Newsletter

Prostate Cancer 101, Inc.

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The Prostate Cancer Information and Support Group of the Mid-Hudson

Depression May Make It Harder to Beat Prostate Cancer

Men with both conditions have worse survival odds, study contends

Friday, July 11, 2014 (HealthDay News) -- Prostate cancer patients are more likely to be diagnosed with aggressive disease, receive less effective treatment and die sooner if they also have depression, a new study suggests.

Researchers analyzed data from more than 41,200 American men who were diagnosed with localized prostate cancer between 2004 and 2007. They followed them through 2009. Nearly 1,900 of the patients had been diagnosed with depression in the two years before their prostate cancer was discovered.

"Men with intermediate- or high-risk prostate cancer and a recent diagnosis of depression are less likely to undergo definitive treatment and experience worse overall survival," study lead author Dr. Jim Hu, a professor of urology at the University of California, Los Angeles, said in a university news release.

"The effect of depressive disorders on prostate cancer treatment and survivorship warrants further study, because both conditions are relatively common in men in the United States," he added. While the study found an association between the two, it did not establish a direct cause-and-effect relationship.

Several factors may contribute to this association, the researchers said. They include: bias against people with mental illness; depression's effect on the cancer's biological processes; a depressed patient's reduced interest in his health or treatment; and missed opportunities by doctors to educate men about prostate cancer screening and treatment.

Depression was more likely in prostate cancer patients who were older, had lower incomes, were white or Hispanic, were unmarried, had other health problems and did not live in cities, the researchers found.

Also, depressed prostate cancer patients were less likely to ask for treatments such as surgery or radiation than those without depression, according to the study published online recently in the *Journal of Clinical Oncology*.

"This was surprising, because depressed men were more likely to see physicians in the two years prior to prostate cancer diagnosis compared to non-depressed men," Hu said.

Next to skin cancer, prostate cancer is the second most common cancer in American men. About 233,000 U.S. men will be diagnosed with prostate cancer in 2014, and nearly 30,000 will die of the disease, according to the U.S. National Cancer Institute.

More information
The U.S. National Library of Medicine has more about prostate cancer.

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Vitamin D deficiency linked to aggressive prostate cancer
Regular vitamin D screenings could especially benefit white and African-American men

CHICAGO --- African-American and European-American men at high risk of prostate cancer have greater odds of being diagnosed with an aggressive form of the disease if they have a vitamin D deficiency, according to a new study from Northwestern Medicine® and the University of Illinois at Chicago (UIC).

Results of the study will be published May 1 in *Clinical Cancer Research*, a journal of the American Association for Cancer Research.

"Vitamin D deficiency could be a biomarker of advanced prostate tumor progression in large segments of the general population," said Adam B. Murphy, M.D., lead author of the study. "More research is needed, but it would be wise for men to be screened for vitamin D deficiency and treated."
Murphy is an assistant professor in urology at Northwestern University Feinberg School of Medicine, a physician at Jesse Brown VA Medical Center and a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

"This is the first study to look at vitamin D deficiency and biopsy outcomes in men at high risk of prostate cancer," said Rick Kittles, senior author of the study. "Previous studies focused on vitamin D levels in men either with or without prostate cancer."
Kittles is an associate professor in the department of medicine at UIC.

Scientists examined data collected from a diverse group of more than 600 men from the Chicago area who had elevated PSA levels or other risk factors for prostate cancer. Each man was screened for vitamin D deficiency before undergoing a prostate biopsy.

The authors were surprised to find that vitamin D deficiency seemed to be a predictor of aggressive forms of prostate cancer diagnosis in African-American and European-American men, even after adjusting for potential confounders including diet, smoking habits, obesity, family history and calcium intake.

"These men, with severe vitamin D deficiency, had greater odds of advanced grade and advanced stage of tumors within or outside the prostate," Murphy said.

