

VirtuaPhysician

A quarterly review for Virtua physicians and their colleagues

Tumor scene investigation via molecular diagnostics



William Manion, MD, PhD, JD

Board Certification: Anatomic, Clinical and Forensic Pathology

Medical School: West Virginia University Hospital

Residency: Pathology, Graduate Hospital

Fellowship: Forensic Pathology, Ohio State University

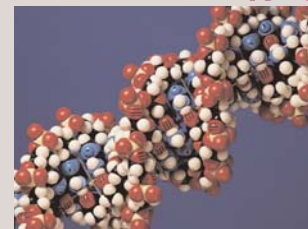
“A dramatic paradigm shift has occurred in pathology,” explains William Manion, MD, chief pathologist, Virtua Memorial Hospital. “We’ve gone from working at the cellular level to now examining molecular and genetic characteristics. New technology such as polymerase chain reaction (PCR), an integral part of the new Virtua molecular diagnostics laboratory, makes these advances possible.”

With PCR, the pathologist or researcher can isolate a segment of DNA or RNA and duplicate it a billion times within a few minutes. Large

amounts of DNA are prerequisite for molecular and genetic testing. Jagjit Chawla, MD, pathologist at Virtua Memorial, gives an example of how “molecular photocopying” (www.genome.gov) excels.

“Take the Pap smear,” says Dr. Chawla. “With conventional testing, we can achieve a 90 percent accurate result. Molecular diagnostics pushes this accuracy to 98 percent. It also provides a way to identify and follow high-risk HPV patients, since HPV can be a precursor to cervical cancer.” In addition, new molecular

Molecular Photocopying



Physicians at Virtua Memorial are currently participating in an analysis of atypical endometrial cells using protein and molecular analysis.

platforms or techniques promise even greater progress in diagnosing infectious diseases and malignancies.

Pharmacogenomics: the genetic basis of drug response

“Another profound advantage offered by the molecular diagnostics laboratory is the ability to perform genetic studies on patients to determine optimal therapies,” says Dr. Manion.

(continued on page 2)

Critical care obstetrics for an elusive disease

“Pregnancy can be a dangerous time for a woman with a pulmonary disorder such as pulmonary hypertension (PPH),” explains Shailen Shah, MD, Virtua critical care obstetrician/gynecologist. “With PPH, pressure in the pulmonary artery rises, which can cause heart failure and high morbidity: Up to 25 percent of these women die during pregnancy or in the months just after.”

Sadly, more than half of these women begin their pregnancies with the lowest New York Heart Association rating for heart failure – of only a one out of four – with four indicating severe heart failure due to symptoms while at rest.

Dr. Shah explains: “Early

recognition of this often elusive disease and its continual monitoring and intervention – throughout pregnancy, delivery and beyond – produces the safest course. We plan for an optimal delivery time and the method is based on the subtle changes in the unique pathophysiology of the mother and her baby.”

Delivery can be a risky time for a healthy woman, and especially so for a PPH mother when blood volume changes are sudden and dramatic. Monitoring hemodynamic functions such as tissue oxygenation, cardiac output, ejection fraction and other functions with a Swan-Ganz catheter is the optimal tool to provide critical information that can

preserve the health of both mother and child.

An overview study that looked at pulmonary vascular disease (PVD) in pregnancy from 1978 through 1996 concludes that:

Maternal prognosis depends on the early diagnosis of PVD, early hospital admission, individually tailored treatment during pregnancy and medical therapy and care focused on the postpartal period.¹

Whereas many maternal-fetal critical care programs focus on the fetal side of the equation, Virtua’s program focuses on both.

¹Journal of the American College of Cardiology, June 31 1998 1650-7 Weiss BM, et al Department of Anesthesiology, University Hospital, Zurich, Switzerland



Shailen Shah, MD

Medical School: Jefferson Medical College

Residency: Obstetrics and Gynecology, Thomas Jefferson University Hospital

Fellowship: Maternal-Fetal Medicine, Thomas Jefferson University Hospital

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Time equals brain function for stroke patients



Mitchell Rubin, MD

Board Certification: Neurology
Medical School: University of Pennsylvania School of Medicine
Residency: Neurology, Columbia-Presbyterian Hospital, New York

“After an initial ischemia, the brain tissue that surrounds the stroke damage – the ischemic penumbra – is also at risk for necrosis,” says Mitchell Rubin, MD, medical director of Virtua’s Neuroscience Program of Excellence. “For patients with an ischemic stroke, administering tissue plasminogen activator (tPA), a thrombolytic agent, within a three-hour window helps preserve tissue and function. Getting them to an emergency room set up to quickly diagnose the problem and administer medication is critical.”

