

January 2003

NIH Clinical Center News

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- Alter continues to make history
- Patient aids in international relief effort
- New guidelines help blood bank

Doctor who admitted first Clinical Center patient dies

Dr. Roy Hertz, 93, a renowned NCI researcher who admitted the first patient to the NIH Clinical Center in 1956, died on Oct. 28. A memorial service was held on Dec. 7 at the Clinical Center Chapel and attended by family, friends and colleagues.

"You often hear that someone's life ended before it should have," said Dr. John Lewis, once a clinical associate of Hertz's. "But Roy Hertz got to follow the whole trail—he had a good run from the top of the mountain."

Hertz came to NIH in 1941. He became chairman of the endocrinology section at the National Cancer Institute, then NICHD's scientific director and then chief of NICHD's Reproductive Research Branch. In 1956, through the sequential use of two drugs, methotrexate and actinomycin-D, cures were achieved in up to 90

percent of women with choriocarcinoma who were treated by 1972; 90 percent of those who were not treated died within a year. This was the first effective chemotherapy for a solid tumor.

"It was the cure for choriocarcinoma and the precise measurement of tumor burden by urinary gonadotropin assay that Roy perfected that actually led to treatment for cure of other cancers, especially leukemias," said Dr. Stan Korenman, associate dean for Ethics and Medical Scientist Training, University of California at Los Angeles, School of Medicine. "I took care of a lot of women with choriocarcinoma, and the change in their lives was the most dramatic event in my long medical career."

Dr. Hertz, who had an M.D. and a doctorate in physiology, was a professor of obstetrics and



Dr. Roy Hertz (l), admitted the Clinical Center's first patient, Charles C. Meredith, on July 6, 1953.

gynecology at New York Medical College in Valhalla in 1972. Born in Cleveland, he earned degrees in physiology and medicine from the University of Wisconsin and a master's in public health from Johns Hopkins.

He married Pearl Fennell in 1934. She died in 1962. In 1965, he married Dorothy Anne Wright Oberdorfer, who died Oct. 17. Surviving are two children from his first marriage, Margaret Brodtkin of San Francisco and Jeremy of Sebastapol, Calif.; a stepson, Michael Oberdorfer of Dickerson, Md.; a stepdaughter, Barbara Verdin of Chesapeake Beach, Md.; 13 grandchildren and nine great-grandchildren.



Jolly hearts and big smiles

Children around the Clinical Center were all smiles this holiday season as NIH employees donated toys and dedicated their time to help children forget about their illnesses and enjoy the holiday.

See photos page seven

Making Clinical Center history...twice

Dr. Alter elected to Institute of Medicine

Dr. Harvey Alter made history last year by being the first Clinical Center physician elected to the National Academy of Sciences.

And he's done it again, by being elected to the Institute of Medicine, a unit of the National Academy of Sciences, making him the first physician in Clinical Center history to be named to both academies.

"It's overwhelming," said Dr. Alter. "I feel guilty and undeserving, but it is a really great honor."

Members are elected into the Institute of Medicine based on professional achievement and demonstrated interest, concern and involvement with problems and critical issues that affect public health.

Established in 1970 as a unit of the National Academy of Sciences, the Institute of Medicine is broadly based in the biomedical sciences and health professions, as well as related aspects of the behavioral and social sciences, administration, law, the physical sciences, and engineering. It is concerned with the protection and advancement of the health professions and sciences, the promotion of research and development pertinent to health and the improvement of health care.

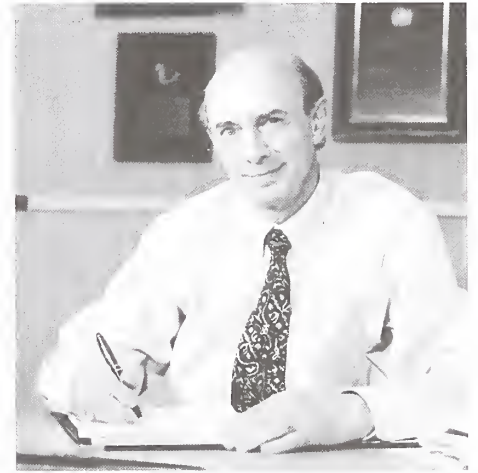
"The research I conduct is long term and has unpredictable payoffs," said Dr. Alter. "Only at NIH could I have had the support necessary to achieve these outcomes."