European-American men and African-American men had 3.66 times and 4.89 times increased odds of having aggres-

sive prostate cancer respectively and 2.42 times and 4.22 times increased odds of having tumor stage T2b or higher, respectively. African-American men with severe vitamin D deficiency also had 2.43 times increased odds of being diagnosed with prostate cancer.

"Vitamin D deficiency is more common and severe in people with darker skin and it could be that this deficiency is a contributor to prostate cancer progression among African-Americans," Murphy said. "Our findings imply that vitamin D deficiency is a bigger contributor to African-American prostate cancer."

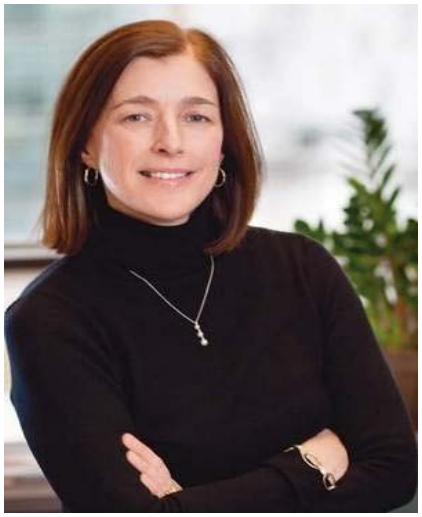
Unless it is severe, vitamin D deficiency is fairly asymptomatic, so more effort needs to be put on screening, Murphy said.
"It is a good idea to get your levels checked on a yearly basis," Murphy said. "If you are deficient, you and you doctor can make a plan on how to reverse it through diet, supplements or other therapies."

The National Institutes of Health and the U.S. Department of Defense funded this study.

Source: CDMRP http://cdmrp.army.mil/pcrp/

U-M research: Late-stage prostate cancer increasing among younger men

8:56 AM, July 17, 2014 |



Dr. Kathleen Cooney

By Robin Erb

Detroit Free Press Medical Writer

Diagnoses of late-stage prostate cancer among younger men are on a surprising increase, with a nearly sixfold rise in diagnoses over two decades — too much of an increase to link solely to better screening, according to a team of researchers at the University of Michigan Comprehensive Cancer Center. Some of these cases turn out to be very aggressive and these men can present with cancer that has already spread to lymph nodes and bone.

That, has the U-M researchers calling for a closer look at the DNA of aggressive prostate cancer tumors — work that could reveal genetic mutations causing the uncontrolled cell growth.

Just as the BRCA2 gene mutation makes women more likely to develop breast cancer and men to develop an aggressive form of prostate cancer, another genetic mutation might be at work causing some of these early-onset prostate cancer cases, researchers said.

"We want to understand these aggressive diseases from the biologic perspective — why are they happening. That (in turn) may have an impact on screening and therapy," said Dr. Kathleen Cooney, U-M professor of internal medicine and urology.

Although prostate cancer is on the rise for all age groups, Cooney and her team were particularly troubled by the increase among those who were diagnosed early, in part because studies suggest that some early-onset prostate cancers are faster-growing and more deadly.

One study found that men between 35 and 44 years old who are diagnosed with late-state prostate cancer have a 50% higher risk of dying than men diagnosed with late-stage prostate cancer between 65 and 74, Cooney said.

To be clear, with treatment, prostate cancer overall is "low risk" compared with oth-

er cancers, even for younger men, Cooney said.
But for a few, the cancer is particularly aggressive. Plus, the treatment may cause other health problems later in life, she said.

Cooney and colleagues analyzed cancer case surveillance data collected by the National Cancer Institute between 1987, when doctors began screening men for prostate cancer using the prostate-specific antigen or PSA blood test, and 2008, the most recent data available for the analysis.

The findings, she said, are a "call to action" for better gene sequencing of tumors, which could lead to better screening guidelines for men who are likely carriers of the gene mutation.

It is estimated that 233,000 new cases of prostate cancer will be diagnosed this year in the U.S., with 29,480 deaths caused by it, according to the National Cancer Institute .

