The Ribbon

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A Newsletter of the Cornell University Program on Breast Cancer and Environmental Risk Factors (BCERF)

Cornell Faculty Address Contaminants in Sewage Sludges

What are sewage sludges?

Sewage sludges, or "biosolids" are the semi-solid material that remains after sewage treatment facilities process wastewater from homes, businesses, medical facilities, and industry. In some communities, runoff from roads, lawns and fields is also sent through the facility. Legislation mandating treatment requirements for wastewater (the Clean Water Act), necessarily resulted in double the amount of sludge produced, and changing sludge management practices (shifting away from ocean dumping, landfills and incineration) include the viewing of sludges as a resource. Organic matter and nutrients make sludges a potentially valuable addition to soils, and sludges are, in fact, widely used as a soil amendment. However, there are no requirements in the US to test for or remediate organic pollutants in sewage sludges and sludges contain a variety of these contaminants that conventional treatment does not eliminate. These contaminants present a range of possible exposure scenarios for wildlife and people. The Cornell faculty in these two interviews address in their work various aspects of the identification, degradation activity, and approaches to management and bioremediation of chemicals in sludges.

(Sludge information adapted from Cornell Waste Management Fact Sheet, "The Production of Biosolids/Sludge" http://cwmi.css.cornell.edu/Sludge.html)

Interview with Anthony G. Hay

Associate Professor, Department of Microbiology, and Director, Institute for Comparative and Environmental Toxicology

Your lab addresses several challenges with regard to contaminants in the environment, from the detection of chemicals in diverse settings – such as sewage sludges – to developing approaches to degrading harmful compounds.

Anthony Hay: Yes, we are interested in some of the contaminants that are in sludge, many of which originate in the home. Most of the wastewater treatment plants that are around today were designed with the idea of meeting wastewater treatment rules that target industrial pollutants. Even today the monitoring and the reporting that is done only has requirements for some industrial pollutants. There are no requirements for chemicals from personal care products, pharmaceutical compounds, or antibiotics. There is a disconnect between some of these newer concerns and what is monitored.

At what stage of a given pollutant's "journey" are the biodegradation processes that you are studying relevant – during wastewater treatment, sludge processing or "digestion," or in the broader environment?

AH: Biodegradation is relevant to all aspects. We are finding that the wastewater plant itself is not well adept at either removing or degrading these compounds, and that's in part because it is optimized for a different suite of compounds. We are interested in knowing if and how biodegradation is happening in the environment. What types of genes would be present in an environment where these things are getting dumped, and is the biological capacity there to degrade these pollutants? By understanding the biology, we can then look at the various environments – whether it is the sewage treatment plant, or the lake that is receiving the treated water, or the soil that is getting the sludge amended to it. We think that by understanding the basic biology we can address questions in all of those realms.

How does a typical municipality treat its wastewater?

AH: The typical municipality treats to remove primary indicators like biochemical oxygen demand,

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fecal coliform bacteria, nitrogen, and phosphorous; those are the main components that they are concerned about and on which the EPA mandates they report. Depending on the size of the facility, they also have to do a yearly assessment of certain industrial pollutants. As we talk a little bit about in the review article on which Ellen Harrison is the lead author *(reference at end of article)*, the types of compounds targeted by the required analyses do not include any of the pharmaceuticals and personal care products that are now being seen at high levels in sludges.

Have you heard of any municipalities that have addressed these compounds?

AH: Some municipalities try to institute various tertiary treatments; those might be ultraviolet treatment, or ozonation, for example. These are usually effective technologies for attacking these kinds of compounds, or organic pollutants in general. Constructed wetlands are another type of tertiary treatment for wastewater. In Ithaca they recently built up a biological phosphorous removal plant, and there is some evidence that you get additional organics removal with this treatment. Concern about phosphorous is pushing a lot of the wastewater treatment changes. But again, these changes are not driven by pharmaceuticals, personal care products, or any other endocrine disrupting compounds; these are simply not on the radar screen yet for wastewater treatment.

There are questions in the scientific literature about how low concentrations need to be for us to stop being concerned about them. Just because a compound is present, doesn't mean it's harmful. And, at this point, everything is everywhere. The question is: are those pollutants present in concentrations sufficient to cause biological harm? The problem is that we don't always know the endpoint of concern: is it, for example, estrogen response, is it enzyme inhibition, or is it some other endpoint we don't know about? An example is tributyl tin, an anti-fouling biocide that is polluting coastal waters. New research is showing that it functions as an environmental "obesogen." That is, it promotes the accumulation of fat and adipocytes. This emphasizes the point that there are endpoints that we don't fully understand. We do have to know the dose-response relationship and that not all doses are important, but the other side is that we have to know the range of endpoints that need to be measured. The more we study, the more we realize that there are additional sensitive endpoints that we have not known about in the past.

Your work focuses on the ability of microorganisms to degrade pollutants. What is an example of that process?

AH: Yes, we like to say, "bugs on drugs." For example, there are microorganisms that grow on ibuprofen. Ibuprofen is the third most consumed drug in the world. Wastewater treatment plants remove about 90% of it, but given the volume that is being consumed, that is still a lot being given out to the environment. No one knew previously how ibuprofen was degraded. Sometimes biodegradation is incomplete, and can result in things that are more toxic than what you started out with. So understanding the biological fate is very important for being able to predict the potential for toxicity of compounds. In the case of ibuprofen we were able to show that it was degraded to non-toxic intermediates.

