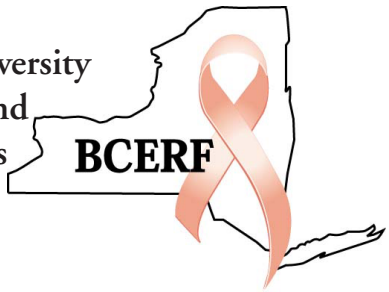
The Ribbon

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



Volume 7, Number 2, Spring 2002

BCERF Faculty Discuss Recent Research

The Ribbon *asked BCERF faculty Suzanne Snedeker and Carol Devine to each discuss a very recent research paper in their fields of expertise. Both studies reviewed involved topics previously covered in BCERF Fact Sheets; these studies — along with any others published in the interim — will be included in future updates of those Fact Sheets.*

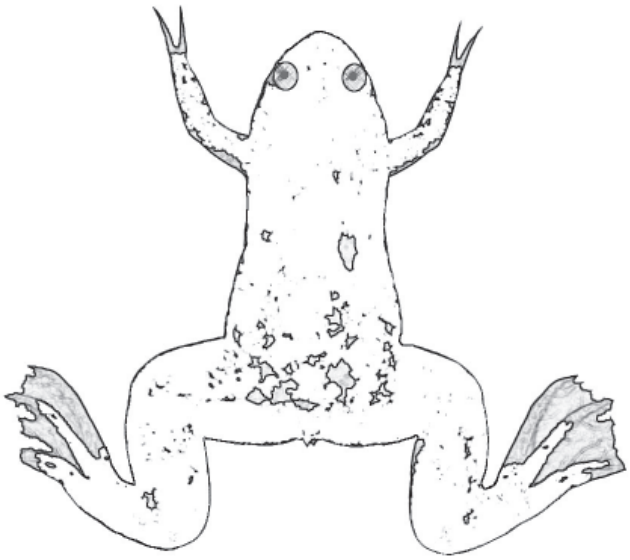
Dr. Tyrone Hayes' Research on the Effects of the Herbicide Atrazine on Sexual Development in Frogs

Suzanne Snedeker, BCERF Associate Director of Translational Research

Late in October of last year, on a rare, cool New Orleans day, I had the pleasure of hearing Dr. Tyrone Hayes, an Associate Professor of Integrative Biology at Berkeley, give an amazing talk on how low levels of the herbicide atrazine affect the sexual development of frogs. This talk was a part of a conference on endocrine disruption hosted by the Tulane University Center for Bioenvironmental Research. This is not a limb deformity, but rather permanent developmental changes in the sex organs of the frogs. You would not notice this change by just looking at the frog, because it is an internal change. Many of the frogs exposed to atrazine were hermaphrodites—they had both testes (male sex organs) and ovaries (female sex organs). Some of the frogs had several sets of sex organs. Not only is Dr. Hayes a dynamic speaker, he also is a thorough researcher. He explained how he had repeated his experiment dozens of times, always with the same results. Male tadpoles exposed to atrazine had abnormal sexual development. These effects were seen at very low levels of atrazine, as low as 0.1 part per billion (ppb), that is, 0.1 millionth of a gram in one liter (1000 grams) of water. These effects were seen at atrazine levels 30 times lower than the maximum contamination limit (MCL) set by the Environmental Protection Agency (EPA) for atrazine in drinking water (MCL for atrazine is 3 ppb). The tadpoles exposed to over 1 ppb atrazine had abnormal development of the laryngeal muscle, which normally develops in response to the male sex hormone testosterone.

I talked with Dr. Hayes the day after this presentation. He told me that while originally his research had been funded by the company that is the major manufacturer

of atrazine, Syngenta (formerly Norvartis, formerly Ciba-Geigy), he had completely cut off ties with the company and secured independent research funding to repeat his experiments. He submitted his unpublished report on atrazine's effects on frogs to the EPA. Atrazine has been under Special Review by the EPA since the mid-1990s, and it is expected that the EPA will release a final risk assessment of atrazine this summer. What is unique about Dr. Hayes' research is that he observed effects on sexual development at very low levels of atrazine, levels commonly seen in the environment.