This marks Dr. Alter's fifth honor in two years. In 2000, he was awarded the prestigious Albert Lasker Medical Research Award, and in 2002 he was awarded The International Society of Blood Transfusion Presidential Award,

named Master of the American College of Physicians, and elected to the National Academy of Sciences.

Dr. Alter is chief of the infectious diseases section and associate director of research in the Department of Transfusion Medicine. A native of New York City, he earned his M.D. at the University of Rochester. He came to the NIH Clinical Center as a senior investigator in 1969.

As a young research fellow, he co-discovered the Australia antigen, a key to detecting the hepatitis B virus. Later, Dr. Alter spearheaded a project at the Clinical Center that created a storehouse of blood samples used to uncover the causes and reduce the risk of transfusion-associated hepatitis. Because of his work, the U.S. instituted blood and donor screening programs that have served to increase the safety of the blood supply.



Dr. Alter used this repository of clinically-linked blood samples to identify another puzzling clinical problem. Most transfusion-related hepatitis was found to be due to a virus different from the two then-known hepatitis agents, A and B. Dr. Alter called this new form of hepatitis non-A, non-B hepatitis and subsequently proved through transmission studies in chimpanzees that it was due to a new agent. This eventually led to the discovery of the hepatitis C virus.



CRIS demos slated for January

Want to know more about the capabilities of the CRIS core system? Stop by the Clinical Center Visitors' Information Center 2-4 p.m. on Jan. 14, 23, or 27 for hands-on demonstrations.

CRIS—the NIH Clinical Research Information System—is a \$60 million project that will tie together and support patient care, research and management at the Clinical Center and the Mark O. Hatfield Clinical Research Center. Work has begun on the largest component of CRIS, the core system that will replace and expand the 25-year-old Medical Information System.

Dr. Stephen Rosenfeld, CRIS project manager, talked about the project in a Dec. 18 Clinical Center Grand Rounds presentation, "An Information Architecture for Clinical Research: Leveraging Technology to Speed Discovery." The presentation can be viewed online at <http://videocast.nih.gov>. Go to "Past Events, Clinical Center Grand Rounds."

For more information about CRIS, go to <http://cris.cc.nih.gov>.

Clinical Center
News

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Clinical Center News online: www.cc.nih.gov/ccc/ccnews/current



Quality of Worklife Initiative & Diversity Council

Do not let holiday debt hold you hostage

Americans charged more than \$100 billion between Thanksgiving and Christmas according to a Maryland-based consumer credit card information company. This means that despite the wonderful holiday that was spent with family and friends, many individuals will face financial crises when the bills arrive in the mail. Employee work life can be adversely impacted by financial worries. The coping tips below may help ease this burden:

- Develop a budget: Realistically assess how much money comes in, and how much is spent. List all expenses and decide which ones can be eliminated.
- Start a payment schedule: Pay the most on the card with the highest interest rate.
- Put away your cards: Don't carry them around with you. You will only be tempted to use them.
- If you are disciplined and can pay more than the minimum amount due, go for introductory rates to take advantage of lower interest rates.
- Start a savings plan for next year so you won't spend what you don't have.
- Call creditors: Explain the situation and work to develop a plan. Don't wait until the account has been turned over to a debt collector.
- Credit Counseling: Credit counseling services are available to help people create and stick to a workable budget, or assist in working out a repayment plan with creditors. Creditors may be willing to accept reduced payments from individuals participating in a debt-repayment plan with a reputable organization.
- Debt Consolidation: You may be able to lower the cost of credit by consolidating debt through a second mortgage or a home equity line of credit. These loans can be expensive, but may also provide certain tax

advantages.