This contrasts with some commonly-used detergents, like alkylphenol ethoxylates, which start out relatively nontoxic, but when they are degraded, the spectrum of activity – the biological endpoints that they target – changes, as well as how long they persist in the environment. The alkylphenols change from something that just has a detergent effect to something that binds with a hormone receptor and can cause a cascade of activities to take place in the body. The concentrations being reported are below levels of concern for most human populations but there are a lot of ecologically sensitive organisms. Fish, for example, have been shown to undergo changes in sex ratios, resulting in fewer males. The question is, what is the long-term effect on populations? We don't really know.

Aquatic effects are what has driven any regulatory activity on these compounds in this country, correct?

AH: Yes. Definitely.

Can you elaborate on this process of the spectrum of biological activity changing toward increased toxicity with biodegradation? Where in the process is it happening?

AH: We call it activation, and it happens all along the way. Alkylphenol ethoxylates can be degraded when oxygen is present or when it is absent. As soon as you have conditions that allow microbes to grow, like the inside of your drain, they can begin to metabolize the ingredients in household products.

Compounds of specific interest in your lab include the alkylphenols and triclosan. How do you determine which chemicals to examine? How much of the load of estrogen potency of chemicals in sewage sludge is accounted for by the alkylphenols?

AH: We have worked on both detecting these chemicals in sludges, and on their biodegradation. Originally we just wanted to determine whether they present in our sludges. We had heard of them being reported elsewhere, and didn't suspect that ours would be any different or worse. But we found that alkylphenol in sludges from the four communities in the Northeast that we studied had levels that were five times higher than other places that had been studied. The ranges we found of 1500-2000 mg/kg, which is .1 - .2% by weight, is quite a lot for any organic pollutant. We then wanted to know if that was a one-time event, or true through all the seasons and over a number of years. So we studied four treatment plants, monitoring them seasonally. We found that there were fairly constant

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levels present. When we portrayed that alkylphenol quantity in terms of what it meant to an estrogen receptor, we found that there was about 15-20 times more alkylphenol-related estrogenicity than has been reported for dairy manures, which are thought to have a high level of estrogenicity due to the lactating cows.

With respect to how much of the total of estrogen-like burden in sludge is accounted for by the alkylphenols, we really don't have a good sense; the level of overall estrogen potency of sewage sludge is a good question.

The four sites you worked on had exclusively domestic input to the wastewater, except one with an industrial mix, correct?

AH: We looked at alkylphenols in Syracuse, Cortland, Ithaca, and Cayuga Heights (a suburb of Ithaca) wastewater treatment plants, and expected Syracuse to have the highest, but that was not always the case, especially when we looked at the estrogen equivalency. Cayuga Heights actually had a lot more octylphenol, which is the alkylphenol with the most estrogenic potency.

So when we looked at total predicted estrogenic potency, it was highest for Cayuga Heights. There are differences in the way the treatment plants are operated. Cayuga Heights has a trickling filter. The others have aeration basins that use a different technology. Other researchers have looked at alkylphenol level in sludges that were produced by different types of processes and have not found consistent links. What really needs to be done is to determine what's coming in versus what's coming out, because the processes do differ so greatly.

Can you speak about the two other chemicals that were included in this work?

AH: Abigail Weiss Porter did this work. She also measured sludge levels of triclosan, a widely used biocide, present in almost all the antibacterial hand soaps that you can buy, as well as in a lot of deodorants, toothpastes, many products. It's not even all that effective. In fact, one of the students working with me, Lauren Junker, looked at antimicrobial effects of plastics with triclosan and found no antimicrobial effect. Yet these things are marketed to what we called the "microbophobic" public. Triclosan was present in all of the sludges in quite high concentrations, in concentrations that would inhibit microbial activity in laboratory media. When they are in a complex mixture like a sludge, however, they are not likely to be as bioavailable, so they are not going to be as potent. We are seeing triclosan increasingly in environmental samples. We are finding triclosan in fish, and it is found in high concentrations in breast milk. Triclosan is an inhibitor of the enzymes that are involved in cleaning out other pollutants from our body; part of phase-2 metabolism.

Abigail also looked at HHCB or Galaxolide, a synthetic polycyclic musk found in perfumes and deodorants, which has endocrine disrupting activities. It is a compound that is very persistent, and doesn't disappear in soils. The levels of HHCB were very constant in our study; we saw it in every sample and the concentrations did not vary very much.

I think we should all be concerned with what we are putting down the drain. I do product searches every year, and I am seeing some voluntary phase out of some of these compounds. Without US regulatory activity on these, it becomes "good business practice," especially with regard to exporting products to Europe, where, under the REACH program, (http://ec.europa.eu/environment/chemicals/reach/reach_intro.htm), regulation of these chemicals is much more rigorous than the US.

You and Abigail Weiss Porter have a new paper coming out addressing the identification of a gene involved in the biodegradation of octylphenol (reference below). What does it mean to have identified this gene? What is the next step?

AH: Abigail's research showed that the organism that we had isolated from the Ithaca wastewater treatment plant was able to grow on alkyphenol and it did that using a flavin monooxygenase. This protein was able to activate oxygen and get that oxygen incorporated into the alkylphenol, making a metabolite that broke off the chain. It went from alkylphenol to a phenol derivative and alkyl group.

That phenol derivative was actually very toxic to the cell and she had a hard time getting the cells to keep wanting to make the enzyme because that phenol derivative, hydroquinone, was toxic to the cells. This goes back to that question of activation. Sometimes pollutants aren't easily degraded in the environment because the degradation products are toxic to the cells. One of the questions we would like to ask about the environmental fate or the relevance of this is: are these things being degraded to intermediates that *prevent further degradation*, therefore killing the very organisms that are trying to degrade them? That has implications for persistence in the environment and might help to explain why these things are so long lived. We are learning from a number of different studies that microorganisms in nutrient poor environments, like a lake, may not be able to withstand the metabolism of toxic compounds as easily as in laboratory settings. Especially if a toxic by-product is being made. Dealing with these toxic insults limits the cells ability to multiply, and therefore could limit any biodegradation that might take place in the environment. We would like to build on Abigail's work by trying to understand if these same pathways are occurring in the environment, and if the levels of degradation are self-limiting because of toxic intermediates.