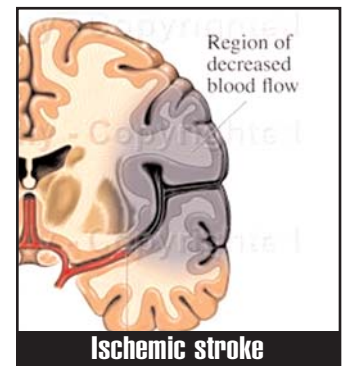
Dr. Rubin explains: “Over the past year, we’ve administered tPA to more acute ischemic stroke patients because of highly defined stroke treatment protocols, a stroke-ready emergency department and a stroke team with a neurologist on

call 24/7. The neurologist together with the radiologist must determine on a CT whether the stroke is ischemic or hemorrhagic, since tPA comes with its own risk of bleeding.” Taking these steps has also earned Virtua Memorial JCAHO’s Primary Stroke Center Certification which is based on guidelines from the Brain Attack Coalition and the American Stroke Association.

An independent tPA review

In May 2002, the National Institute of Neurological Disorders and Stroke (NINDS) asked for an independent review of the data from the initial 1995 NINDS Stroke Study. Upon review, the committee found that:

When the drug was administered according to the study protocol, there was a statistically significant, and



clinically important, benefit of tPA treatment measured by an adjusted tPA to placebo odds ratio of 2.1 (95% CI: 1.5 - 2.9) for a favorable outcome at three months.¹

For a stroke patient, this could mean the difference between someone who is wheeled into his three-month post-stroke appointment or a person who walks through the door.



¹www.ninds.nih.gov (search tPA Review Committee)

Tumor scene investigation via molecular diagnostics (continued from page one)

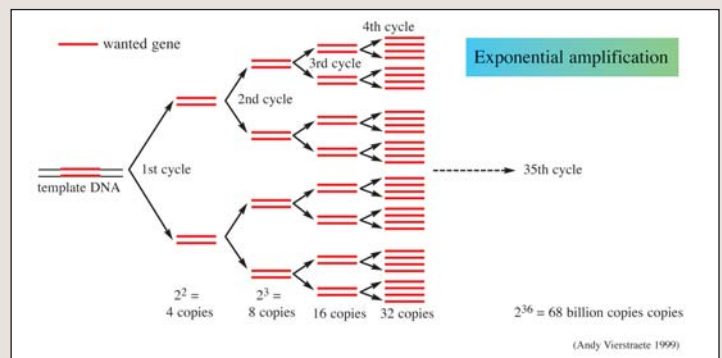


Jagjit Chawla, MD

Board Certification: Anatomic, Clinical, Hemato-Pathology
Medical School: Lady Hardinge, New Delhi, India
Residency: Pathology, Philadelphia General Hospital

Pharmacogenomics provides: a better understanding of the genetic determinants of chemotherapeutic response and ... will enable prospective identification of patients at risk for severe toxicity or those most likely to benefit from a particular treatment regimen. Such studies can be translated to clinical practice via molecular diagnostics (genotyping) in order to guide selection of the optimal drug combination and dosage...¹

For example, a recent clinical trial to address the impact of



dose on the chemotherapeutic response of irinotecan, an agent used to treat colorectal cancer: “showed that patients with the UGT1A1*28 allele are at higher risk for grade 4 neutropenia.”²

Dr. Manion observes: “Through molecular diagnostics, we are entering an era of

increased testing sensitivity, improved testing specificity and individually tailored therapies. It is a brave new world in the very best sense.”



¹Woojin Lee, et al *The Oncologist* 2005;10:104-111 (www.TheOncologist.com)

² Ibid

Stopping the critical cascade



"A patient with sepsis is like a house on fire," declares Jewelle Sutherland, MD, Virtua pulmonologist and critical care specialist. "You may not locate the source of the fire, but empiric therapy and supportive care must be started until the specific infection source is identified."

