed. I am pretty tough. I can handle a lot of physical pain, but I am a total wimp when it comes to nausea and vomiting. Surprisingly, it wasn't the nausea that hit me the hardest during chemo (although there were moments that I thought I couldn't bear it), but the constant, burning diarrhea that kept me bound to the toilet. I quickly learned that whenever I ate or drank anything, I would have to dash for the bathroom almost instantaneously. Getting anywhere fast got harder as the chemo progressed. I lost all my physical strength and could barely walk, let alone run. Climbing stairs was out of the question.

Ironically, with all that diarrhea and the chemical taste of food keeping me from eating too heartily, I gained weight. The steroids I was given to help combat the side effects of the chemo bloated me up – including my head (which was not a good look when hairless). Lymphedema, another side effect from the surgeries and chemo, caused my arms, hands, back and trunk to also retain fluid. I felt like a blimp!

Perhaps the longest-lasting side effect from the chemotherapy treatment is what is referred to as "chemobrain" – a brain fog that envelops a percentage of patients who've received strong chemotherapy. What I do remember from those first early days of chemo was feeling like I was outside my body looking down on things that were happening and that I wasn't really present. Then I couldn't remember things – places, people, conversations, words, where I was going, how to get places, where I put things . . . the list goes on. And that was in direct contrast to my pre-cancer life, where my work required me to think quickly and accurately at all times. The speed at which this change came about after starting the chemo was shocking. It was like a light switch plunging me into darkness. Although now, several years later, this has improved a bit, I think I will now always have to write copious lists, put reminder sticky notes around the house and allow extra time to find my belongings whenever I leave the house.

As I approach that all-important five-year mark, I can now reflect on how far I've come. I'm one of the lucky ones, really. My hair has grown back (and I'm keeping it long in spite). I had good friends and loved ones to cheer me up, make meals, taxi me to hundreds of chemo and doctor appointments, and listen to me vent; hardworking doctors and nurses to see me through every step; and the wonders of modern medicine to keep me alive. One of the chemo drugs I was given, Herceptin, was developed specifically to destroy HER2-positive cancer cells, and it has been highly successful. Had I been diagnosed with HER2-positive just a few years before, I might not be here today writing this.

And that's the real bottom line isn't it? I'm here. Puffier and spacier, perhaps, but I'm here. When I was first diagnosed, I didn't know if I would get to see my daughters graduate high school, and now, my eldest is due to graduate college in a few months. I am hoping to hold my grandchildren someday.

Anne Wright, a former journalist, received her BA from Tufts University.

Paradigm Shift in Management of Advanced Lung Cancer

Maryann Cooper, PharmD, BOCP

More than half of patients diagnosed with non-small cell lung cancer (NSCLC) are diagnosed when the disease has already metastasized to a distant site.[1] For this group of patients, the outlook is bleak, with a five-year survival rate of less than 5%. First-line treatment for patients newly diagnosed with metastatic lung cancer will vary based on the presence or absence of driver mutations, gene rearrangements or the overexpression of programmed death ligand 1 (PD-L1). Unfortunately, the vast minority of patients are diagnosed with a driver mutation or a gene rearrangement that can be targeted with drug therapy (Table 1). PD-L1 overexpression defined as a tumor propensity score (TPS) of ≥ 50% occurs in about 25% of patients.[2,3] For the remaining patients, first-line treatment involves multiple cycles of platinum-based combination chemotherapy that is accompanied by a slew of toxicities and limited survival.

Table 1: Prevalence of Driver Mutations and Gene Rearrangements at Diagnosis in NSCLC[4-7]

Driver Mutation or Gene Rearrangements	Prevalence
EGFR	10% Caucasians, 50% Asians
BRAF	3%
ALK	<7%
ROS1	1-2%

ALK = anaplastic lymphoma kinase; BRAF = v-Raf murine sarcoma viral oncogene homolog B; EGFR = epidermal growth factor receptor

The outlook and treatment approach for metastatic NSCLC has begun to shift in the era of immune checkpoint inhibitors. Of the two current classes of checkpoint inhibitors, the programmed death 1 (PD-1) inhibitors are emerging as game changers in NSCLC. Tumors that overexpress the programmed death ligands enhance signaling through the PD-1 pathway, ultimately allowing the tumor to evade T-cell mediated immune surveillance.[8] By blocking the interaction between the programmed death receptor and the ligands, immune checkpoint inhibitors stop the blockade of the immune system, allowing it to eliminate cancer cells. In NSCLC, PD-L1 inhibitors have a role as first-line therapy, as well as in the second-line setting when the tumor has progressed. In the first-line arena, pembrolizumab is FDA approved in combination with chemotherapy or as a single agent in those with a TPS ≥ 50%.