Can you comment on related work going on at Cornell and the history of Cornell's contribution to these research questions about biodegradation and their applications?

AH: Marty Alexander is the "godfather" of biodegradation. As a soil microbiologist here in Crop and Soil Sciences,

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he really helped pave the way for understanding what affects the biological fate of pollutants in the environment. He is extremely well respected in the field, and made significant contributions to understanding the factors that limit biodegradation.

I can't begin to list all the work that is being done here at Cornell, but more specific examples of ongoing research include that by James Gossett in the School of Civil and Environmental Engineering and Stephen Zinder in the Microbiology department, who discovered the bacterium that's able to grow on chlorinated ethanes like DCE and vinyl chloride, which are important groundwater pollutants. This process which they discovered has been shown to be working in aquifers and sediment environments all over the world, and, together with Ruth Richardson (also in the School of Civil and Environmental Engineering), they have developed tools to monitor that process. They have done a great job in focusing on a specific problem and bringing to bear biological and engineering expertise that is now resulting in cleaner environments in local areas all over the US and the world.

Beth Ahner in Biological and Environmental Engineering looks at phytochelins and other components of the cell that mobilize heavy metals like lead and cadmium. Christopher Ober and Emmanuel Giannelis in Materials Science and Engineering are looking for replacement compounds for things like tributyl tin; they are looking at polymers that can be used as anti-fouling coatings on ship hulls so toxic chemicals are not needed. Ann Lemley in the Department of Fiber Science & Apparel Design has a very focused program looking at the degradation of pesticides at the point source, and developing a technology that can one day be an inexpensive way to destroy leftover pesticides.

There is a group of people at Cornell beginning to look at nanomaterials in the environment. Len Lion and

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Interview with Ellen Z. Harrison

Director, Cornell Waste Management Institute, Department of Crop and Soil Sciences

Would you start by telling us about the use of sludge as a soil amendment?

Ellen Harrison: The management of sludges is a significant component of the cost associated with wastewater treatment and disposal. Applying sludge as a soil amendment is often the cheapest option. The majority of sewage sludge produced in the US is being applied to agricultural, forest, mine or park lands. Some is being sold or given away to private citizens. Before being applied to land, sludges must be treated to reduce pathogen concentrations, but no treatment is required that addresses the chemical contaminants. And, no labeling is required, so citizens may be unknowingly purchasing sludge products. Some products are even using the term "organic" on their labels.

You, Dr. Hay, and your research team produced a major gap-filling work in recent years: a thorough review of the existing peer-reviewed and governmental reports on the presence of organic chemicals in sewage sludge. First of all, can you explain the possible implications of the presence of contaminants in sewage sludge?

EH: Current sludge regulations address only a handful of contaminants and we have little information on thousands of chemicals that go down the drain. Our concern is that we are spreading such a complex mixture of chemicals – from pharmaceuticals and personal care products to PCBs – across the landscape where we eat, work and play. Given our lack of knowledge about what is in sludges and of the risks associated with even those chemicals we have identified, the impacts on human and ecological health are impossible to assess.

With our ability to measure very small concentrations, an important question is whether the amounts of chemicals detected in sludges have environmental or health significance. To address that question, we used a measure suggested by the National Academy of Sciences, National Research Council, in their assessment of sludge. We compared the measured concentration of sludge contaminants to US EPA Soil Screening Levels (SSLs). We found that most of the chemicals were found in some sludges at concentrations exceeding these SSLs, indicating that they are present at levels high enough to warrant concern.

"We post all our work on our much-used web site **(http://cwmi.css.cornell.edu/)** so that people can have free access to the work we do."

What did you find in the available reports, and, equally important, what data were not available?

EH: Finding relevant data was not easy. Since testing is not required, we had to rely on research conducted by academic and governmental institutions. Out of the many thousands of chemicals that are probably in sludges, we were able to find data on only 516. Many of the research papers did not contain information on the type of treatment processes or the characteristics of the industries contributing sewage, so we could not draw general conclusions about the sources and control of various chemicals. The lack of standard analytic methods also

Claude Cohen have developed nanomaterials to remove pollutants from solids; others are looking at the toxic effects of nanomaterials to see if they act differently than the bulk chemicals we are used to studying. There are far too many examples to list them all but this gives you a flavor for some of the things that are going on at Cornell.

Let's close by returning to the problem of contaminants going down the drain and, in many communities, resulting in sludges or "biosolids" that contain toxic compounds. What can communities do?

AH: Although tertiary treatments like ultraviolet treatment or ozonation can dramatically reduce a lot of these trace organics that are making it through traditional wastewater treatment plants, these technologies are expensive and most communities have little incentive to install them. In the absence of legislation it really is the consumer that is going to drive changes right now; we can each make the choice to change the products we buy and think more carefully about what we put down the drain.

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Porter, A.W., and Hay, A.G. (2007). Identification of *opdA*, a Gene Involved in Biodegredation of the Endocrine Disruptor Octylphenol. Applied and Environmental Microbiology, 73. Doi: 10.1128/AEM.01478-07

This article can be found on our website at: http://envirocancer.cornell.edu/Newsletter/articles/v12contaminants.cfm

makes it difficult to compare results of different studies, since large differences in measured concentrations can result from using different laboratory methods.

What classes of chemicals found strike you as especially important for additional attention, and why?