African clawed frog (Xenopus laevis)
courtesy Kraig Adler

Atrazine is the most widely used herbicide in the US. 61 to 73 million pounds were used per year during the 1990s by the US alone. Atrazine is used to control weeds primarily in fields where corn and sorghum are grown. Atrazine is usually applied in the spring to fields during the planting season to prevent weeds from choking the new emerging plants. After application, atrazine can be washed from the fields by the heavy spring rains into streams, rivers and reservoirs, and levels can exceed 20 ppb. The time when atrazine levels are highest in rain runoff in the spring exactly coincides with the season when frog tadpoles are developing. While atrazine is frequently detected in surface and groundwater during other times of the year, levels are typically much lower than the 3 ppb MCL set for drinking water. But, it is not uncommon to see atrazine in drinking water in the range of 0.001 to 1.0 ppb; Dr. Hayes observed inter-sex frogs with both ovaries and testes at levels of atrazine as low as 0.1 ppb. Atrazine can also be transported in the air, and levels exceeding 1 ppb and as high as 40 ppb have been detected in rainwater in Midwestern states with high use of atrazine.

Dr. Hayes has recently published his research "Hermaphroditic, demasculinized frogs after exposure to the herbicide atrazine at low ecologically relevant doses" in the journal *Proceedings of the National Academy of Sciences, USA* (vol. 99, pp. 5476-5480). Dr. Hayes notes that about 20% of his atrazine-treated male frogs had multiple sex organs, or had both male and female sex organs. None of the control animals had any abnormalities. Dr. Hayes reported that he sampled the blood of adult frogs that had been exposed to atrazine as tadpoles. Exposed frogs had low levels of the male sex hormone testosterone. Testosterone levels were 10 times lower in the frogs raised in water with 25 ppb atrazine compared to untreated frogs. What could cause this abnormal hormonal change? This suggests there is a change in the way the frogs synthesized steroid hormones. Dr. Hayes thinks that atrazine may cause an increase in the levels of an important enzyme called aromatase which helps convert the male sex hormone testosterone to the female sex hormone, estrogen. Higher levels of estrogen with low levels of testosterone would explain the inter-sex frogs. However, Dr. Hayes has not tested this idea experimentally, and more work needs to be done to see if the aromatase pathway is disrupted.

Might this have implications for other species? The testosterone to estrogen conversion pathway is not just present in frogs. It is also important in mammals, including humans. After menopause when the ovaries no longer make estrogen, the major source of circulating estrogen is the conversion of testosterone in a series of steps to estrogen, via an aromatase pathway in body fat. Whether atrazine can have any effect on increasing the activity of aromatase in humans is not known. In other species atrazine does not have an effect on sexual development. For instance it does not appear to have a major effect on the sexual development of other wildlife like alligators, which are also very sensitive to changes in sex hormones. And, humans are certainly not frogs. We do not live in water nor do we drink water to the extent frogs would. However, because of other data on the endocrine disrupting effects of atrazine in laboratory animals, it is important that further research be done to rule out any possible disruptive effects on hormonal pathways in humans.

Dr. Hayes is continuing his studies, extending his research to frogs in the wild. However, his research is not without controversy. In an article written for the *National Geographic*, other researchers have not been able to duplicate the atrazine-effect at the very low levels of atrazine used by Dr. Hayes. However, they did see similar effects at higher levels of atrazine.

Currently, the importance of this study is finding that the sexual development of frogs can be adversely affected, resulting in multiple sex organs (gonads) or inter-sex frogs at levels of atrazine commonly found in the environment.

For more information on the EPA atrazine risk assessment (note: many documents listed on this page are hundreds of pages long) see: http://www.epa.gov/oppsrrd1/reregistration/atrazine/index.htm

More on Dr. Hayes and his research interests:

http://www.berkeley.edu/news/media/releases/2002/04/15_frogs.html

Abstract of Dr. Hayes article published April 16, 2002:

http://www.pnas.org/cgi/content/abstract/99/8/5476

More on Dr. Hayes and his research interests:

http://www.exploratorium.edu/frogs/researcher/

On-line National Geographic article on Dr. Hayes' research: http://news.nationalgeographic.com/news/2002/04/0416_020416_TVfrog.html

Vegetarian Eating and Breast Cancer – Evaluating the Evidence

Carol Devine, BCERF Education Leader and Associate Professor, Division of Nutritional Sciences

A recent headline declared that being vegetarian was linked to having a lower risk of breast cancer. Like many of you, I found this headline intriguing and went to the original article to see for myself. Some questions I considered as I read were:

Who was studied? The researchers recruited women up to 75 years of age who had been born in South Asia (India, Pakistan, Bangladesh) and later immigrated to England. Some of these women had been lifelong vegetarians, avoiding meat and eggs but consuming milk. Other women had been meat eaters, except for pork.