This summer at the American Society of Clinical Oncology (ASCO) Annual Meeting, Lopes, et al., presented the results of Keynote-042, a large, randomized controlled trial that compared pembrolizumab to traditional chemotherapy as first-line therapy for metastatic NSCLC.[9] Patients were included in this study if their PD-L1 TPS was at least 1%. The primary outcome of the trial was overall survival (OS), which was assessed in those with a TPS of ≥50%, ≥20% and ≥1%.

A total of 637 patients were included in each group, with 599 (47.0%) and 818 (64.2%) having a TPS ≥50% and ≥20%, respectively.[9] After a median of 12.8 months of follow-up, 13.7% of patients remained on pembrolizumab compared to 4.9% of patients receiving chemotherapy maintenance.

OS was significantly improved with pembrolizumab compared to chemotherapy (Table 2).[9] Interestingly, this improvement was seen in all TPS groups. In addition, patients receiving pembrolizumab experienced significantly fewer treatment-related grade 3 to 5 adverse events compared to chemotherapy patients (17.8% vs. 41.0%).

Table 2: Overall Survival Data from Keynote-042[9]

	PD-L1 TPS					
	≥50%		≥20%		≥1%	
	Pembrolizumab n = 299	Chemotherapy n = 300	Pembrolizumab n = 413	Chemotherapy n = 405	Pembrolizumab n = 637	Chemotherapy n = 637
Hazard Ratio	0.69 95% CI: 0.56-0.85 P value: 0.0003		0.77 95% CI: 0.64-0.92 P value: 0.002		0.81 95% CI: 0.71-0.93 P value: 0.0018	
Median Survival	20.0 months 95% CI: 15.4-24.9	12.2 months 95% CI: 10.4-14.2	17.7 months 95% CI: 15.3-22.1	13.0 months 95% CI: 11.6-15.3	16.7 months 95% CI: 13.9-19.7	12.1 months 95% CI: 11.3-13.3

This open-label, phase III trial was the first study to evaluate OS with pembrolizumab compared to chemotherapy in patients with metastatic NSCLC.[9] These significant results have the potential to expand the role of pembrolizumab as a first-line treatment for this disease to include those with a TPS as low as 1%. This would include almost all patients diagnosed with metastatic disease that do not also harbor a driver mutation or gene rearrangement.

At this time, Keynote-042 is still ongoing and several questions remain. Since patients in each TPS group overlapped, it is difficult to determine which TPS score benefits the most from this therapy. In addition, pembrolizumab in combination with platinum-based chemotherapy has been shown to significantly improve both OS and progression-free survival compared to chemotherapy alone.[10] Until pembrolizumab monotherapy is compared to pembrolizumab with chemotherapy, it will not be known which treatment is superior.

Despite the unanswered questions, the preliminary results of Keynote-042 have produced great buzz in the oncology world. The potential to offer a treatment that not only improves survival but also minimizes toxicity for patients receiving such a devastating diagnosis is very exciting. Only time will tell if immunotherapy will replace chemotherapy as the new standard first-line treatment for metastatic NSCLC.

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Reasons for Hope: New Advances in Cancer Therapy

Jonathan M. Gerber, MD

Jonathan M. Gerber, MD

We are now entering a highly promising era in cancer treatment, made possible by a number of recent groundbreaking advances in research. These include particularly exciting discoveries in the molecular basis of cancer, cancer stem cell theory and immune-based approaches. Collectively, these findings are leading the way to more personalized cancer care, with improved diagnosis, better prognostication and more effective, yet less toxic, therapies.