EH: A number of endocrine disrupting chemicals (EDCs) are found in relatively high concentrations in sewage sludges, including brominated flame retardants, and nonylphenols, as well as pharmaceutical hormones. The ecological impact of EDCs is of great concern. Our survey also found that short-chained chlorinated aliphatic compounds (trichloroethylene for example) and monocyclic hydrocarbons (benzene and toluene, for example) were reported at concentrations in sludges that routinely exceeded the SSLs. Almost no data were found for nitrosamines which is surprising given their toxicity and the fact that they are likely to be formed during sewage treatment. Unfortunately, a current effort at the US EPA to examine additional contaminants in sludges is not addressing these contaminants.

Within the Cornell Waste Management Institute, which you direct, sewage sludge is one of several areas of focus. What are your objectives in this area of the Institute?

EH: Our role at the Cornell Waste Management Institute is to promote and conduct applied research and outreach to help people, from governmental policy makers to farmers and gardeners, make decisions based on sound science. To ensure our independence, we have a policy not to take funding from anyone with a financial stake in the outcome of our work. We post all our work on our much-used web site (**http://cwmi.css.cornell.edu/**) so that people can have free access to the work we do.

As with all environmental health issues, a lot of different players need to come to the table in order to make progress. Who are the necessary players for cleaning up sewage sludge?

EH: Elimination or reduction in use, as well as upstream controls at the point of industrial discharge into the sewer, have reduced concentrations of some contaminants. However, we send such a mixture of chemicals down the drain, that I do not think that it is realistic to clean up sewage sludges to a point that I would be comfortable with their use as a soil amendment. Separating the wastewater from homes from that coming out of industrial and other non-domestic sources could help reduce the burden of chemicals in sewage sludges, although residential sewage also contains pharmaceuticals and personal care products. In my view, we need to develop other ways to manage sludges. There are new energy recovery options that may provide a better option.

Is there a role that the public can play?

EH: Many of the contaminants of concern in sludges are "bad actors" wherever they are found. Working to ban such chemicals from use will limit our exposure. California, for example, has banned the use of the more toxic brominated flame retardant, which is a good step.

People should find out where the sludge from local treatment plants is being disposed. They should also be aware of whether sludges are being used on the grounds of the schools and parks where their children play. When they obtain compost or soil amendments for use on their yards, they should find out whether they contain sewage sludge. And of course, they should try to use products that don't contain toxic chemicals and should not flush unwanted chemicals or pharmaceuticals down the drain.

Reducing the Risks of Golf Course Management

By Jennifer A. Grant, NYS IPM Program and Frank S. Rossi, Department of Horticulture, Cornell University

Golf course superintendents, owners and staff are motivated to reduce pesticide use due to pending regulation, economic factors, and their own environmental consciousness. However, golf turf managers faced with operating facilities with fewer pesticides need the best information on course conditioning that is less reliant on chemical pesticides and also meets golf client expectations. At the same time, those advocating pesticide restrictions need to be aware of the costs of implementing the policies and the resulting impacts on revenues in the case of widespread turf loss. In an effort to address the environmental, economic and practical aspects of pesticide restriction we are exploring golf turf management with little to no chemical pesticides.

Our approach has been to compare traditional putting green management to a strict IPM approach and to biologically-based, reduced-risk management. We chose putting greens because they are the most intensively managed golf course areas, have the highest quality expectations, and will therefore be the most difficult to manage without chemical pesticides.

Frank Rossi, Jennifer Grant, and Andy Wilson, Supervisor of the Green Course at Bethpage State Park, make an early season visit to the course.

A primary focus of our work is to reduce the plant stress associated with putting green management that often leads to pest problems. These stress-reducing strategies include altered mowing, watering and feeding practices. They result in turfgrass that is sometimes poor in visual quality, but meets the playability standards of the game.

Our project is unique for many reasons. We look at the full suite of management practices performed on a golf course – not just one aspect, and our research site is an operational golf course. The Green Course at Bethpage State Park on Long Island is a high-use public course, getting 50,000 rounds of play each year.

The project is long term – we're just completing our seventh year. It's an experiment using full putting greens as experimental units, and it also serves as a demonstration to the many thousands of golfers who play the course each year.

What have We Learned?

Diseases, caused by fungi similar to organisms that cause athlete's foot, are the main pest problems on putting greens. These organisms attack weakened, stressed grass more easily and severely than healthy, non-stressed plants. In the early years, we managed six greens without pesticides (no EPA-classified I, II, or III chemical pesticides). The greens, composed of creeping bentgrass and annual bluegrass *(Poa annua)*, eventually became unplayable and died each year from the intense heat and humidity of increasingly warmer Northeastern summers. Three of the greens were converted to a more disease-resistant grass species, velvet bentgrass, but have also proven to be difficult to manage without chemical pesticides.

We conceded that for these older surfaces that had been treated with chemical pesticides for more than 30 years, nonchemical management was not sustainable given the current technology and negative impact on revenue from reduced golfer play. Consequently, we modified the management of these greens to "reduced risk" – incorporating low-risk chemical pesticides. Reduced risk pesticides have characteristics such as very low toxicity to humans and non-target organisms including fish and birds, low risk of groundwater contamination or runoff, low potential for pesticide resistance, and demonstrated efficacy and compatibility with IPM.

Throughout the project, we have been able to apply fewer chemical pesticides on the IPM and reduced-risk (or nonchemical) greens as compared to traditionally managed greens. The IPM greens have consistently received 30-60% fewer applications, while maintaining equal quality. However, numbers of applications do not tell the full story. Numbers of pesticide applications are easily compared, but they reveal nothing about the qualitative effect of these pesticides. As traditional chemical pesticide applications have decreased, reduced-risk and biological product use has increased. So how can we tell which products are "better" to use, and when we are improving?