Martin Topiel, MD, Virtua infectious disease specialist, explains: "Sepsis can cause a violent inflammatory chemical cascade where a patient deteriorates, within hours, into severe sepsis, septic shock and multiple organ dysfunction syndrome (MODS). It's critical to make the earliest diagnosis and begin immediate intervention."

Sepsis, as defined by the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM), is a systemic inflammatory response syndrome (SIRS), resulting from an infection: bacterial, viral, fungal or parasitic. Peritonitis, a kidney infection, or community-acquired pneumonia (CAP) are common triggers. Also at increased risk are patients taking chemotherapy, steroids or those

with Foley catheters. However, in up to 30 percent of sepsis cases, the cause of the infection is not known.

The SIRS complex of symptoms include: tachycardia, fever > than 38c or < 36c, a white count > 12,000, and oliguria. Dr. Sutherland adds: "A change in a patient's mental status may point to sepsis as well as other medical diagnoses. The change can be due to under perfusion of the brain as well as a more global response to the inflammatory cascade."

Goal-directed therapy

The most advanced evidence-based recommendations¹ for treating sepsis now include the addition of early fluid resuscitation, along with empiric antibiotics to cover gram positive, gram negative and anaerobic infections. Many patients with severe sepsis may be candidates for Xigris, an activated protein C monoclonal antibody shown to reduce the risk of death in this population. However, there is a risk of serious bleeding in some patients.

New protocols in place

Virtua is fighting sepsis as part of the Institute of Healthcare Improvement's national 100,000 Lives Campaign. A multidisciplinary team of pulmonary critical care and infectious disease physicians, nurses and technicians, along with hospital infection control personnel have put enhanced hospital and ICU protocols into place. These are formulated to reduce and eliminate evidence of central-line-associated bacterial infection and ventilator-related pneumonia, both of which can lead to sepsis.

What causes sepsis is not entirely clear. Dr. Topiel explains: "It is now believed that the pathophysiology of sepsis is characterized by circulatory derangements and changes in the microvasculature."

Understanding these changes may unlock the mystery of why some people develop sepsis or go into septic shock and others do not.²

¹ *Critical Care Medicine* 2004, Vol.32, no.3

² Kevin J. Tracey, *Fatal Sequence the killer within*, p190



Jewelle Sutherland, MD

Board Certification: Pulmonary Medicine

Medical School: Temple University Medical School

Residency: Internal Medicine, Medical College of Pennsylvania

Fellowship: Pulmonary and Critical Care Medicine, Medical College of Pennsylvania

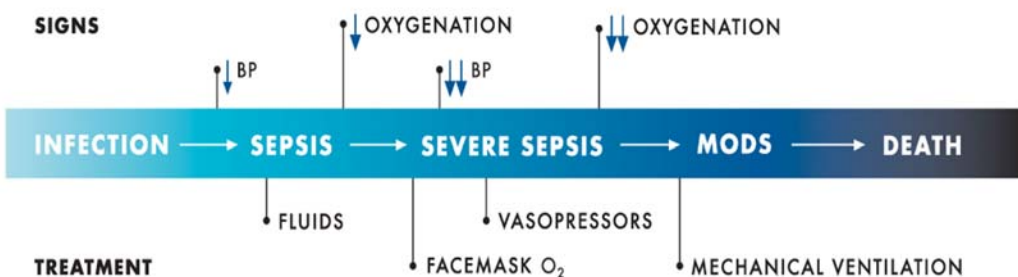


Martin Topiel, MD

Board Certification: Infectious Disease
Medical School: New York University School of Medicine

Residency: Infectious Disease, George Washington University Hospital

Common clinical criteria that may be used to screen patients for severe sepsis



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"It is now believed that the pathophysiology of sepsis is characterized by circulatory derangements and changes in the microvasculature."