Molecular Medicine

The approval of imatinib in 2001 for the treatment of chronic myeloid leukemia (CML) ushered in the era of molecular medicine for cancer.[1] The impact was immediately game-changing, transforming CML from a universally fatal disease to one in which most patients will live a virtually normal lifespan and selected patients will remain in durable remission even after stopping therapy. Since the introduction of imatinib, genomic characterization of numerous cancers has followed, with countless new drug approvals over the ensuing 17 years, many of which selectively target cancer-specific mutations. Indeed, more than 50 new oncology drugs were approved by the FDA in the past five years alone.

Molecular medicine is now part of routine clinical practice for many cancers. Gene sequencing panels are now commonplace for diagnosis, guidance of management and assessment of disease response. Targeted molecular inhibitors are now regularly utilized alone, or in combination with more traditional chemotherapy, for the treatment of a variety of solid and hematologic malignancies, often with dramatic responses. In fact, even the tricarboxylic acid (a.k.a. Krebs) cycle, which many physicians had fully forgotten from their undergraduate and first-year medical school courses, has now proved clinically relevant, with the approval of two isocitrate dehydrogenase inhibitors over the past year for the management of relapsed/refractory acute myeloid leukemia.[2,3] Unfortunately, despite their remarkable effectiveness and often favorable side effect profiles, in most cases, molecular inhibitors are not curative, and relapse is too often an inevitable outcome.

Cancer Stem Cell Theory

The cancer stem cell (CSC) theory provides an excellent explanation for the observation that most patients achieve complete remission after initial therapy, only to later relapse.[4] The CSC theory was first mentioned in the literature as early as 1959, but it wasn't until decades later that technology had sufficiently advanced to test the theory.[5]

The CSC theory posits that all cancer cells are not created equal. Cancer is theorized to arise from CSCs, which, by the time a patient presents, are typically diluted out by their vastly more common offspring – the "bulk" tumor cells. While the CSCs typically represent only 1% or less of the total tumor burden at diagnosis, they possess two key qualities: (1.) they harbor all the regenerative potential of the tumor, and (2.) they are, unfortunately, also quite resistant to treatment. According to the theory, most therapies effectively kill only the bulk cancer cells, sparing the rarer, but more resistant, CSCs. The surviving CSCs are typically too few to be detected by clinically available means, hence, patients appear to be in complete remission. However, they subsequently relapse, as the CSCs regenerate the cancer. Therefore, the theory suggests that the CSCs must be eliminated to achieve cure.

Over the past decade, we and others provided proof of the clinical relevance of the CSC theory, particularly in acute myeloid leukemia (AML), where the concept has been best validated. We were able to demonstrate that CSCs in AML are indeed more resistant to chemotherapy than are the bulk leukemic cells and that the CSCs could be detected at miniscule levels in patients who achieved complete remission but subsequently relapsed, just as the theory had predicted.[6] Although the CSCs utilize a variety of defense mechanisms to withstand therapy, we are now developing better means to detect and target these resistant cells, with the goal of curing more patients.

Immunotherapy

One of the few available therapies that can reliably eradicate CSCs, at least in the hematologic malignancies, namely allogeneic blood and marrow transplantation (BMT), represented a tremendous breakthrough in immunotherapy, demonstrating the ability of a new immune system to cure the otherwise incurable.[7] However, this great potential has come with the risk of life-threatening, treatment-related complications, such as infection and graft vs. host disease. Recent refinements in BMT have significantly improved outcomes and extended this potentially curative therapy to more patients, especially the elderly, but the risks remain considerable.[8] Newer advances, including antibody-based therapies, tumor vaccines, immune checkpoint inhibitors and chimeric antigen receptor (CAR) T cells, have sought to harness the therapeutic potential of the immune system and expand this to other cancers, but with less toxicity.