To address this predicament, we incorporated the "Environmental Impact Quotient" (EIQ) (Kovach et al. 1992), to both select low-impact pest management products and to evaluate the relative effect of our various management regimes. The EIQ model provides information on pesticide effects on non-target organisms, applicators and golfers. The superintendent chooses the lowest risk product amongst the legal products expected to be effective under the specific circumstances encountered. In comparing management strategies, we use the EIQ to evaluate the effect of each approach. From 2004 to 2006, the environmental impact of the IPM and reduced-risk treatments have been up to 85% less than that of the conventionally managed greens *(see Figure 1)*.

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Research Brief

DDT, Breast Cancer Risk, and Age at Exposure

By Suzanne Snedeker, Ph.D., BCERF Associate Director of Translational Research

Cohn, Barbara A., Wolff, Mary S., Cirillo, Piera M., and Scholtz, Robert I. (2007). DDT and Breast Cancer in Young Women: New Data on the Significance of Age at Exposure. Environmental Health Perspectives 115, 1406-1414.

Cohn and colleagues examined breast cancer risk and DDT exposure of women diagnosed before the age of 50 who lived in the Oakland, California area. Blood samples were obtained from the women while they were still in their 20s (shortly after they had given birth) and were stored for up to 40 years. The study is unique because it examined risk according to age of exposure, including exposure in a subset of women who were 14 years of age or younger when DDT was introduced for general use in 1945. For instance, while all the women were exposed for the same number of years (1945 to 1963) their age at first possible exposure (their age in 1945) differed considerably.

The investigators analyzed blood samples for three different forms of DDT in both cancer cases and age-matched controls without breast cancer. These forms included p,p'-DDT, the predominant form in technical DDT ("technical DDT" is the form used in insecticide sprays); o,p'-DDT, an estrogenic form that constituted a small proportion of technical DDT; and the persistent metabolite, p,p'-DDE.

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Reducing the Risks of Golf Course Management *continued from page 6*

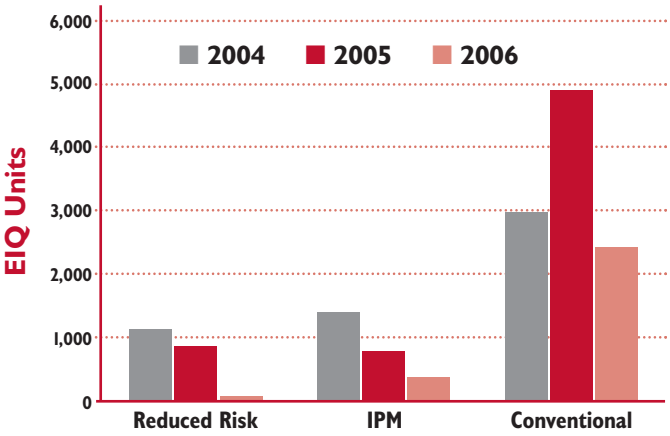

Figure 1. *Environmental Impact of Pesticide Applications, expressed as Field EIQ*

The quality of the IPM greens has equaled that of the conventionally managed greens, almost without exception throughout the seven years of our study. Quality of the reduced-risk greens has been acceptable, if not equal to conventional, through most seasons, with the common exception of approximately one month during the hottest weather each year. Golfer surveys have further attested to the quality, with all treatments rated as good to very good, with few exceptions from 2003-2006. It appears, to date, as though we are getting closer to meeting our environmental and economic goals.

Where will we go from here?

Perhaps most important in this project is that we have developed a suite of reduced-risk practices that is feasible for use on public golf courses in New York State. We have seen our "experimental" practices begin to be implemented on the other courses at Bethpage and we look forward to more widespread implementation. We plan to produce an operations manual that can be used as a guide throughout the Northeast by other courses interested in reducing their dependence on chemical pesticides. At the same time, we will continue testing new products and practices for environmentally compatible golf course management.

Further reading

A more detailed discussion of methodology and results from 2001 through 2003 can be found at http://usgatero.msu.edu/, and the 2004-2006 reports at http://nysipm.cornell.edu/grantspgm/projects/default.asp

Acknowledgements

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This article can be found on our website at:
http://envirocancer.cornell.edu/Newsletter/articles/v12GolfRisk.cfm

FALL 2007
REGIONAL CANCER AND ENVIRONMENT FORUM IN NEW YORK CITY

Advances in Endocrine Disruption Research, Breast Imaging, Cancer Vaccines, and Outreach Efforts

Two leading researchers on health effects of exposure to endocrine-disrupting chemicals, Dr. Andreas Kortenkamp, Head of the Centre for Toxicology at the University of London School of Pharmacy, and Dr. Mary Wolff, Professor of Community and Preventive Medicine at the Mount Sinai School of Medicine in New York City, presented their work on September 27, 2007.

Speakers also included two faculty members of the Weill Medical College of Cornell University: Dr. Ruth Rosenblatt, Director of Women's Imaging, who spoke on the latest developments in breast cancer detection, and Dr. Kevin Holcomb, Assistant Professor of Clinical Obstetrics and Gynecology, who presented the latest research on vaccines against the human papilloma virus, a virus known to cause cervical cancer.

A panel including representatives from the Young Survival Coalition, the Witness® Project of Harlem, Susan G. Komen for the Cure/Greater NYC, and the New York State Breast Cancer Support and Education Network, rounded out the day with a lively discussion on challenges, successes, and opportunities for collaborative efforts to reduce the risk of breast cancer.