•Bankruptcy: Personal bankruptcy is a last-resort option, which is far-reaching and long-lasting. It stays on a person's credit report for 10 years, making it difficult to acquire credit. However, if the rules are followed, a court order may possibly be obtained to release one from repaying certain debts.

Portions of this article were abstracted from the Federal Trade Commission publication, "Knee-Deep in Debt."

Copies may be obtained from the FTC website at <http://www.ftc.gov/bcp/online/pubs/credit/kneedeep.htm>.

The Clinical Center QWI/Diversity Council does not endorse any groups or individuals who provide services pertaining to these topics.

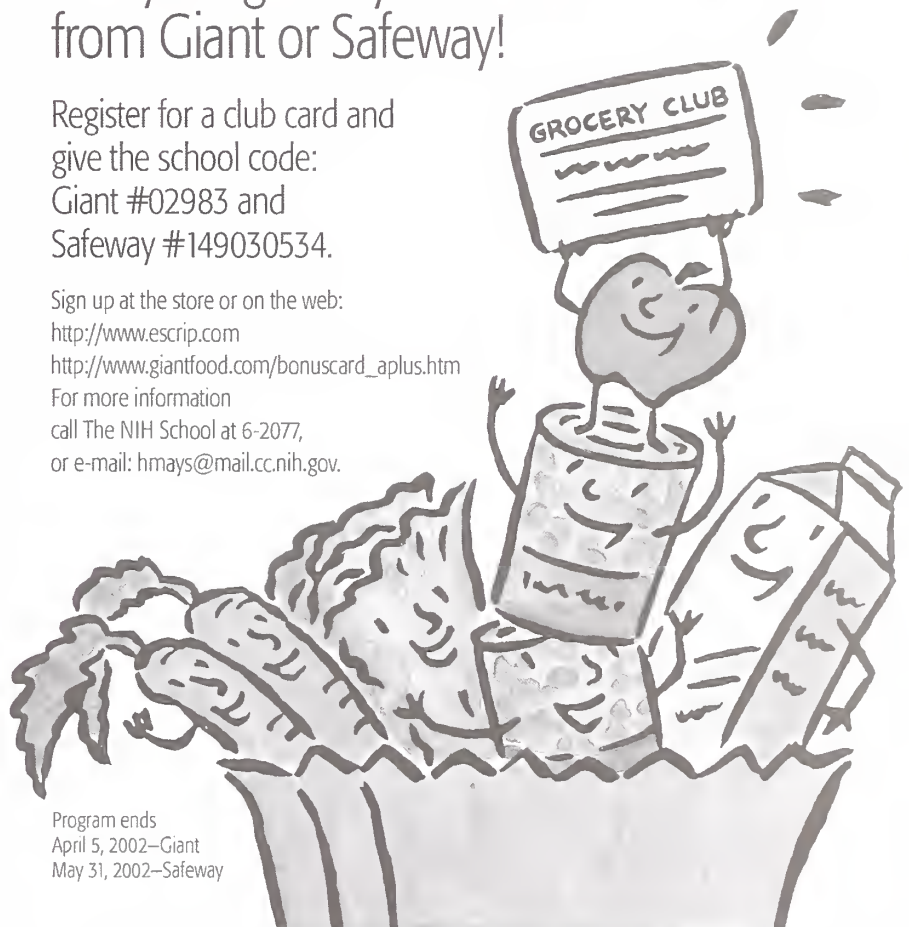


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Program ends
April 5, 2002—Giant
May 31, 2002—Safeway

Children a world apart find common connection

NIH patient selected as youth ambassador for international relief effort

For Lesley Clementi, turning 13 on Dec. 20, was a big deal, but this birthday was extra special. While serving as a national youth ambassador this holiday season for Operation Christmas Child, an international kids-helping-kids-relief effort, Lesley joined hundreds of other children in New York City for an early December massive airlift of gifts for African children with HIV/AIDS. Among those 83,000 gifts was a box Lesley had personally packed with items she selected and a letter she had written. Lesley didn't know that several folks were planning a surprise for her upcoming birthday.