Among the most promising of these new immunotherapies, the immune checkpoint inhibitors (for which the 2018 Nobel Prize in Physiology or Medicine was awarded) have shown remarkable activity in metastatic melanoma and other solid tumors, as well as lymphoma.[9] These agents work by overcoming a cancer's ability to evade the patient's immune system; however, they are still limited by quite significant side effects in some patients and suboptimal responses in others. Work is ongoing to better identify predictors of response to these drugs and to figure out how best to combine them with other therapies to improve responses.[10,11]

CAR T cells represent perhaps the most highly promising of the attempts to exploit the capabilities of the immune system to fight cancer. The patient's own T cells are genetically re-engineered to target an antigen on the tumor cells. The technique has proved dramatically effective in treating relapsed/refractory acute

lymphocytic leukemia, achieving durable remissions even in patients who relapsed after BMT, receiving FDA approval last year.[12] Despite such promise, CAR T cells are hindered by the need for specialized expertise (both for the manufacture and administration of the cells), potentially life-threatening side effects, enormous cost and a dearth of tumor-specific targets in most cancers. Additionally, some cancers have managed to evade this therapy via "antigen escape," whereby the tumor cells drop the target of attack from their surface.

Future Directions

Armed with a better understanding of cancer at the molecular and cellular levels, we are now developing therapies that are far more effective and, in many cases, much better tolerated therapies than the regimens of old. Indeed, we are now able to treat patients well into their 80s and beyond with gentler, yet still effective, therapies (some of which are chemotherapy-free), stretching not just quantity but also quality of life. We are also now realizing some successes against diseases which once seemed insurmountable. However, there is still much work to be done, as cancer is rapidly closing in on heart disease as the leading cause of death in the U.S.

Our ongoing research is focused on targeting the most resistant cancer cells, i.e., the CSCs. Additionally, we are exploring means to improve the personalization of care – identifying biomarkers that better predict prognosis, as well as treatment efficacy and side effects. As we build upon these promising advances, refining existing therapies and designing new ones, we are optimistic that this new era will be paradigm-shifting for cancer care.

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Harmony on the Wards: The Role of Music Therapy in Pediatric Oncology

Alex Newbury

It was a crisp, sunny fall afternoon as I walked up to the pediatric floor of the UMass Children's Health Center (CHC). I planned to spend a few hours with the Child Life Department to learn more about music therapy in the inpatient setting. As a musician, I'm always fascinated to learn about new modalities and settings where music can play a role. So when I discovered that our pediatric department had a music therapy division, I jumped at the chance to learn more about what was offered to such a vulnerable population.

I was greeted by Trish Jonason, a board-certified music therapist who warmly ushered me onto the floor. She spent the first 10 minutes of my visit explaining the extent of her services, which range from individual sessions with patients in their rooms to five-member bands taking up residency in the common playroom. Jonason spends two days a week bringing joy and ease to the children of 5 East. She promotes improvisation, encourages lyric composition and even offers guitar and ukulele lessons at the patient's request. One scene that stuck with me involved a patient who was anxiously awaiting discharge due to an unanticipated delay in her return home. Jonason was asked by the medical team to see if there was anything she could do to help with the patient's angst. Armed with an acoustic guitar slung over her back and a bag of percussive bells, drums and maracas, Jonason entered the patient's room and immediately began engaging her with songwriting that used the patient's name and objects of her affection as part of the lyrics. The tension in the room melted away, while the girl strummed a ukulele and sang a song made just for her.

Music therapy falls under the realm of CAM, or complementary alternative medicine, and is defined as "the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program."[1] Working alongside traditional medicine, music therapy addresses the psychosocial and cognitive components of a patient's care and is especially helpful in providing useful coping skills and positive distraction during painful or long-duration procedures like chemotherapy infusion or extended hospital stays. In general, children use coping strategies such as seeking support from a parent or participating in normalizing activities when placed in the hospital or outpatient clinic in an attempt to reduce, or at least tolerate, stress.[2] In a study specifically involving pediatric oncology patients, researchers found that patients who participated in active music engagement through music therapy had a higher frequency of positive coping-related behaviors than those who passively listened to music or audiobooks. Further, children actively engaged with the environment via positive coping skills tend to manage the trauma of hospitalization in a more appropriate way.[3] In their review of CAM modalities among pediatric oncology patients, Poder and Lemieux suggest that interactive music therapy, similar to the style provided by Jonason, has an overall positive effect on patients, improving a patient's stress and pain, reducing anxiety and improving the overall behavior of the child.[4] While more research is needed to better tailor an individual CAM treatment plan for each patient, music therapy provides a clear benefit to those in extended or painful hospital stays, such as those children with cancer.