Contact Robin Erb: rerb@freepress.com or 313-222-2708. Follow her on Twitter https://twitter.com/FreepHealth

Source: Detroit Free Press

Study May Alter Approach to Prostate Cancer

By ANDREW POLLACKJUNE 1, 2014

A study supports chemotherapy for men early in their treatment for advanced prostate cancer. Credit Gerry Broome/Associated Press

CHICAGO — Many men with prostate cancer put off using chemotherapy as long as possible, fearing its side effects.
But a new study has found that men given chemotherapy early in their treatment for advanced disease lived a median of nearly 14 months longer than those who did not get early chemotherapy. The result could upend the established treatment practice, researchers said here on Sunday.
"We haven't seen survival benefits like that for any therapy in prostate cancer," said Dr. Michael J. Morris, an associate professor at the Memorial Sloan-Kettering Cancer Center, who was not involved in the study but was selected to publicly comment on it at the annual meeting of the American Society of Clinical Oncology.

Another study being presented on Sunday found that drugs called aromatase inhibitors might be better than the standard drug tamoxifen in preventing a recurrence of disease in premenopausal women with early breast cancer.
Both studies are being featured in the plenary session on Sunday, meaning they were deemed among the most noteworthy of the more than 5,000 studies being presented at the meeting. In a conference that typically celebrates the latest and greatest drug, all four studies chosen for the plenary session this year are about better ways of using older drugs, showing that there can be a lot to learn even after drugs get to market.

Dr. Nicholas J. Vogelzang, an author of the study on prostate cancer, said that the findings would change practice and that he had already started discussing this option with patients. The challenge, he said, is getting men to agree.
"Not many of them want to do chemotherapy, even though the numbers are convincing," said Dr. Vogelzang, who works at the Comprehensive Cancer Centers of Nevada.

The study's findings apply to a fairly narrow group of patients — men whose cancer has already spread beyond the prostate gland at the time of diagnosis, or whose cancer has come back after surgery or radiation treatment and still remains susceptible to hormone therapy.

Only a small fraction of men have metastatic prostate cancer at the time of the initial diagnosis because prostate cancer screening using a blood test typically detects the disease before it has spread.
But screening is expected to become less common because

a government advisory committee, the United States Preventive Services Task Force, has recommended against routine screening, saying that more men are harmed by unnecessary treatments for prostate cancer than are saved from death by screening. That could lead to an increase in men whose initial diagnosis is metastatic cancer, Dr. Vogelzang said.

The study, sponsored by the National Cancer Institute, involved 790 men who received either only hormone therapy or hormone therapy in addition to at most six infusions of docetaxel spaced three weeks apart.
Those who received the chemotherapy lived a median of 57.6 months, compared with 44.0 months in the control group, a difference of 13.6 months. The difference in survival was even greater — 17 months — for the patients whose cancer had spread more extensively. Dr. Morris of Sloan-Kettering said those men were the best candidates for early chemotherapy.

Docetaxel is sold under the brand name Taxotere by Sanofi, but generic versions are also available. It was approved for metastatic prostate cancer in 2004. In the last few years, several other drugs have been approved, like Zytiga from Johnson & Johnson and Xtandi from Medivation and Astellas Pharma.
But docetaxel and the newer drugs are typically used after hormone therapy has stopped working. In that setting, each of them has extended median survival by about two to five months in clinical trials.

Dr. Matthew R. Cooperberg, associate professor of urology at the University of California, San Francisco, said doctors were starting to use the newer agents before docetaxel, pushing chemotherapy further back in the sequence.
So the new study "is, to an extent, bucking the tide," he said. "This trial may be evidence that the role for chemo is earlier, when patients are healthier and the disease burden is relatively low."

The results also raise the question of whether the other prostate cancer drugs would also provide a much greater survival advantage if used earlier. Some trials are underway to determine that.
One issue is that early treatment is often handled by urologists, not oncologists. And many urologists do not administer chemotherapy.
Dr. Morris said he did not think earlier use of docetaxel would diminish sales of the newer agents. Men will eventually become resistant to hormone therapy, he said, and will need the newer agents.