Chemical "Cocktails" and Breast Cancer Risk

BCERF was honored to bring Dr. Andreas Kortenkamp to address the Forum to present his cutting-edge toxicology research on how exposure to mixtures of environmental pollutants may increase the risk of breast cancer. Many environmental pollutants may mimic estrogen, a hormone known to increase breast cancer risk.

His talk, entitled *Estrogens, Environmental Pollutants and Breast Cancer: a Re-evaluation from a Mixture Effect Perspective* focused on new thinking with regard to the role of chemical exposure in breast cancer risk. Two concepts inform this new line of thought: the timing of exposures with regard to critical early life periods, and "cocktail effects;" that is, the combined action of multiple chemicals, also taking into account the presence of the individual's own natural hormones. These two concepts, Dr. Kortenkamp explained, increase the biological plausibility for a role of environmental pollutants in breast cancer risk.

Dr. Kortenkamp laid out the paradoxical role of natural, or endogenous, estrogens: they are essential for breast development, but also involved in breast cancer risk (hence the established risk factors of early menarche and late menopause, which result in more estrogen reaching the sensitive structures in the breast over a lifetime). Recent pooled analysis of nine prospective, case-control studies on blood serum levels of estradiol (the more potent of the endogenous estrogens) showed significant increases in breast cancer risk with higher levels. This work further strengthens scientific understanding of the important role of estrogen in breast cancer development.

Dr. Kortenkamp then described the most pronounced example of involvement of "outside" or exogenous estrogens in breast cancer risk, with two large epidemiological studies in the US (the Women's Health Initiative) and Britain (the Million Woman Study) finding tens of thousands of excess breast cancer cases associated with the use of hormone replacement therapy (see *The Ribbon*, Volume 12, Number 3, *The Recent Decline in Breast Cancer Incidence: What is its Relationship to Hormone Therapy Use?*)

What other exogenous estrogens might play a role in breast cancer risk? Organochlorine chemicals, such as DDT and its metabolite DDE, have endocrine disrupting behavior, and DDE is highly persistent in the environment. Over 50 studies in the last decade and a half have tried to examine the role of these compounds in breast cancer risk. There have been, Dr. Kortenkamp pointed out, far fewer studies of other estrogen-mimicking environmental pollutants, such as PCBs, and fewer yet of phenolic compounds, such as parabens and bisphenol A. With regard to the organochlorine studies, the results were very mixed. Earlier studies, especially with DDE, demonstrated a link with breast cancer, but other studies did not see this link. A pooled analysis of all these studies came to the conclusion that the data provided do not support an association between DDE body burden levels and breast cancer risk.

Dr. Kortenkamp warned against dismissing a role for these chemicals in breast cancer risk based on this previous generation of studies, and identified their important methodological limitations and conceptual shortcomings. He mentioned a very recently published epidemiological study that does address the issue of critical early life periods, which found a strong association between exposure to a form of DDT in childhood and subsequent breast cancer risk (see *Research Brief* by Dr. Suzanne Snedeker in this issue). He encourages epidemiologists to address combined exposures, as well as to continue addressing windows of vulnerability

Dr. Rodney Page, BCERF Director, facilitates the panel discussion.

to exposures, as this recent DDT study will need corroboration.

In his own current work Dr. Kortenkamp provides toxicological data to fill these research gaps. "The estrogen hypothesis of breast cancer should be extended to encompass mixture effects between weakly estrogenic agents and endogenous hormones," he says. One of his research questions is: are mixture effects to be expected when every component is present at low, otherwise ineffective doses? His research group addressed this in a model experiment combining estradiol with eleven weakly active estrogenic agents at levels that individually did not produce any detectable effects. They found that, in combination, these chemicals were able to more than double the effect of the endogenous hormone, "demonstrating that," Dr. Kortenkamp explained, "in principle, weak outside estrogens, at low levels, can exacerbate the actions of potent endogenous hormones." This is not synergism, but rather low levels of multiple environmental estrogens acting in concert with estrogens from the body.

He goes on to ask, will cocktail effects occur at environmentally relevant doses? He discussed data on estrogenic agents measured in European human tissue samples, showing the closely correlated expected and observed effects from mixtures, as well as a scenario modeled on data from a highly contaminated population in Spain. He also discussed how this data could contribute to better prioritization of chemicals for biomonitoring.

Dr. Kortenkamp's own and other research he discussed at the Forum is demonstrating that the added contribution of estrogenic environmental pollutants to endogenous estrogenic load is likely in certain situations, although the contribution of any single chemical – including, for example, the organochlorines that have been studied individually – is small. He points out that all mixture analysis to date is based only on those chemicals that are currently known to be estrogen mimics, and that the effect of conjugations have not yet been taken into account.

As Dr. Kortenkamp encourages a proactive approach in a recent briefing paper for the World Wild Life Fund – UK (link at: http://www.wwf.org.uk/news/n_0000003135.asp): "Given the role of estrogen in breast cancer, it would be prudent to reduce exposures to chemicals that can mimic estrogen. Consideration should therefore be given to replacing such chemicals with safer alternatives, where possible."

A "New Generation" of Endocrine Disruptor Research

Dr. Mary Wolff (who presented later in the day but whose talk is described here due to its relevance to Dr. Kortenkamp's) presented on *Relevant Environmental Exposures in the 21st Century: Hormonally Active Agents and Potential Health Effects*. She discussed the history of interest in endocrine-disrupting chemicals, its beginning marked by the Wingspread Conference in 1991, leading into a list of such chemicals published in *Environmental Health Perspectives* by Theo Colburn and colleagues in 1993.

Dr. Wolff described the history of studying the better-known exposures, such as dioxins, DDT, PCBs and lead, which, although in decline in the west in recent decades, can still be found at significant levels in the developing world. The "new generation" of endocrine-disrupting chemical research addresses, for example, phthalates and bisphenol A; toxicological and epidemiological work on these chemicals is at a much earlier stage.