I had the pleasure of exchanging emails with Jonason about her involvement with the CHC and her work as a music therapist. She has been at UMass for three years, where she has worked in multiple settings, including the inpatient pediatric floors, pediatric ICU and the outpatient oncology/hematology clinic. She mentioned that her career began as a music therapist for a predominantly pediatric oncology population at Lutheran General Hospital in Park Ridge, Ill. When asked about any subtleties or differences working with these types of patients, Jonason mentioned, "Music therapy with pediatric oncology patients differs from other [music therapy] work in how the family is involved. Most often, a session occurs bedside with a parent sitting by. Cancer affects the entire family; jobs are put on hold; other family members take on caregiving roles; and routines change." Similar to the research noted above, she uses music before a procedure such as a dressing change or port placement. She notes, "More often than not, after a music therapy session, a parent will tell me that they haven't laughed with their child in weeks."

One of the best parts of her job is giving ukulele lessons to the patients. "I love giving ukulele lessons! I love putting an instrument in somebody's hands and teaching them how to navigate those four strings to create something recognizable. There are so many benefits to learning a new instrument during weeks of chemotherapy or an inpatient stay. Cognitively, the brain is busy learning a new skill, following a lead sheet with chords and lyrics. Neurologically, the body is coordinating movements between the right and left hands to create chords. Physically, the patient is maintaining a level of activity that can sustain the holding of the instrument and sitting up in bed. Emotionally, the patient is choosing music that brings joy and meaning." More importantly, the patients do not need to be skilled in an instrument in order to derive benefits. Jonason said music therapy's impact derives more from the connection of playing with someone rather than through the skill of the performance. "If the music is not meaningful, then the connection will not be made and no benefit will come of the session. That requires me to be skillful on multiple instruments, comfortable with musical styles and technologically savvy."

The music therapy program at UMass CHC began in 2013 with the help of an anonymous donor and continues to be mostly funded by private donations, most notably from the Sleepers family, which has donated to the CHC for 16 years, along with oncology grants and some pediatric budgeting. Despite the incredible work that Jonason and her fellow Child Life team members do for our pediatric patients, the funding only exists for 16 hours a week in the face of an enormous need for her services. Jonason is always looking to expand what she can provide to her patients. Most notably, she utilizes studio-quality headphones and microphones for recording both the original music performed by her patients and their heartbeats to create "heartsongs," which are music pieces comprised of the patient's heartbeat as a backing track with instrumental or vocal tracks mixed in. These touching works are helpful for both survivorship and bereavement.

"Sometimes songwriting projects are born, or the rewriting of lyrics to express exactly what they want to say in that moment. The change that happens in music therapy can last for hours after a session. A patient will often have a change in mood, which will allow caregivers to feel more relaxed. CNAs will have more success with taking the vitals of a restless toddler during or after music therapy. Nurses and physicians will often come and listen to their patients making music. This is what I love: the ripple effect of a meaningful session on the rest of the patient's day."

Jonason's passion for both her patients and for music underscores the need for such a service. To support this vital aspect of our pediatric patient care, contact Kendra Frederick, the manager of the UMass Child Life Program at childlife@umassmemorial.org or donate to Child Life via https://www.umassmemorialhealthcare.org/umass-memorial-medical-center/services-treatments/childrens-medical-center.

Alex Newbury is a fourth-year medical student applying for residency in diagnostic radiology. He would like to thank Trish Jonason, MT-BC, for contributing to this article and for all her work with the UMass Department of Pediatrics.

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The Eldred Case: A Troubled Encounter of Law and Science

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In July 2018, the Massachusetts Supreme Judicial Court ruled that a judge exercised appropriate discretion in ordering a woman, who was on probation for stealing jewelry to support her heroin habit, to jail as a result of her violation of the "drug-free" condition of her probation. Since the ruling was issued, it has been mischaracterized in a variety of ways. Some commentators have argued the decision stands for the proposition that substance use disorder does not eliminate an addict's "free will." Others have claimed the decision criminalizes drug addicts' relapses. A close reading of the decision shows a court struggling with conflicting public policies, the need to enforce a probation violation in the course of a disease process and a developing understanding of SUD patients' needs and capabilities.