In breast cancer, women with estrogen-responsive disease typically take drugs for at least five years after their tumor has been removed surgically, to prevent cancer from recurring.
Aromatase inhibitors are generally considered a better choice than tamoxifen for postmenopausal women. But aromatase inhibitors work only when women have low estrogen levels, which usually rules them out for premenopausal women.

The new study — actually two studies being analyzed together to accumulate nearly 4,700 patients — involved suppressing the functioning of the ovaries so that the younger women could take an aromatase inhibitor.
Five years of an aromatase inhibitor in addition to ovarian suppression proved superior to five years of tamoxifen in addition to ovarian suppression. After five years, 91.1 percent of those who received the aromatase inhibitor, exemestane, were free of cancer, compared with 87.3 percent of those who received tamoxifen with ovarian suppression. (In the United States, tamoxifen is typically used without ovarian suppression.)

Some experts said they were a bit skeptical that the results would change practice, noting that so far there was no difference between the groups in how long the women lived. And side effects must be evaluated, they said. Those include both the joint pain caused by aromatase inhibitors as well as the hot flashes and bone loss that could come from putting women into early menopause so they could use the aromatase inhibitor.
Ovarian suppression is typically accomplished using drugs like goserelin. Another study presented here on Friday showed that goserelin could help preserve fertility in young breast cancer patients.

Exemestane is sold under the brand name Aromasin by Pfizer, though generic versions are commonly used.
Source: New York Times

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In Defense Of Prostate Cancer Screening

Guest post written by **Benjamin Davies**
Benjamin Davies is an Associate Professor in the Dept. of Urology at the University of Pittsburgh School of Medicine.
Davies is writing in response to "More Health Care Is Better Health Care: Medical Myth Or Reality?" by Robert Pearl, Chief Executive, Permanente Medical Group and a Forbes contributor.
Have you ever asked your plastic surgeon advice on prostate cancer screening? Or the utility of an annual physical exam? Or how to treat that nagging back pain? Of course you haven't and why would you? Still the CEO of the Permanente Medical Group, the physician group part of Kaiser Permante, Dr. Pearl (a respected plastic and reconstructive surgeon) feels comfortably equipped to comment on these issues and has in his recent Forbes column. As a doctor who specializes in the treatment of prostate cancer patients, I have to object.
"Unfortunately, in most cases, doctors can't differentiate between cancer that will become harmful and cancer that won't," Pearl wrote. "So, when tests suggest the presence of prostate cancer, most men pursue treatment."
That statement is wrong. The data on prostate cancer screening actually indicate that, when done right, prostate cancer screening does save men's lives. And prostate cancer is probably the most studied carcinoma in the world when it comes to stratifying patients by the risk of their disease. New diagnostic tests, some of them based on genetics, will allow us to do this in an even better way.
Of course, Pearl isn't alone in besmirching prostate cancer screening. His essay parrots the findings of the increasingly powerful (and controversial) U.S. Preventative Services Task Force (USPSTF), a group convened by the government that tries to evaluate which treatments and procedures are supported by evidence and which are not. Notably, this group made its decision without an academic urologist, oncologist, or radiation oncologist.
It says prostate cancer screening is not warranted based on two big clinical trials; the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the Prostate, Lung, Colorectal, and Ovarian Cancer Study (PLCO). Unfortunately, defini-

tive conclusions were made on incomplete data. For instance, the USPSTF relied on the 9yr outcome data from the ERSPC which is not even close to its prespecified main follow-up time (the later results showed significant reduction in prostate cancer mortality in the 11 year follow-up data)

The USPSTF's stated goal was to see if PSA-based screening decreased all-cause mortality. Yet the study based in the United States is not a screening study (PLCO). Think of it more as a study of screened patients vs. sort-of screened patients. That's because in America the control group ("unscreened") was screened over 25% of the time. That is what scientists call contamination. Sorting out anything meaningful from the PLCO is – I would argue – impossible. Had the epidemiologists accounted for this contamination (which they didn't) the study would have been woefully underpowered to look at all-cause mortality. The European trial, where screening groups where properly handled, showed an impressive overall survival benefit.