What was the study design? This was a case-control study. The diets of women diagnosed with breast cancer within the past 2 years (the cases) were compared to the diets of women with similar characteristics and living in the same area who did not have cancer (the controls).

What was the research question? Was breast cancer incidence less likely among women who had been life-long vegetarians compared to women who had been meat eaters?

What data were collected? Women were asked what they had customarily eaten 2-3 years before they were interviewed (before cancer diagnosis among the cases). They were also asked about other breast cancer risk factors (e.g. family history of breast cancer, body weight etc.)

What were the findings? Women who were lifelong vegetarians were only slightly less likely to have had breast cancer than women who were meat eaters. In addition, the difference in breast cancer risk was small enough that it could have occurred by chance. But there were strong trends toward significantly lower breast cancer risk for the women who ate the greatest amounts

of vegetables and pulses (peas, beans and lentils) compared to women who ate the least amounts of these foods. All of the difference in risk between vegetarians and non-vegetarians could be accounted for by differences in vegetable and pulse intakes, even after taking into consideration the other known risk factors for breast cancer.

How big were the differences in the diets in the two groups? Women who ate the most vegetables and pulses (and had about half the incidence of breast cancer) ate more than 406 grams (about 8 cooked cups) of vegetables and 107 grams (about 3/4 cooked cup) of pulses a day. Women who ate the least vegetables and pulses (and had the highest incidence of breast cancer) ate less than 210 grams (about 2 cups) of vegetables and less than 35 grams (about 1/4 cup) of pulses a day.

What was the conclusion? The researchers concluded that higher consumption of vegetables and pulses by the vegetarian women may account for their lower rates of breast cancer, rather than differences in their consumption of meat.

What are the limitations of this study for western women? The East Asian vegetarians in this study had been lifelong vegetarians; many western vegetarians adopt vegetarian diets in adulthood. The amounts of vegetables and pulses eaten by the women in this study were much higher than those found in typical western diets, and the kinds of vegetables and pulses in the East Asian diet are different from those of the typical western diet. In addition, there may also be other lifestyle factors that make these women different from western women. For example, few of these women drank alcoholic beverages, a risk factor for breast cancer.

How do these results compare to those of other studies? These results are generally consistent with those of the few existing studies of vegetarians. Many case-control studies have reported similar protective effects of vegetable consumption on breast cancer risk. Several cohort studies have reported no protective effect of vegetable consumption on breast cancer risk, but some of these may have suffered from limited information on vegetable intake, especially the range and type of vegetables eaten in this study. Case-control studies collect dietary information after diagnosis and depend on memory. Cohort studies collect information before the disease occurs.

What are the take-home messages? First, vegetables and beans once again may have a protective effect on health. Second, read beyond the headlines, it wasn't being a vegetarian that was protective in this study, but eating more vegetables and beans. Third, when considering a study like this, consider how closely you, your diet, and your life style compare to the women in this study.

For more information go to: Dos Santos Silva I, Mangtani P, McCormack V, Bhakta D, Sevak L & McMichael, A. Lifelong vegetarianism and risk of breast cancer: a population-based case-control study among South Asian migrant women living in England. *International Journal of Cancer* 99(2002):238-244.

Evaluations from April 4 Satellite Conference Give Guidance for Future Plans

70 downlink sites in 20 states participated in BCERF's April 4, 2002 satellite videoconference, *Environment and Breast Cancer: Education for Change.* Each of these downlink sites provided "train-the-trainer" events in which educators of all kinds could come together within their communities to learn strategies for integrating research results and risk reduction strategies into their daily work. The conference featured many New York State educator voices, research information and perspectives, and two question-and-answer periods, during which faxes and phone calls streamed in from many sites.