Martin Topiel, MD

Pre-implantation genetic diagnosis



Stephen Sawin, MD

Board Certification: Reproductive Endocrinology (OB/GYN)

Medical School: University of Rochester School of Medicine & Dentistry

Residency: Obstetrics and Gynecology, Hospital of the University of Pennsylvania

Fellowship: Reproductive Endocrinology and Infertility, Hospital of the University of Pennsylvania

Geneticists have identified more than one hundred monogenic defects that can be identified with pre-implantation genetic diagnosis (PGD). Some of these include cystic fibrosis, Tay Sachs, and sickle cell anemia.

At the forefront of this technology are George Taliadouros, MD, Peter Van Deerlin, MD, and Stephen Sawin, MD, Virtua obstetricians/gynecologists and reproductive endocrinologists.

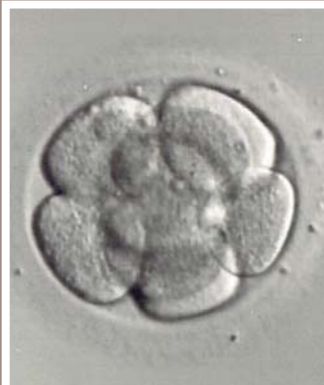
These physicians offer PGD to patients with family histories of genetic disorders in order to determine, before pregnancy, if embryos are at risk for carrying specific genetic abnormalities.

“The science behind this labor-intensive and time-sensitive technology first became available in 1990, but has been improved dramatically and continues to evolve,” says Dr. Taliadouros.

Refinements in PGD have led to its application in situations where patients, particularly women 35 and over, have experienced recurrent miscarriage due to aneuploidy in the fetus. Dr. Taliadouros says: “Research indicates that 60 percent of those miscarried fetuses have chromosomal abnormalities.”

A study published in *Fertility and Sterility*, Vol. 84, No. 2, August 2005, concluded that by using PGD to diagnose aneuploidy – either from the translocation of chromosomes or from the presence of an

Pre-biopsy, day 3, 8 cells



Post-biopsy, day 5, blastocyst



abnormal numbers of chromosomes – it was possible to reduce the recurrent miscarriage rate in women 35 and older from the average 36 percent to 17 percent.

All applications of PGD begin with a blood test of the patients to determine either the necessary genetic probe that should be used to detect the presence of a monogenic disease; or to determine if a chromosomal translocation is present. A genetic probe is a complementary piece of a DNA strand, usually labeled with a radioactive or fluorescent tag, used to locate the abnormal gene by hybridization (matching and attaching itself to a like copy).

Next, the woman undergoes hormone therapy in order to grow multiple eggs.

Using ultrasound guidance and mild anesthesia, the eggs are removed, fertilized with the male’s sperm, and then allowed to grow into embryos over a three-day period.

At that stage, a biopsy of one or two cells from each embryo is performed; and, in cases where patients seek to determine if a genetic mutation is present, the specific probe is applied to determine which, if any, of the embryos are affected.

Dr. Van Deerlin notes that usually two, but no more than three, of the healthy embryos are then implanted in the woman’s womb to establish pregnancy.

However, he points out that if other healthy embryos remain, they can be cryo-preserved for later use.

“Success rates are generally good with PGD – about 50 percent per try – because most patients undergoing the technique are not infertile,” explains Dr. Van Deerlin. Still, both he and Dr. Taliadouros underscore that other factors, such as the age of the woman and the quality of the sperm, can affect the outcome.



Peter Van Deerlin, MD

Board Certification: Reproductive Endocrinology (OB/GYN)

Medical School: Washington University, St. Louis

Residency: Obstetrics and Gynecology, Washington University

Fellowship: Reproductive Endocrinology and Infertility, Hospital of the University of Pennsylvania



Appropriate candidates for PGD are patients who know they are predisposed to certain genetic abnormalities for which there exists a probe; and couples for whom it would be morally or religiously intractable to terminate a fetus after prenatal testing indicated abnormalities were present.

PGD is also appropriate for patients who have experienced recurrent miscarriage, which the American Society for Reproductive Medicine defines as three or more. It is also applicable in situations where there is concurrent infertility.

According to Dr. Sawin, PGD broadens the options available to couples facing the potential for giving birth to a child with genetic or chromosomal defects. "You could leave it to chance, wait and do prenatal testing such as amniocentesis or CVS, use donor gametes, adopt, decide to live child-free, or you could use PGD."