Dr. Wolff plays a leading role in two major epidemiologic efforts to move forward the research on endocrine-disrupting chemicals and health effects. She leads the Mount Sinai Center for Children's Environmental Health and Disease Prevention Research, one of eight centers established by the NIEHS in conjunction with the EPA. She also leads one of the sites (Fox Chase Cancer Center/Mount Sinai collaboration) of the Breast Cancer and Environment Research Center's (BCERC) "Environmental and Genetic Determinants of Puberty" study. Both of these efforts produce data on the effects of hormone disrupting chemicals prenatally and in young girls.

The Mount Sinai Center, which is running a number of studies, includes efforts to monitor prenatal exposures and birth outcomes in over 400 mothers in the NYC region. Maternal blood and urine is collected in the third trimester of participants' pregnancies, and infants/children are examined at three days old, and at one, two, four, and six years of age. Chemicals monitored include DDT/DDE (though in dramatic decline), PCBs, organophosphate pesticides, phenols, and phthalates. Endpoints monitored include birth

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outcomes such as birth weight and length, and neurodevelopment. The study model, Dr. Wolff explained, includes analysis of any relationship between each compound and the various outcomes. Dr. Wolff emphasized that her own focus is becoming the lesser-studied chemicals, such as bisphenol A and phthalates, which are international in scope, widely detected in children and pregnant women, and showing links with some of the outcomes the Center is examining. She discussed where exposures to these chemicals might be coming from, suggesting sources ranging from diet, to air contamination, to personal care products.

Dr. Wolff also discussed work on early puberty that she is conducting with the BCERC. The Environmental and Genetic Determinants of Puberty study hypothesis is that hormonal environmental exposures may alter pubertal onset. The collection of urinary and blood biomarkers of environmental chemicals is one of the exposure measurement approaches in the study, about which Dr. Wolff and colleagues published an article early this year. (This article, "Pilot Study of Urinary Biomarkers of Phytoestrogens, Phthalates, and Phenols in Girls," published in *Environmental Health Perspectives*, January 2007 was reviewed by Dr. Suzanne Snedeker in *The Ribbon*, Volume 12, No 1).

This work includes a variety of hypothesis-generating findings, such as the implications for various race/ethnicity differences in exposure biomarker measurements. In her talk, Dr. Wolff provided data on four biomarkers (two phthalates, two phenols) for the black, Hispanic and white participants, showing dramatically different patterns for each: white participants showing the highest levels for benzophenone-3, a phenol found in sunscreens; blacks and Hispanics showing higher levels of monoethyl phthalate, found in personal care products; whites with the highest levels of mono93-carboxypropyl) phthalate, found in soft plastics; and black participants with the highest levels of 2,5-dichlorophenol, found in mothballs.

Dr. Wolff displayed a chart showing significant research gaps in the cumulative animal and human evidence on health effects for endocrine disrupting chemicals. The multiple studies in which she plays a leadership role will be contributing significantly to closing those gaps.

Updates from Weill Medical College of Cornell University Faculty

Holding the Forum in New York City gave BCERF the opportunity to feature Weill Medical College faculty. Forum participants received up-to-date information on two areas of focus at Weill, from faculty who generously came to join us between seeing patients at the Medical College.

Prophylactic human papilloma virus vaccines. Dr. Kevin Holcomb, Assistant Professor of Clinical Obstetrics and Gynecology, presented the latest research on vaccines against the human papilloma virus, a virus known to cause cervical cancer. He described the clinical trials being conducted and the extremely high prophylactic efficacy they are showing in preventing incident HPV infection and subsequent pre-cancer. Dr. Holcomb also discussed the challenges of delivering vaccines in low-resource settings, and responded to questions about the presence of aluminum in the vaccine, as well as confirming the absence of mercury.

New developments in breast cancer detection. Dr. Ruth Rosenblatt, Director of Women's Imaging, spoke on the latest developments in breast cancer detection, covering digital mammography, breast magnetic resonance imaging (MRI), and breast specific gamma camera (BSGI). She compared conventional and digital mammography, showing the same results for detecting breast cancer in women over 50 (postmenopausal), the same results for women with average and low breast density, and more sensitivity for detecting breast cancer in women with dense breast tissue and younger women. There are advantages to digital mammography, such as the speed of image acquisition, the greater contrast, and the ability to efficiently share images, but also many challenges and limitations, such as high maintenance costs. She described ultrasound as an important adjunct tool. Dr. Rosenblatt described MRI, and when it is indicated, for example when other imaging studies are ambiguous or difficult, as with implants, or for high-risk women. She emphasized that MRI does not replace mammography. She then shared information on BSGI, which involves injecting a small amount of a "tracer." The tracer is taken up in cancerous cells because they have increased blood flow and metabolic activity, and then a specially developed camera show the image. She gave examples of indications for use of this technology, such as to sort out scar tissue from recurrent breast cancer in women with history of breast cancer.

Panel Discussion: Local Efforts on Breast Cancer Research, Education, and Activism

At most BCERF Forums we are able to provide time for representatives from breast cancer or other relevant organizations, local to the region in which the Forum is bring held, to address participants about their organizations' goals and activities. This Forum's panel featured the following organizations and representatives.

The Young Survival Coalition (YSC)

http://www.youngsurvival.org/

CEO Michelle Przypyszny, who has been with YSC for seven years, has seen this organization, headquartered in New York City, grow to 14,000

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constituents, 11 staff and eight affiliates. The YSC was founded by three young breast cancer survivors in 1998, all who were under the age of 35 at diagnosis. The YSC has grown to fill the gap in information and resources that were available to young women then, and remains the only international, non-profit network of breast cancer survivors and supporters dedicated to the concerns and issues that are unique to young women and breast cancer.