"...I am writing you because I know what it is like to have HIV because I was born with it. I want to let you know that I care for you and I always will no matter what happens in our lives. I also have some advice to give to you that has helped me a lot of times: never give up hope; always have faith and keep faith; if someone chooses not to be your friend it's their loss not yours; you are always going to have a friend, all you need in life is one, and here I am; if you have a problem or any fears, turn to God and he will guide you; and last but not least, another thing that helps me is to write letters to God explaining what is hurting me. Love your friend, Lesley (Florida, USA)."

Lesley who is HIV positive has been an NIH patient for the past seven years. She is currently in a research study in the HIV and AIDS Malignancy Branch, NCI. In the study, children who have been treated for long periods of time with combination therapy against HIV using a class of drugs targeting HIV called protease inhibitors, are carefully followed to see how their immune system responds to the therapy and whether the children develop any toxicities due to the long-term therapy. The study is led



Music star Bono of the rock group U2 hugs NIH Clinical Center patient Lesley Clementi at the Dec. 10 airlift of shoe box gifts for Operation Christmas Child.

by NCI principal investigator Dr. Steve Zeichner. Lesley, accompanied by her mom, Tracey Dannemiller who is also HIV positive, had her latest visit to the Clinical Center the day before her birthday. She is a bundle of smiles and energy as she explains her motivation for working with Operation Christmas Child. "This is for kids like me. I hope these gifts in some small way help other kids with HIV/AIDS overcome the pain, sadness and loneliness."

During her Clinical Center visit Lesley was a trooper as her nurse and doctor performed the routine tests and blood draws, her upbeat attitude unwavering. Helping with a project like Operation Christmas Child is typical of Lesley, according to her mom. "She always wants to help. The ridicule and all the negative things—this (the shoe box of gifts) was taking something so simple and turning it into something so positive by bringing hope and joy to someone who doesn't have much. Lesley truly has an amazing giving heart."

Nachos with cheese and soda and friends coming over were among

Lesley's birthday requests. She got that and a bit more. Courtesy of NBC Nightly News team members and Operation Christmas Child representatives, Lesley was surprised with a videotape of her gift box and letter being given to an African child, who also is infected with HIV. She also received the child's response letter. Lesley and her mom echo the same sentiment about the birthday surprise, "awesome and special."

"...I am a Ugandan girl with HIV. Nine years old. We lost our Daddy in Nov. 1999 that was AIDS which killed him. I was told that my friend you're also HIV+. Sorry for the problem but only Jesus cares about us—I have received my gift from you. Thank you very much and I am asking our God lord to give you life so you never know one day we will meet if God wishes. I have three sisters and one brother. I am the second last born. I am unlucky because among us I only found HIV+ with also my mum she is HIV+. We only thank God because we are still alive. May God be with you, reward you and live for long. Bye Bye, Emily (Kampala, Uganda)."

Worldwide, there are 42 million HIV-positive people. According to a report by the United Nations' AIDS agency, sub-Saharan Africa is home to 75 percent of HIV-positive people.

According to Dr. Zeichner, HIV-infected children in resource-rich countries can often remain healthy for a long time, given the right care, the proper choice of antiretroviral therapy and good adherence. Children in poor countries however, confront a very different future. "The gift that Lesley gave to a child in Uganda serves to connect these two children with the same disease living in two very different worlds and to highlight the differences in the care that they receive and the fates they face."

—by Dianne Needham

Celtic curse opens new doors for blood banks

In the cold, barren lands of northern Europe, where famines and warfare were common, what is today regarded as a common blood disorder may have been a vital genetic defense mechanism to help ensure survival under unusually harsh conditions. The mutation resulted from two defective copies of a particular gene causing the intestine to absorb excessive iron—a good thing if there’s no food and frequent blood loss. But some of the descendants of these northern Europeans today are suffering because of this mutation.