The USPSTF is guilty of the sin of omission. It never considered the important work of Dr. Ruth Etzioni at the Fred Hutchinson Cancer Research Center who has used retrospective data to create models that show the large impact screening has had on prostate cancer mortality in the United States. This exact type of complicated statistical modeling was used in the USPSTF breast cancer recommendations. And the USPSTF did not take into account basic prostate cancer epidemiology. Between the years 1994 and 2005 the prostate cancer mortality rates in the US fell about 4% a year and the rates are still declining (for now). There is no plausible explanation for this except for screening. Accordingly there has also been a 40% decrease in the rates of prostate cancer metastasis since screening began – again there is no plausible explanation for this except for screening.

This is a fact: We can differentiate between harmful tumors and slow growing tumors, which means many men can safely not be treated. Hundreds of thousands of men who have slow growing prostate cancers are monitored and not treated here in the US and worldwide. It has been painful to see many urologists reject active surveillance of prostate cancer and treat many men inappropriately. In fact I would posit that as a group we have contributed to the PSA screening conundrum precisely because we failed to promote active surveillance of slow growing prostate cancer tumors.

Our ability to follow slow growing tumors is a product of decades of careful epidemiologic research into the natural history of the disease. Carefully constructed prediction calculators have been made by our leading researchers (called the Partin Tables or CAPRA scores) that can help counsel our patients on their risks of the disease affecting them over time.

Important advances in prostate cancer screening are upon us. Witness the birth of a new lab test called Prostate Health Index (PHI) that can discriminate fast growing tumor better than the current PSA lab test. The advance radiologic techniques called MRI fusion technology also has the ability to diagnosis high grade tumors with amazing ability (does miss a few though..). We are also seeing the emergence of real genomic tools that risk stratify prostate cancer patients based on their pathology results (using gene singatures) when combined with clinical parameters.

I don't mean to suggest that Pearl and the USPTSF don't have a point. Many urologists do overtreat low grade prostate cancer tumors in elderly men (or over use androgen deprivation), and this is shameful. I truly believe there will be a day that insurance companies (and medicare) should not pay for treating 80 year olds with low grade, low volume prostate cancer. This is a complicated, fraught, and challenging topic. But I think many critics of screening go much too far without even acknowledging the limitations of the data at hand. To do so is dangerous, intellectually dishonest, and – in my opinion – might shorten the longevity of American men. We need screening, and we can make it better.

Benjamin Davies is an Associate Professor in the Department of Urology at the University of Pittsburgh School of Medicine. You can follow him on Twitter at @daviesbj.

Source: Forbes http://www.forbes.com/sites/matthewherper/2014/07/17/in-defense-of-prostate-cancer-screening/

Making Science Real: Scientists moving forward in addressing research integrity; learning from past mistakes

Poor scientific reproducibility is a product of poor reagents, sloppiness, selective publishing of data, and on occasion – outright fraud. Drug development will continue to fail if results from published studies cannot be relied upon. How are scientists working to right these wrongs?

July 2, 2014 -- Scientific fraud makes headlines – particularly in cases where the findings were thought to be earth-shattering—such as the infamous falsification of stem cell studies by Korean scientist Dr. Woo Suk Hwang in 2006, and just recently, the retraction of stem cell studies published by Japanese RIKEN researchers who ruled that fellow scientist Dr. Haruko Obokata had intentionally manipulated data in a misleading fashion. But problems with the reproducibility of findings are rarely due to outright fraud. Research reagents might be of poor quality, or get mixed-up or contaminated. The execution of experiments or their analysis might have been done in a sloppy or inexperienced fashion. And hard-pressed researchers may only publish select pieces of their data that support their conclusions. These reasons contribute many-times more than fraud, to the prevalence of poor quality, irreproducible data in the scientific literature.