55 sites have returned their evaluations to BCERF so far, representing the responses of 548 individuals. The majority of those participating work in health care, health education, breast cancer education or advocacy, or nutrition. Environmental professionals also participated, representing the areas of household environment, environmental engineering, wildlife biology, pest management, hazardous waste remediation, and conservation. Other participants included epidemiologists, cancer researchers, students, social workers, concerned parents or parent educators, tribal health providers, and members of breast cancer support groups.

Five key number scale questions plus two open-ended questions provided an evaluation which was not overly

Continued on Page 6

Cancer Research at Cornell: *Professor Danny Manor*

Mechanisms Underlying Malignant Transformation, and Applications of Such Findings Toward Cancer Prevention and Intervention Strategies

BCERF strives to build awareness of environmental health and cancer-related Cornell University research, and help facilitate interaction and outreach activities. The work of Danny Manor, Assistant Professor in the Division of Nutritional Sciences, is highlighted here in a conversation with him. For overviews of the work of two other cancer researchers at Cornell, Dr. Rodney Page and Dr. Rui Hai Liu, please see ***Environmental Update****, a publication of the Cornell Center for the Environment, Spring 2002. http://cfe.cornell.edu/cfe/publications.cfm*

What is the focus of your research program?

Our efforts can be divided into two general areas: one is to gain a better understanding of the basic mechanisms that regulate cell growth, and how are they perturbed in malignant diseases. Separately, we ask what are the mechanisms by which some treatments — such as vitamin E supplementation — may prevent malignant pathology. Conceptually, these are two very different questions: in the first we ask what happens once a malignant process has started. In the second we study how to minimize the initiation of the disease.

Vitamin E is an anti-oxidant that is claimed to have some anti-cancer effects. How might this happen?

The first thing we must understand is that cancer is a disease that stems from accumulation of multiple mutations in our DNA. Some of these mutations can be inherited, as in the case of the breast cancer genes *BRCA1* and *BRCA2*, thus increasing a person's overall risk for cancer. The rest of the mutations are sporadic, that is, acquired throughout our lives due to chemical modification in cellular DNA from environmental factors. One such mutagenic process involves the action of Reactive Oxygen Species (ROS); these by-products of normal metabolism are extremely reactive, oxygen-based molecules that damage cellular components, including DNA. Anti-oxidants, such as vitamin E, chemically neutralize ROS, and thereby eliminating the mutagenic and carcinogenic risk associated with them. The above explanation is the "dogma" of anti-oxidants effects. This said, however, there have been a number of biological activities of vitamin E that are NOT associated with its activity as an anti-oxidant. These are issues under intensive experimental research.

How is your research on vitamin E and cancer applicable to breast cancer?

First, different malignant diseases share many common biochemical properties, regardless of the affected tissue. Thus, our studies on basic mechanisms of cell transformation bear relevance to all cancers. In addition, we will soon be starting experiments in which we will directly assess the possible protective effects of vitamin E on breast cancer – both in tissue culture (breast cancer cell-lines) and in animal model systems (mouse strains that develop breast cancer in high frequency).

Can one make a clear-cut statement about the effectiveness of vitamin E in cancer prevention?

I have read multiple epidemiological studies on this topic that, unfortunately, do not share a solid and common conclusion. I therefore do not feel I can give you a simple answer. However, there are published reports from animal models that show a strong protective effect of vitamin E in some malignant diseases.

Can you please tell us about your new Cancer Protein Expression Laboratory?

We recently received funding from the National Cancer Institute to establish a centralized protein expression facility on the Cornell campus. The main goal of the facility is to aid in elucidating the structures of cancer-related proteins. Knowing the molecular architecture of these molecules is critical to the development of new intervention strategies. The project is an interdisciplinary endeavor, with investigators from the departments of Molecular Medicine, the Comparative Cancer Center, Chemistry, Molecular Biology and Genetics, and Nutritional Sciences. Please see the web site at **http://cancerpxl.cornell.edu/**

Satellite Conference (continued)

cumbersome for the participants, but quickly revealed useful information about the strengths and weaknesses of the conference. Through the number scale questions we sought information about whether, as a result of the conference, the participant :

- *Expanded his or her knowledge of breast cancer risk factors* **82.2%**
- *Knows how to help reduce breast cancer risk through his or her work* **78.2%**
- *Understands the reasons for the intergenerational approach to risk reduction* **93.5%**
- *Knows how to use the BCERF Tool Kit in his or her work* **58.6%**
- *Plans to use what he or she learned in the conference in his or her work* **78.2%**

(The percentage in bold is how many responses were "agree" or "strongly agree.")