The Witness Project® of Harlem and Esperanza y Vida

http://www.witnessproject harlem.org/

Lina Jandorf, the Director of Cancer Community Outreach in the Department of Oncological Sciences at Mount Sinai Hospital, directs these two faith-based community projects. The Witness Project® is a breast and cervical education program targeting African American women, and is based on an educational model first developed at the University of Arkansas in 1991 in response to racial disparities in breast cancer. The project seeks to address these disparities by having cancer survivors share their stories about diagnosis and treatment in community settings. Similarly, Esperanza y Vida is a breast and cervical education program that reaches out to the Hispanic/Latino community in churches and community centers across the city.

Susan G. Komen for the Cure/Greater NYC

http://www.komennyc.org/

Board member Marge Neuwirth sat in for Executive Director Donna Lawrence, representing the New York City affiliate of this national support and granting organization. Ms. Neuwirth discussed the uniqueness of the NYC affiliate. For example, up to 75 percent of funds raised are distributed to programs in the NYC region, including the Witness Project®. In 2007, Komen Greater NYC is awarding close to $3.2 million in grants: $2 million will support 34 community-based organizations that provide breast health programs to underserved women, $245,000 will increase capacity of local researchers to enroll women in breast cancer trials and help fund local breast cancer conference and education programs, and close to $1 million will go for research.

New York State Breast Cancer Support and Education Network (SEN)

http://nysbcsen.org/

Susan Cohen is Chair of the SEN, the only statewide network of community-based breast cancer organizations in the state. SEN facilitates the over 20 member organizations sharing programs and resources, inter-organization referrals for services, and a support and education system. Public health and environmental policy initiatives are one strong focus of the Network, and Ms. Cohen shared details of 2007 efforts. She also represented Manhattan Legal Services on the panel, where she uses advocacy skills developed in anti-poverty work, and transfers them over to breast cancer advocacy.

BCERF thanks all the speakers and the over forty participants, all of whom contributed to a lively event of information sharing and collaborative thinking. We also thank Ms. Ali Beck, Coordinator of the Cancer Prevention Program at NewYork-Presbyterian Hospital for all her assistance in planning the event.

This article can be found on our website at:
http://envirocancer.cornell.edu/Newsletter/articles/v12ForumFall07.cfm

http://envirocancer.cornell.edu/turf/

BCERF's Turf Pesticide and Cancer Risk Database

Receiving tens of thousands of hits and being used nationwide

There is a tremendous amount of activity surrounding BCERF's Turf Pesticide and Cancer Risk Database. This searchable database includes cancer risk information on 111 pesticide active ingredients found in over 2800 individual turf and lawn care pesticide products, an extensive glossary, information on interpreting cancer risk, and links to fact sheets and other documents from the US EPA. Collectively, these web-based resources received over 180,000 hits from July through September 2007. Project leader Dr. Heather (Clark) Dantzker is conducting a wide range of outreach projects to ensure that pesticide safety educators nationwide are able to use and instruct others in the use of this database. Heather and her research assistant Devi Chandrasekaran developed an instructional CD – with a slide show, a movie and other features – for this purpose. The CD is now in the hands of hundreds of pesticide safety educators in the majority of the states, four US territories, Canada, and several Central American countries. The CD is being distributed to over 100 educators and staff in Cornell Cooperative Extension, with offices throughout New York State. An information sheet about the database is available (html or PDF format) in both English and Spanish (new!) at http://envirocancer.cornell.edu/turf/Info.cfm. These and future efforts are helping to ensure that anyone who needs to know the cancer risk potential of the active ingredients in turf pesticide products has access to that information.

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Editor
Carmi Orenstein, M.P.H., *Assistant Director*

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Research Brief: DDT, Breast Cancer Risk, and Age at Exposure *continued from page 7*

While breast cancer risk didn't differ when the researchers compared levels of o,p'-DDT or p,p'-DDE in cases and controls, differences in breast cancer risk were observed when looked at levels of p,p'-DDT. When they analyzed the results by the age of first exposure in 1945, the authors reported an odds ratio (OR) of 5.4 in the women who were less than 14 years of age in 1945. This means the breast cancer risk was 440% higher in women with the highest levels of p,p'-DDT (highest tercile, the upper third of p,p'-DDT levels) compared to women with the lowest levels of this chemical (lowest tercile). This effect was statistically significant (OR 5.4, 95% CI 1.7-17.1, p for trend 0.01). While the reason for this effect is not known, it is possible that an "imprinting" effect may have occurred. Development of the breast from gestation through puberty has been shown to be affected by exposure to ionizing radiation in humans (Japanese women, atomic bomb survivors) as well as to a variety of endocrine disrupting chemicals in animal studies. These other studies suggest the breast is very sensitive to environmental stressors during this critical window of development.

While this study was small, and results need to be examined carefully (small studies sometimes are more prone to results being due to chance rather than to the chemical being evaluated), it shows the need for studies that evaluate if and how exposures to environmental chemicals during this critical window of breast development affects the lifelong risk of breast cancer. This study focused on breast cancer that occurred by age 50. To what extent early exposures may affect post-menopausal breast cancer risk needs further investigation.

This article can be found on our website at:
http://envirocancer.cornell.edu/Newsletter/articles/v12DDT.cfm

BCERF

Cornell University
Program on Breast Cancer and Environmental Risk Factors
Vet Box 31
College of Veterinary Medicine
Cornell University
Ithaca, NY 14853-6401

Phone: (607) 254-2893
Email: breastcancer@cornell.edu
Web: http://envirocancer.cornell.edu

Cornell University