This problem is critical because there is only an estimated 5% success rate in drug development, and a significant amount of these failures are linked to the selection of drug targets from these poorer quality science publications. Time and resources of scientists are wasted when hypotheses are based on incorrect or inadequate prior studies. At the 2014 AACR Annual Meeting held in April in San Diego, CA, a session was devoted to Scientific Reproducibility –garnering huge attention from attendees, and indicating the seriousness with which this issue is being taken by the scientific research community. Everyone hopes to make the next headline -- but for the quality and impact of their work, not for the lack of it.

Identifying and combating the reasons scientists publish unreliable data

Dr. Lee Ellis discussed issues with the reproducibility of scientific studies – i.e., whether another researcher performing the same experiments can obtain the same results. "Not all non-reproducible events are due to evil people," said Ellis. He defined a spectrum of problems that contribute to this issue – from honest mistakes, to sloppiness, selective reporting, and the most serious —falsification and utter fabrication.

To identify the causes leading to publication of poor quality or even false data, Ellis conducted a survey on data reproducibility at his institution, the University of Texas MD Anderson Cancer Center, and gathered anonymous responses from 171 research trainees and 263 faculty members. He hypothesized that trainees and faculty would have different reasons for feeling the pressure to "massage data" for scientific publications. On average, more than 50% of those surveyed had at some point been unable to reproduce published data. Of trainees, 22% reported that they had felt pressure to publish findings for which they had doubt, and 31% had felt pressure to prove a mentor's hypothesis was correct, even though the data spoke otherwise. Particularly worrisome, is when the VISA status of foreign students comes into play – those who don't make progress on their projects may fear losing their mentor's support for their VISA. Thus, for trainees, the culture of trying to please a mentor who is set on seeing a specific set of results – such as proving the mentor's hypothesis—may drive some to find a way to produce the desired results. Other reasons include the need to have high-impact publications to complete a PhD or to obtain a job. For

faculty, "publish or perish" is a key driving force leading to data-massaging – meaning that without publications, a scientist will not be able to maintain and advance in his/her career. "Impact factor mania" refers to the sought-after status of publishing in prestigious "high impact" scientific journals. Such journals require a "perfect story," which may influence researchers to manipulate data by removing experimental results that do not fit the hypothesis. Publishing in higher impact journals or having a larger number of publications is necessary to obtain grants, get promotions and tenure, and are desired for stature or financial gain, such as the development of patents.
Fascinatingly, the higher the impact factor (a numeric measure reflecting influence) of the journal, the more often retraction -- a public announcement of a study's scientific inadequacy followed by its withdrawal from publication -- occurs. Retractionwatch.com is a website that tracks and writes cynical articles on scientific publications that get retracted. A quick glance at the website reveals reasons for retractions ranging from honest mix-ups of reagents, to outright fraud, to journals astoundingly caving to corporate demands because a publication on a controversial topic harmed the company's profits (i.e. Monsanto and GMOs).

Dr. Ellis despaired on the weak consequences doled out to researchers found guilty of committing fraud: retraction of publications, "supervision" of research for 3 years, and exclusion from service committees for 2-3 years, while most can still receive NIH funding. Clearly these "consequences" are not significant enough, when such people should simply be expelled from science. Emphasizing this problem, David Wright, the recent director of the US Office of Research Integrity, which monitors and investigates alleged scientific research misconduct, quit in February, claiming he was unable to get anything accomplished due to the oppressive political environment he had to operate within.

Efforts are being made to curb these issues. The NIH aims to raise awareness and educate researchers on these occurrences and their causes. The Reproducibility Initiative, recently begun by the Scientific Exchange, provides a platform for independent reproduction of studies, and rewards independently validated publications with special recognition. Ellis emphasized the importance of implementing other changes to reduce the culture of "impact factor mania." He suggests overhauling grant application and publication practices, and encouraging publication of negative data, which would have an added benefit of reducing time and resources that researchers spend testing hypotheses that someone has already found to be wrong.