Dr. Taliadouros stands next to *The Beginning of Life*, a reproduction of the painting by Spanish artist Joan Miro.

George Taliadouros, MD

Board Certification: Obstetrics and Gynecology

Medical School: National & Capadistrian University, Athens

Residency: Obstetrics and Gynecology, Northeastern Ohio University

Fellowships: Reproductive Endocrinology, National Institutes of Health, Reproductive Endocrinology & Infertility, Case Western Reserve University

Staying current while working a 12-hour day

"Each year, Virtua provides hundreds of hours of high quality, balanced CME programs to help physicians maintain the highest standard of clinical competence," explains Jeffrey Komins, MD, Virtua's director of medical education. Each program provides category one credits and is accredited by the Medical Society of New Jersey. Programs include all current clinical issues and patient care as well as scientific, ethical, legal, safety and socio-economic topics. Quality and patient satisfaction are also covered. Virtua physicians, visiting professors and scientific experts are among the presenters. Forums include medical grand rounds, lectures, conferences, clinical skills workshops and seminars. All Virtua CME programs are open to Virtua physicians, physicians in the community as well as nurses, technicians and other health-care professionals. For more information about our CME program, contact Shama Nix at 609.267.0700, ext. 43224.

Free software for mobile patient information system

Virtua physicians now can access lab results, diagnostic reports and medication lists from Virtua's hospital information system via a SmartPhone – a combination of phone, PDA, e-mail and Internet access.

And, Virtua will install MData® software from MercuryMD on a SmartPhone. This technology allows physicians secure access to patient data at any time, any place with Internet connectivity. Whether in the office or at home, this software quickly gets up-to-date information to doctors so that patient-care decisions can be made.

"When I'm rounding in the hospital, I use my SmartPhone constantly to review patient information and to make treatment decisions," says Mary Campagnolo, MD, chief of family practice at Virtua Memorial Hospital. "It's gratifying to practice at a place, like Virtua, that continues to leverage the newest technology to improve patient care."

To learn more, call 1-888-Virtua-3.

Arthroscopic rotator cuff repairs



Mark Schwartz, MD

Board Certification: Orthopedic Surgery
Medical School: Mt. Sinai School of Medicine

Residency: Orthopedic Surgery, Mt. Sinai Medical Center, New York

Fellowship: Sports Medicine & Arthroscopic Surgery, Hughston Orthopedic Clinic



Merrick Wetzler, MD

Board Certification: Orthopedic Surgery
Medical School: Temple University Medical School

Residency: Orthopedic Trauma and General Orthopedics, Boston University Medical Center

Fellowship: Sports Medicine, Thomas Jefferson University Hospital

“About 80 to 90 percent of the rotator cuff repairs I perform now are arthroscopic,” says Mark Schwartz, MD, a Virtua Health orthopedic surgeon. He notes that with arthroscopy: “There is much better cosmesis and patients report significantly less pain in the first six to eight weeks post-op because there has been less trauma to the associated areas, especially the deltoid muscle.” Unlike open surgery, adds Dr. Schwartz: “With arthroscopic repair, we can begin rehabilitating patients within the first week.”

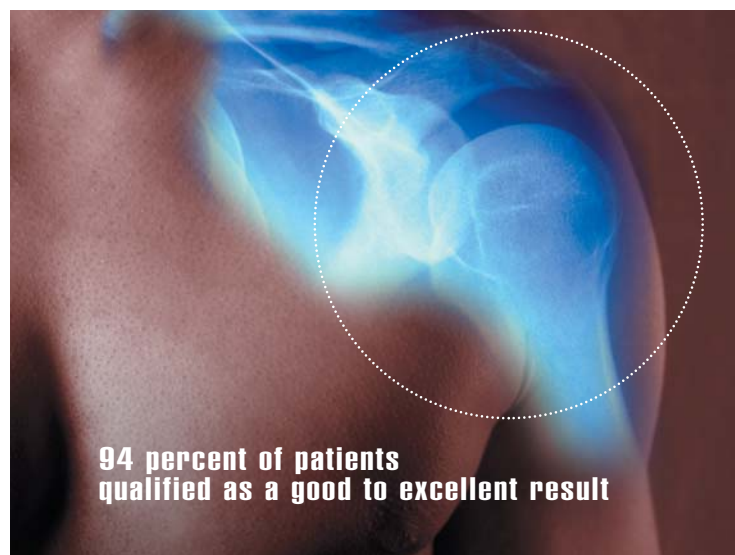
Alternative to open surgery

“It’s incredible. The evidence is conclusive that this procedure is at least as good as open surgery, which has always been the gold standard,” says Dr. Schwartz.