On Aug. 22, 2016, a District Court judge imposed on the defendant a one-year term of probation, which required her to remain drug-free, submit to random drug screens and attend outpatient substance abuse treatment three times a week. That outpatient treatment began Aug. 29. On Sept. 2, the defendant failed a random drug test administered by her probation officer. The probation officer encouraged the defendant to enter inpatient treatment, but the defendant allegedly refused. A probation detention hearing was then held that same day because the probation officer noted that it was the Friday before Labor Day, the defendant's parents were out of town, and the probation officer did not want the defendant to leave his office testing positive for fentanyl. Defense counsel was unable to secure an inpatient placement for the defendant, so the judge ordered the defendant to be held in custody until such a placement became available. The defendant was released to an inpatient treatment facility after 10 days in custody.

On Nov. 22, a hearing was held on the defendant's probation violation. At that hearing, the defendant argued that her SUD rendered her incapable of remaining drug-free and asked that the "drug-free" probation condition be removed. The judge declined to remove that condition but added the condition that the defendant continue inpatient treatment. The question of the "drug-free" condition was appealed, and the SJC took up the matter because "this question presents issues of significant magnitude that require resolution." Importantly, the court stated that "the defendant's claim of SUD rests on science that was not tested below" in the trial court.

The defendant had claimed that a SUD patient cannot comply with a "drug-free" probation condition because she is unable to refrain from drug use. This, the defendant argued, made the SUD defendant analogous to the probationer defendant in another case who was homeless and was required to wear a GPS monitoring device. However, because the homeless shelter where the defendant lived could not accommodate such devices, the defendant's violation was ruled not to be a willful non-compliance with that probation condition. In this case, the court noted that "the appellate record before this court is inadequate to determine whether SUD affects the brain in such a way that certain individuals cannot control their drug use." Thus, the SJC left the door open for another case to raise the claim, based on a judicially recognized theory of addiction, that a SUD probationer cannot be expected to be able to comply with a "drug-free" condition of probation.

The court began its analysis by looking at the public policy goals of probation: rehabilitation of the defendant and protection of the public. With specific reference to drug cases, the court referred to its 1998 "Standards of Substance Abuse," which created a framework that would "promote public safety, provide access to treatment, protect due process, reduce recidivism and ensure offender accountability." Given these disparate goals, the court noted that judges can set any probation condition that is "reasonably related" to the goals of sentencing and probation. The court also stated that prior to agreeing to the probation conditions, the defendant did not claim that her SUD made her unable to abide by the "drug-free" condition. Consequently, the court concluded that the judge did not abuse her discretion by initially imposing that probation condition.

It is possible that, should another case be brought to the SJC in which a claim is properly made that SUD makes a "drug-free" probation condition unfair because it's practically impossible to comply with, the court might revisit the 1998 Standards to try to strike a different balance among the stated goals. The role of the threat of legal consequences for drug use for those with SUD is controversial and directly concerns the goals of providing access to treatment and ensuring offender accountability, which may be difficult to reconcile. Also, the significance of multiple relapses in the recovery process might be better accommodated in individual probation enforcement decisions, in light of new models of addiction that have been evaluated in court. (The court noted in particular that on appeal, the defendant advanced the "brain disease" theory that addiction makes it impossible for a patient to abstain from using drugs, contrasted with the Commonwealth's "behavioral model" holding that SUD only affects, but does not eliminate, the patient's "free will.") This would not be the first nor the last time courts adjust legal doctrine in light of advances in scientific knowledge.

At the probation violation proceedings after the failed drug test, the court expressed sympathy for trial court judges, "particularly judges in the drug courts, [who] stand on the front lines of the opioid epidemic." Where a probationer's probation violation arises out of the defendant's relapse, the confrontation between judicial and disease processes is stark: "The core of this dilemma is that although probation violations often arise out of a defendant's relapse, we recognize that relapse is part of recovery." What is a judge supposed to do, when he or she is confronted with a single incident of relapse that is undoubtedly a probation violation, in the context of the knowledge that those with SUD often relapse multiple times as part of their recovery? In the particular circumstances of the Eldred case, the judge felt the defendant, and the public, would be best protected by detaining her until an inpatient treatment placement could be found. (It should be noted that the defendant's counsel argued in her brief that the judge could have chosen to seek the defendant's civil commitment.)