The condition was dubbed the “Celtic Curse” by some, but is more commonly known today as hereditary hemochromatosis (HH). Its effects can be devastating: arthritis, fatigue, heart palpitations, non-specific stomach pain, impotence, loss of menstruation, and infertility. In advanced stages, the skin can take on a gray or bronze hue and serious problems like cirrhosis of the liver, liver cancer, diabetes, heart and joint disease, severe fatigue, cardiac arrhythmia, and congestive heart failure may develop, resulting in disability or death.

“It’s one of the most common genetic disorders in persons of northern European Caucasian descent,” said Dr. Susan Leitman, chief, Blood Services, Department of Transfusion Medicine. “Many people don’t even know they have it, although it affects them from early childhood.” According to Leitman, one in 200 people in this category suffer from HH. She adds, it should be something that’s tested at infancy or in childhood.

“Many physicians are opposed to universal screening for HH because it labels people as having a genetic disorder early on,” she said, “and it might negatively affect that person’s ability to get health insurance.” Such attitudes, she added, need serious rethinking.

One reason she feels that way is because the treatment for this

potentially debilitating disorder is as simple as taking blood, a process blood donors know as phlebotomy. In other words, the ancient practice of “bleeding” may have had a very real foundation in medical science.

Although phlebotomies may be simple, they are not cheap. Bills for going in to have blood removed in a doctor’s office on a regular basis can quickly add up. On the other hand, blood centers, increasingly hobbled by new restrictions on who can and can’t give blood, are facing record blood shortages. Leitman and other researchers believe the time has come to stop viewing people with HH as sufferers and began seeing them as a potential national asset.

“The fact is, we’ve taken a hit because of these restrictions,” she said. “If a person’s been to England for greater than three months, or

“In every way this is a win-win situation...”

—Dr. Susan Leitman



Dr. Susan Leitman believes that people with HH are a national asset.

served more than six months on a European military base, or resided in Europe for five years or longer, they are unable to donate blood. These new policies have robbed us of many of our best donors.”

Because hereditary hemochromatosis is considered a disorder and those with it need to have blood removed for therapeutic reasons, the Food and Drug Administration was initially wary about letting them donate blood. People who want to donate because they’re doing something good for somebody else is one thing, it was reasoned. If someone needs to give blood, their motivations may keep them from revealing details that would otherwise prevent their blood from being accepted. Thus, any blood drawn from HH subjects was tracked and, if used, the source of the blood had to be disclosed to transfusion recipients in advance—more trouble than it was worth for most centers.

The impasse is real, but not insurmountable, Leitman said. In January 2001, the Clinical Center’s Department of Transfusion Medicine joined a growing number of blood centers receiving waivers for the restrictions. But as with anything, there were conditions.

First, all HH subjects must be treated free of charge whether or not they meet the present criteria for donating blood. They must be under a physician’s care, must have a prescription for phlebotomy treatment written by a physician and must undergo periodic monitoring of blood iron levels. In return, the blood that is removed therapeutically can be made available for transfusion into others.

“In every way this is a win-win situation,” Leitman said. “All that’s required is a simple finger-stick blood test at the time of phlebotomy to see if the hemoglobin is high enough to donate. Schedules are established, there are fixed guidelines

see **Blood Bank**, page six

West Nile Virus observed in MRI images

Extensive changes in deep brain tissue or gray matter caused by West Nile Virus (WNV) encephalitis have been observed in magnetic resonance images for the first time. That finding is described in a case report from scientists at the NIH Clinical Center.