Studies such as that published in the January 2004 issue of *Arthroscopy*¹ support this assertion. At the California Pacific Medical Center in San Francisco, between 1990-1996, researchers conducted one of the largest studies ever on arthroscopic repair outcomes. Patients who had either open, mini-open, or arthroscopic rotator cuff repairs were surveyed and evaluated for results.

The study concluded that:

Of the patients available for follow-up evaluation, 94 percent of patients qualified as a good to excellent result, and that patients treated with



arthroscopic rotator cuff repair technique have maintained excellent clinical outcomes four to 10 years after surgery.¹

Merrick Wetzler, MD, a Virtua orthopedic surgeon specializing in shoulder arthroscopy, says: “Finding an experienced surgeon is important. The shoulder is the most intricate joint in the body, so each tear has its own demands. You can’t treat them all the same.”

While Dr. Wetzler says that half of the rotator cuff repairs he has performed have been arthroscopic, he cautions, “If the rotator cuff is massively torn and retracted, it cannot be repaired no matter what technique you use.” The best candidates for this surgery are those with small- to medium-sized tears (three centimeters or less). “Within that group, the success rate for arthroscopy is excellent, particularly now that there are better suture passing devices and stronger suture materials,” Dr. Wetzler says.

Latest technology

Recent advancements include a knotless suture device that simultaneously implants both the anchor and the suture to the humeral head. Dr. Schwartz also reports that dissolvable anchors and orthobiological tissue implants are now available. “These devices not only promote new tissue growth, but also help heal the existing tear. It’s just amazing what we can do now.”

Dr. Schwartz’s and Dr. Wetzler’s respective levels of experience with the procedure are significant. According to researchers at the University of Washington’s School of Orthopaedics and Sports Medicine in Seattle, the best outcomes occur when the procedure is performed by a “highly specialized surgical team that is familiar with the various techniques and instruments and who perform this surgery often.”²

¹ *Arthroscopy*, 2004 Jan; 20(1):5-12.

² <http://www.orthop.washington.edu/uw/arthroscopic>

Honors and Awards

Ronald Librizzi, DO, chief of maternal-fetal medicine at Virtua Health, was appointed to the Liaison Committee for Obstetricians and Gynecologists (LCOG). LCOG is a national committee that represents 17 OB/GYN organizations and three government agencies. Members meet twice a year to discuss relevant women's health issues such as worldwide clinical trials for the HPV vaccine to combat cervical cancer, the need for more funding and research for perinatal depression, and protocols for emergency contraception.

Paul Quintavalle, DPM, after 20 years of directing the Virtua West Jersey Podiatry Residency, has re-focused his energies on the new Wound Healing Center at Berlin. **John Girimonte, DPM**, has been named acting director of the podiatry residency.

Virtua Memorial Honors its Finest

In recognition of medical staff contributions, Virtua sponsors physician recognition awards each year. Recipients are chosen by their peers for their outstanding contributions to medicine and for their exceptional dedication to patients. Congratulations to this year's recipients.

Rodolfo C. Pascual, MD, chief of surgery, Virtua Memorial, received the Lindley Reagan Award for his exceptional longstanding leadership and for his commitment to medicine, Virtua Health, and the greater community. An oil painting of Dr. Pascual will be displayed in the hospital alongside past award recipients of which there have only been four since 1984.

Robert Hirsh, MD, chief of anesthesia, Virtua Memorial, and **William A. Morowitz, MD**, chair of medicine, Virtua West Jersey, received Distinguished Career Awards for their outstanding leadership within the medical staff, excellence in medicine and significant contributions to Virtua Health and its surrounding community.

Alan Weinstein, MD, chief of oncology, Virtua Memorial, and **David S. Zalut, MD**, chair of family medicine, Virtua West Jersey, received Physician Recognition Awards for emerging as physician leaders, demonstrating excellence in medicine and making significant contributions to Virtua Health and the community.