In particular, the court denied that placing the defendant into custody under these circumstances constituted punishment for her relapse and positive drug test. Instead, "the judge was faced with either releasing the defendant and risking that she would suffer an overdose and die, or holding her in custody until a placement at an inpatient treatment facility became available," as one did after 10 days. The court also noted the lack of a suitable inpatient placement at the time the decision had to be made by the judge: "Although we recognize that the number of inpatient treatment placements is limited, the resolution of that problem concerns public policy and cannot be addressed by a judge." Had better alternatives been available to the judge at the time the decision had to be made, perhaps the question of "incarceration" might not have arisen at all.

This case highlights the tensions that arise when courts are faced with legal processes that may not adequately accommodate current theories of disease and human behavior, with pressing decisions in the context of long-term medical conditions and with reconciling such disparate public policy goals. What seems clear is that these issues will be revisited in future cases.

Peter J. Martin, Esquire, is a partner in the Worcester office of Bowditch & Dewey, LLP, his practice concentrating on health care and nonprofit law.

Worcester District Medical Society

Calendar of Events

2018

September 14 — Friday, 7:30 a.m., Beechwood Hotel

27TH ANNUAL WOMEN IN MEDICINE BREAKFAST

Speaker: The Honorable Harriette L. Chandler, Massachusetts State Senator for the 1st Worcester District

Cosponsored by Physicians Insurance Agency of Massachusetts (PIAM)

October 11 — Thursday, 5:30 p.m., Beechwood Hotel

13TH ANNUAL LOUIS A. COTTLE LECTURE

Topic: TBD

A generous bequest from the Louis A. Cottle Trust was received allowing WDMS to establish an annual lecture series in memory of Dr. Cottle, a dedicated Worcester physician.

November 14 — Wednesday, 5:30 p.m., Beechwood Hotel

FALL DISTRICT MEETING AND AWARDS CEREMONY

The dinner meeting includes the Dr. A. Jane Fitzpatrick Community Service Award, the WDMS Career Achievement Award, and Scholarship Award Presentations.

November–December 30 & 1 — Friday and Saturday, 9:00 a.m., MMS Headquarters and the Westin Hotel, Waltham, MA

2018 INTERIM MEETING AND MEETING OF THE MMS HOUSE OF DELEGATES

All WDMS members are invited to attend as guests and may submit a resolution to the Massachusetts Medical Society.

December 13 — Thursday, 5:30 p.m., Washburn Hall, Mechanics Hall

HOLIDAY RECEPTION AND A NIGHT AT THE MOVIES

Join us for a holiday buffet and movie with a group discussion to follow.

For more information about WDMS
Visit our website:
www.wdms.org

2019

February 13 — Wednesday, 5:30 p.m., Beechwood Hotel

223RD ANNUAL ORATION

Hope for Haiti: Healing One Patient at a Time

Orator: Jane Lochrie, MD

Dr. Lochrie is the medical director of the St. Anne's Free Medical Program, editor of *Worcester Medicine*, past-president of the WDMS, and current chair of the Personnel Committee. She recently traveled to Haiti for a medical mission.

March 1 — Friday, 7:00 p.m. reception; 8:00 p.m. program, Mechanics Hall

CZECH NATIONAL SYMPHONY

100 Years of Leonard Bernstein, *Candide Overture*, *West Side Story* Dances, Selections from *Trouble in Tahiti* and *Songfest*, and *Mass* Meditations

March 13 — Wednesday, 5:30 p.m., Beechwood Hotel

WOMEN IN MEDICINE LEADERSHIP FORUM

Program to be determined

March 30 — DOCTORS' DAY

Event to be announced

March 30 is National Doctors' Day when patients, friends, family and colleagues honor physicians and express their gratitude for physicians' continuing commitment to patients and exceptional medical care.

The event will be sponsored by the Worcester District Medical Society Alliance.

April 10 — Wednesday, 5:30 p.m., Beechwood Hotel

ANNUAL BUSINESS MEETING

Meeting includes presentation of the 2019 Community Clinician of the Year Award.