Using serial magnetic resonance imaging, physician-researchers monitored West Nile disease progression in a 55-year-old white male. MRI was conducted six times over approximately five weeks (days 5, 8, 11, 18, 23, and 37). Deep gray matter involvement in WNV encephalitis was not found until day 11 of fever – day 7 of neurological symptoms. “The serial images enabled us to follow the disease progression over a protracted timeframe. This aids us in understanding the impact on brain function,” said John A. Butman, M.D., Ph.D., staff neuroradiologist, Diagnostic Radiology Department, Clinical Center

Dr. Butman and co-authors Juan C. Gea-Banacloche, M.D., Michael W. Haley, M.D., Paul A. Nyquist, M.D., and Avi S. Retter, M.D. presented the case report at the 88th Scientific Assembly and Annual Meeting of the Radiological Society of North America held Dec. 1-6, in Chicago.

According to the case report, the MRI findings lag behind the clinical picture of WNV encephalitis, indicating that a patient’s condition can be much worse than initial MRI findings suggest. “Progression of disease may be seen on MR examination between days 7 and 14,” said Dr. Butman.

The researchers noted that the sites of brain involvement with WNV encephalitis have a high overlap with viruses in the same family, and produce similar symptoms. “St. Louis encephalitis is like WNV encephalitis in that it is very unusual to have early MRI findings, whereas Japanese encephalitis often has early MR

findings,” said Dr. Butman.

The most serious consequences of WNV, which is typically asymptomatic or accompanied by mild, flu-like symptoms that last a few days and do not appear to pose any long-term health threat, are encephalitis and meningitis. However, explained Dr. Butman, an estimated 1 in 150 WNV cases become clinically apparent with neurological symptoms. Of those cases approximately 50 percent develop into encephalitis.

Most often found in Africa, Asia and the Middle East, WNV has been in the U.S. since mid-1999 or earlier, according to the Centers for Disease Control. In a 1999 New York City WNV outbreak, MRI documented evidence of meningitis but did not observe infection of the brain tissue. “It is likely that encephalitis was present but undetected visually by MRI,” said Dr. Butman.

A normal MRI does not exclude WNV encephalitis, Dr. Butman pointed out. “This report reinforces that there can be very subtle findings of the disease early on in WNV. The absence of MRI visible disease does not indicate disease status,” he said. He added that a negative initial MRI is to be expected with WNV encephalitis and that there may be fairly extensive disease present in the brain despite a negative MRI. “The consequences of what was likely there from the start may be seen in a week or two.”

The case report’s results, emphasized Dr. Butman, do not render the initial MRI irrelevant. While physicians wait for spinal fluid pathology results, MR findings can be used to rule out the presence of other neurological disease with overlapping symptoms. “This case gives us the knowledge that MRI is not particularly sensitive to the type of infection caused by WNV encephalitis. Consequently, fairly extensive progression occurs before the disease becomes visible,” he said.

Blood bank benefits from new guidelines

continued from page five

for monitoring, and the care is streamlined and standardized.”

Since January of last year, the Clinical Center’s blood bank has accrued 116 new subjects—one of the fastest accruals ever. Word is spreading by the Internet, newsletters and articles, and word of mouth. Organizations such as the American Hemochromatosis Society, Iron Overload Disorders Organization and Iron Disorders Institute have also spread the word. The stipulations surrounding the use of HH donor blood for transfusion guarantee an increase in the amount of usable blood for blood banks and hospitals.

“The treatment is simple and highly effective...”

—Dr. Susan Leitman

At the same time, the guidelines remove any incentive on the part of the donors to hide risk factors that may make them ineligible for donation.

Phlebotomy treatments do not stop once excess iron has been removed. Leitman recommends that iron levels continue to be monitored throughout life in people with HH, and that phlebotomy treatments continue, at a slower pace, to prevent iron reaccumulation.

“The problems associated with hereditary hemochromatosis can be prevented simply by keeping the iron from accumulating,” Leitman said. “The treatment is simple, highly effective, and has been known and available for more than 50 years.”