Learning from failure: lessons from retracted articles

Dr. Ferric Fang, of the University of Washington School of Medicine, discussed what can be learned by evaluating retracted papers. If the integrity of a scientific publication is called into question, an investigation can be held, usually by the institution of the scientist who led the study. If the publication is deemed to be enough of a failure for any reason, honest or dishonest, it is retracted from the literature.
Despite the prevalence of non-reproducible studies found in the scientific literature, only 1 in ~10,000 publications have been retracted, the majority being due to scientific misconduct: plagiarism (including duplication or self-plagiarism, in which data from previously published studies is recycled – a no-no for all reputable scientific journals) and fraud. Studies that are non-reproducible due to honest mistakes, sloppiness, and selective reporting, have only very rarely been retracted, despite their prevalence. Out of the list of the top 17 scientists who have had the most papers retracted, only one was due to a contaminated reagent, while all the others committed fraud. Why the disparity – that retraction is almost exclusive to misconduct, while the vast majority of irreproducible publications are

due to lesser evils? Simple – the cost of an investigation is estimated at over $500,000 per allegation. Therefore, institutional investigations are performed almost exclusively when blatant scientific misconduct is suspected.

Due to the hugely negative connotation associated with retraction – deliberate misconduct– when scientists discover errors in their publications, they instead submit "errata" – corrections to the previously published data. Problematic though, is when the study was so poorly performed that it should be retracted, but to avoid retraction, a significant number of errata are added – to the point that the conclusions of the study are called into question. A alternative mechanism to red-flag publications with incorrect or non-reproducible data may be appropriate, so that the negative implications of misconduct associated with "retraction" do not mar a scientist's reputation (for instance, the hundreds of papers already published on a "breast cancer " cell line later discovered to be melanoma, should be red-flagged).

PubMed, the NIH database of published scientific articles, lists about 3,000 publications that have been retracted, 17% of which are in cancer research – an overrepresentation, as only 12% of all publications are in the cancer field. Biomedical research as a whole is overrepresented for retraction rates, compared with fields such as math and physics. Fang presented an analysis of the scientific journals with the most retracted publications. High-impact factor journals such as the New England Journal of Medicine, Science, Cell, and Nature ranked among the top for retractions due to fraud or suspected fraud, while mostly obscure, lower-impact factor journals ranked highest for retractions due to plagiarism and duplication. Publications retracted for accidental errors tended to be from higher-impact journals. The US, followed by Germany, led amongst countries with the most retractions due to fraud or suspected fraud. China and India ranked highest along with the US, among countries most prominent for retractions due to plagiarism and duplicate publication. This indicates that the reasons for scientific misconduct, retraction, and/or investigation into misconduct, differ between developed and developing countries.

In addition to the factors discussed above by Ellis, the roots of misconduct in the US include increasing competitiveness for diminishing research funding--leading some researchers to take sloppy short-cuts or resort to desperate and dishonest practices. Frighteningly, the rate of fraud and misconduct appear to be increasing, but reassuringly, so is the attention on it. Still, peer reviewers either assume honesty and integrity in experimentation and reporting, or are too busy , to assess a manuscript under review for issues such as fraud or plagiarism. New policies, including education and awareness, should be instated to deal with this double edged sword – decreased federal funding alongside increased bad publications.

Raising the standards for biomedical research

"Cancer is evolution. Cardiology is just plumbing. Of course the advantage that they [cardiologists] have, is that most Americans believe at least in plumbing," joked Dr. Glenn Begley, of TetraLogic Pharmaceuticals, CA. His talk at the AACR was focused on how to set the bar higher for the quality of the data that is published.

Pharmaceutical companies rely heavily on studies published by academic scientists, but have had low success rates in drug development due to the poor quality of published studies. Begley was part of a team of scientists at Amgen that tried to reproduce a number of high-impact, "landmark" academic publications – with devastating results: only 6 of 53 studies could be validated.