May 2 & 4 — Thursday and Saturday, 9:00 a.m., the Seaport Hotel and World Trade Center, Boston

2019 MMS ANNUAL MEETING AND HOUSE OF DELEGATES

All WDMS members are invited to attend as a guest and may submit a resolution to the Massachusetts Medical Society.

May 16 — Thursday, 5:30 p.m., University of Massachusetts Medical School

MEET THE AUTHOR SERIES

"Attending"

Author: Ronald Epstein, MD, professor of Family Medicine, Psychiatry, Oncology and Medicine (Palliative Care), University of Rochester School of Medicine and Dentistry

Cosponsored by WDMS and Humanities in Medicine Committee of the Lamar Soutter Library at the University of Massachusetts Medical School

2018 FALL DISTRICT MEETING & AWARDS CEREMONY

WEDNESDAY, NOVEMBER 14, 2018 • 5:30 PM
BEECHWOOD HOTEL, WORCESTER

PROGRAM:

SOCIAL HOUR / BUSINESS MEETING / DINNER
SCHOLARSHIP AWARDS PRESENTATION
AWARDS CEREMONY

AWARD PRESENTATIONS:

ERIK J. GARCIA, MD

2018 DR. A. JANE FITZPATRICK COMMUNITY SERVICE AWARD

DANIEL H. LASSER, MD, MPH

2018 WORCESTER DISTRICT MEDICAL SOCIETY CAREER ACHIEVEMENT AWARD

AWARD PRESENTATIONS:

Britney Atwater-Class of 2020
University of Massachusetts Medical School

Laurel Banach-Class of 2019
University of Massachusetts Medical School

Regina Brown-Class of 2020
University of Massachusetts Medical School

Alexander Buslov-Class of 2019
University of Massachusetts Medical School

Colleen Flanagan-Class of 2020
University of Massachusetts Medical School

Kelly Flanagan-Class of 2021
University of Massachusetts Medical School

Melinda Futran-Class of 2021
University of Massachusetts Medical School

Caitlin Gauvin-Class of 2019
New York Institute of Technology College of Osteopathic Medicine

Matthew Heard-Class of 2019
Drexel University College of Medicine

Jamie Horrigan-Class of 2020
Albany Medical College

Kelsey Jones-Class of 2021
University of Massachusetts Medical School

Akshay Kapoor-Class of 2020
University of Massachusetts Medical School

Kara Kennedy-Class of 2021
University of Massachusetts Medical School

Lucy Li-Class of 2019
University of Massachusetts Medical School

Daniel Marsden-Class of 2021
George Washington University

Alex Newbury-Class of 2019
University of Massachusetts Medical School

Aarane Ratnaseelan-Class of 2021
George Washington University

Michelle Shabo-Class of 2021
University of Massachusetts Medical School

William Sidelinger-Class of 2020
University of Massachusetts Medical School

Marian Younge-Class of 2019
University of Massachusetts Medical School

TO REGISTER EMAIL: WORDMSA@MASSMED.ORG OR CALL: 508-753-1579

13TH ANNUAL LOUIS A. COTTLE LECTURE, OCTOBER 11, 2018
"PUBLIC HEALTH IMPLICATIONS FOR DEREGULATING MARIJUANA"

DR. MARK J. NEAVYN, ASSISTANT PROFESSOR OF EMERGENCY MEDICINE, UMASS






27TH ANNUAL WOMEN IN MEDICINE BREAKFAST
"WOMEN IN LEADERSHIP"

SENATOR HARRIETTE L. CHANDLER





MUSIC WORCESTER

MUSIC WORCESTER 160th ANNIVERSARY

THE 2018-2019 CONCERT SEASON

NEW WORK FOR GOLDBERG VARIATIONS
SIMONE DINNERSTEIN & PAM TANOWITZ DANCE
THE HANOVER THEATRE FOR THE PERFORMING ARTS
TUESDAY, JANUARY 15, 2019 AT 7:30 PM

THE HAVANA CUBA ALL STARTS: FIESTA CUBANA!
MECHANICS HALL // THURSDAY, JANUARY 15, 2019 AT 7:30 PM

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KEEP YOUR HEART FAILURE PATIENTS OUT OF THE HOSPITAL

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