—by John Iler

Giving from the heart: NIH'ers help spread holiday cheer

The NIH Police and Fire Department received more than 500 toys from NIH employees for their seventh annual *Toys to Share Because We Care* program. Nearly 400 employees donated a bundle of Barbies, stuffed animals and board games to children throughout the Clinical Center. Members of the Police and Fire Department along with Santa Claus and the Washington Redskins Cheerleaders delivered toys to nearly 60 children. Children who were hospitalized on Christmas day woke up to gifts around their bed. "The NIH employees have always given generously," said Lt. Laurence Brown. "They have a giving spirit and as our country continues to go through challenges, NIH employees respond."



Erasmio and Paola Lopez participate in the "Holidays Around the World" activity held on the 14th floor. Volunteers and employees donated their time to help kids make holiday crafts.





And the prize goes to...

Amanda Caruso, 10, pictured with Sheila Barrett, was one of the winners of the Department of Laboratory Medicine's annual holiday raffle. Amanda bought six tickets for \$5 and won a 20-lbs. basket of chocolate, cookies and coffee. The basket was donated by the Social Work Department. Three other baskets, donated by DLM, and one other donated by the local community were won by Sharon Wentcel, Sue Frodigh, Becky Kazebee, and Quandra Freeman. Amanda is one of the youngest winners in the history of the 30-year-old fundraiser. DLM holds its annual holiday fundraiser to benefit the Friends of the Clinical Center and the Patient Emergency Fund. This year they raised \$3,900.

j a n u a r y

1

**Grand Rounds
noon-1 p.m.
Masur Auditorium**
No Grand Rounds

**Wednesday Afternoon
Lecture, 3 p.m.
Masur Auditorium**
No Wednesday Afternoon
Lecture

8

**Grand Rounds
noon-1 p.m.
Masur Auditorium**
*Microanalytical Techniques:
Application to Clinical
Medicine*

Terry Phillips, Ph.D., D.Sc.,
ORS, OD, NIH
*Dietary Factors and
Neurodegenerative Disorders*
Mark Mattson, Ph.D., Johns
Hopkins University School of
Medicine

**Wednesday Afternoon
Lecture
3 p.m.
Masur Auditorium**
*Molecular Mechanisms of
Protein Sorting in the
Secretory Pathway*
Randy W. Schekman, Ph.D.,
University of California,
Berkeley

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**Grand Rounds-Great
Teachers
noon-1 p.m.
Masur Auditorium**
*Cancer Pain: Its Science,
Ethics, and Politics*
Kathleen Foley, M.D.,
Memorial Sloan-Kettering
Cancer Center

**Wednesday Afternoon
Lecture
3 p.m.
Masur Auditorium**
*Biological Circuits With
Small RNA Switches*
Susan Gottesman, Ph.D., NCI

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**Grand Rounds
Bench to Bedside
noon-1 p.m.
Masur Auditorium**
*New Strategies for Diagnosis,
Treatment, and Prevention of
Infections in Oncology
Patients and Blood and
Marrow Transplant
Recipients*
Andreas H. Groll, M.D.,
Wilhelms University Medical
Center, Germany
Elizabeth O'Shaughnessy,
M.D., NCI

29

**Wednesday Afternoon
Lecture
3 p.m.
Masur Auditorium**
*Telomerase and the
Consequences Of Telomere
Dysfunction*
Carol W. Greider, Ph.D.,
Johns Hopkins University
School of Medicine

**Grand Rounds
noon-1 p.m.
Masur Auditorium**
*Finally: A Vaccine for
Typhoid Fever with
Implications for Other
Enteric Pathogens*
Shouson Szu, Ph.D., NICHD
*Genotype Phenotype
Comparisons in Parkinson's
Disease Across Ethnic Groups*
Katrina Gwinn-Hardy, M.D.,
NINDS

**Wednesday Afternoon
Lecture
3 p.m.
Masur Auditorium**
*The Epidemiology Of Breast
Cancer Among Older Women
Between 65-79 Years: An
Understudied Age Group*
Janet R. Daling, Ph.D., Fred
Hutchinson Cancer Research
Center, Seattle