Dr. Begley described six red flags for identifying scientific studies of poor integrity: studies were never blinded, not all results from all experiments were shown (i.e. data from selected experiments were

presented as "representative data"), experiments were not properly repeated, positive and negative controls were not performed or shown (i.e. the appropriate comparisons to know an experiment and reagents are working), reagents were not validated or used properly, and statistical tests were not appropriate to determine if the results should be considered as significant. To assure that published scientific studies are of the highest integrity, Begley suggests that all studies be blinded, and that all of these red flags be addressed by the study researchers, peer reviewers, and journal editors, prior to publication.

Raising the quality of biomedical research reagents

Dr. William Sellers, of Novartis Institute for BioMedical Research, MA, discussed problems and solutions surrounding poor quality scientific research reagents. Cell line contamination has been found to be a prolific problem– including mix-ups or contamination with other cell lines, and contamination with mycoplasma – a slow growing microorganism that frequently contaminates laboratory cell cultures. The Cancer Cell Line Encyclopedia (CCLE), a collaborative effort between Novartis and the Broad Institute, purchased ~1000 cell lines from various vendors. They shockingly found that 70-90 of these were not the cell line they were purported to be, and 5% were entirely "rogue." In fact, a commonly used "breast cancer" cell line was instead found be melanoma. In response to reports such as these, Prostate Cancer Foundation (PCF) now requires annual progress reports submitted by PCF-funded researchers to include results from genetic tests validating cell line identity and evaluating potential contamination for all cell lines used.

Another large-scale problem is the quality – particularly the relative activity—of drugs and reagents used for research. Different drugs and reagents with the same putative function can have vastly different activities, depending on molecular structure (different drugs can be used to target the same molecule) and agent preparation. The cross-reactivity of drugs and antibodies is also an underreported issue—many have multiple molecular targets and these should be robustly evaluated and the results made freely available. Dr. Sellers discussed possible solutions to these problems, including the establishment of a reference ID for every research agent, and/or a "wiki," where researchers can review and comment on agent quality. Scientific journals could require full disclosure of methods and reagents used, and studies that use poor reagents could be flagged in PubMed.

Finally, Dr. Sellers discussed the problems that arise in this era of new technologies that execute genome-sized experiments, such as whole-genome sequencing: The large amount of data generated comes with a significant amount of "noise," or incorrect data that arises by chance-- which must be filtered out. Thorough methods of statistical analysis and many experimental steps are needed to validate results from these important, yet noisy, data-rich experiments. Allocating further funding for validation of results is critical in order to gain the clearest and most relevant insight from these large data sets.

The value and impact of the scientific enterprise stands on the integrity of the work done – and the social impact that it leads to. While there is a substantial economic and time cost associated with research both leading to and resulting from flawed publications, the most devastating effect is when untrue "science" affects public health policies or ideologies, or leads to bad drugs entering clinical trials. No prize should ever be given to the scientist who brushes aside the central dogma of science –that systematic observation and sound experimentation performed in a repeatable fashion-- forms the base of all knowledge.

Source: Prostate Cancer Foundation
http://www.pcf.org/site/c.leJRIROrEpH/b.9166841/k.D0E0/

Making_Science_Real_Scientists_moving_forward_in_addressing_research_integrity_learning_from_past_mistakes.htm

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1st	3rd
Tuesday	TBA

4:30 p.m. monthly

SEMINAR For Newly Diagnosed	**Distinguished Lecturer Series**

Hurley Reformed Church Hall, Hurley, NY

Poughkeepsie
Men to Men Group
Our brothers in support and education

Meetings are held the First Thursday of the month at the Central Hudson Auditorium on South Road in Poughkeepsie, starting at 6:30 p.m. Various doctors and speakers are on the agenda and one on one help is available after the meeting.

Contact
Paul Totta 845 297-7992
or Jim Kiseda 223-5007

If you need or want to help:

PCa 101 Seminar
First Tuesday of every month

Fred Bell 845 338-1161
Fwbelljr1@aol.com

Gene Groelle 338-1805
Gro226@aol.com

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