Mitchell Rubin, MD, chief of neurology, Virtua Memorial, received the President's Award for his outstanding commitment to quality care.

New Services

ACE Program Implemented at Virtua Memorial: The Acute Care for Elders (ACE) program is designed to prevent the functional decline that often occurs among older adults during hospitalization. This inpatient program involves daily assessments of the older adult patient by a multidisciplinary healthcare team. It allows for early identification and intervention of common geriatric syndromes. The goal is to promote independence with an emphasis on the patient returning to home. Benefits of the ACE program include improved functional status, decreased iatrogenic illness, decreased restraint use, improved continuity of care and decreased discharges to long-term care facilities. Virtua Memorial's ACE program complements an existing ACE unit at Virtua Berlin.

The Pre- and Post-Procedural Care Unit at Virtua Marlton was renovated and features a six-bed pre-surgical area, a 10-bed PACU/recovery area with isolation rooms, a 10-bed Phase II recovery/discharge area, all digital cardiac monitoring system, a fully digital nurse communication system and medication system. And to ensure the comfort of patients and their loved ones, the patient areas have been enhanced with windows, TVs and new lounge chairs.

Virtua office forms now will be delivered to your door. And when they are revised or new ones developed, Medical Affairs will notify you of the changes by e-mail and will send replacements to you. Forms can be ordered directly from Virtua's copy center:
Phone: (856) 355-0910
Fax: (856) 355-0921
E-mail: copycenter@Virtua.org
Mail: 20 West Stow Road
Suite #3
Marlton NJ 08053

Accreditations and licensures •

The **Dental Center at Virtua Camden** has been approved as a state-designated loan redemption site. This official recognition encourages full-time attending dentists to work in underserved communities such as Camden and enables them to receive educational loan forgiveness. The dental center treats approximately 6,000 patients annually.

The **postpartum depression program (PPD)** at Virtua has received a grant for \$195,000. The program provides comprehensive resources to help women overcome PPD. In fact, Virtua is one of the first hospitals in New Jersey to offer PPD screenings within one day of delivery. There's also PPD education in prenatal classes, a support group called Talking, Listening & Caring (TLC) for Moms, and a postpartum adjustment information line to help mothers find the support they need.

A wireless EKG system



Cardiac care has been revved up with the installation of General Electric MUSE – a fully-digital, wireless system that transmits and stores EKG data for immediate retrieval anytime, anywhere. The system allows Virtua’s

physicians to provide a faster diagnosis, and it eliminates both the wait time for doctors to receive results and the paper-based filing system. The system utilizes secure web technology that transforms the EKG data into a virtual electronic patient record available for physician review on Virtua’s Health Information System. After simply entering a secure patient ID number, physicians are able to view clear waveforms and images from any computer in the wireless hospital system or from anywhere in the world for comprehensive cardiac interpretation and diagnosis. Doctors can view the data in real-time and obtain results for a quicker diagnosis. Virtua Memorial cardiologist Vincent Spagnuolo, MD, says: “It provides the right information in real-time to anticipate or prevent an attack.”

Elective angioplasty project

Virtua Marlton has been approved to participate in a demonstration project to perform elective angioplasty without the ability to perform open heart surgery onsite. While eight other New Jersey hospitals will participate in this project, Virtua Marlton is the only one in South Jersey. This project is part of a national pilot program that was launched by Johns Hopkins University and includes hospitals in Pennsylvania, Ohio, Illinois, Alabama and Georgia. It also aligns with trends in cardiac care that show the demand for cardiac surgery has declined steadily whereas the need for angioplasty has grown by 26 percent over that last four years. There are, however, not enough angioplasty sites in South Jersey to meet the growing need for this service.

VirtuaPhysician

Peer Review

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Donald Orth, MD, *President Elect, Virtua West Jersey Medical Staff*

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VirtuaPhysician

A quarterly review

Virtua Physician is a review of the work conducted by Virtua physicians in the areas of diagnostic, medical, surgical and rehabilitative medicine.

We hope you find this issue informative, and we look forward to your comments.

We also encourage you to share your work and interesting case studies with your colleagues. Simply e-mail VirtuaPhysician@virtua.org.

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