The first open-ended question asked participants, "As a result of this program I plan to…" Responses to this question showed a range of plans, from personal behavior change to all the various educational uses of the Tool Kit. Many participant statements paralleled the objectives of the Tool Kit in terms of the approach, audiences and settings to which the risk reduction messages, strategies and materials might be applied. For example, (as a result of this program I plan to…)

- *"personally read labels more carefully, choose less dangerous products, wear correct gloves, etc., and professionally use the material ... in health and wellness education."* (Carver County, Minnesota)
- *"use this information with patients whenever I have the opportunity.*" (Meadville, Pennsylvania)
- *"continue to reinforce and teach risk reduction methods, with an emphasis on starting 'early' re: age."* (Suffolk County, New York)
- *"while my job is to teach breast self exam, I will add information about risks from chemicals.*" (Seattle, Washington)
- *"use less toxic methods for cleaning my home; take another look at my diet; think about these issues when I talk to girls, when I buy products, and when I vote."* (Tompkins County, New York)
- *"explore the ways that I, retired and a breast cancer survivor, can learn more about and keep up with environmental risk factors, help spread the message and push for more research on causes of cancer.*" (State College, Pennsylvania)

The second open-ended question simply provided the opportunity for participants to add any additional thoughts. Here is where we learned about their overall assessments of the satellite conference. These responses (and any additional input received) will help BCERF make decisions about future widely disseminated educational programs. For example, we are very aware of the need to provide materials at various levels; hence our publication of materials ranging from lengthy scientific documents to "tip sheets." We also have the challenge of wanting to reach educators new to working with these issues, as well as the more seasoned educator who may have a lot of knowledge already. A majority of participants seem to have found the conference appropriate to their needs and their level. There were also many participants who clearly had extensive existing scientific knowledge and were looking to expand upon it. These participants especially appreciated the presentations of Drs. Suzanne Snedeker and Barbour Warren, as well as the interactive panels, and hoped for both more science and more interaction. Some participants would have preferred that we spend more time on science and less time on presentation of the Tool Kit. BCERF staff plan to further explore this question, as we strategize how to best provide our national — even international — group of colleagues in risk reduction education with appropriate information about the materials we have developed.

We thank all facilitators and participants for a lively and successful satellite broadcast. We welcome any further comments about the program.

Thank you to Neil Rotach, BCERF Administrative Assistant, for compiling the data.

Videotape of satellite conference

We have sold out of the original order of videos we had made following the conference. If we receive enough additional interest, we are happy to have more copies made. If you are interested, please contact Mary Maley through the BCERF office or at mm153@cornell.edu

PUBLICATIONS AVAILABLE!!

Single copies available at no cost.
For multiple copies please contact BCERF (address below).

EDUCATIONAL TIP SHEETS

Five *Tip Sheet*s on practical strategies to reduce the risk of breast cancer from environmental factors have now been developed. These *Tip Sheets* have been written at or below the 7th grade reading level.

__**What Do We Know About Breast Cancer?** discusses breast cancer risk factors and general, practical tips about how to reduce your risk.

__**Eating Well and Staying Active** offers risk reduction tips associated with food, alcohol, breastfeeding and physical activity.

__**Pesticides in Your Environment** addresses various pesticide-related concerns, including tips for accessing information about pesticides in drinking water, schools and workplaces, and how to reduce your exposure at home.

__**Using Home and Garden Products More Safely** provides an easy-to-read, step-by-step guide on how to reduce exposure to harmful chemicals in and around your home.

__**Breast Cancer Resources On...** tells you where to get answers to frequently asked questions related to the topic of breast cancer. Resources refer to New York State and beyond.

FACT SHEETS

Revised: *(Please replace your old versions)*

__FS #1--Phytoestrogens and the Risk of Breast Cancer (July 2001)

__FS #2—Pesticides and Breast Cancer Risk, An Evaluation of DDT, DDE (March 2001)

New:

__FS #40—Hormone Treatments and the Risk of Breast Cancer

__FS #41—Polycyclic Aromatic Hydrocarbons and Breast Cancer Risk

__FS #42—A Woman's Body Type and the Risk of Breast Cancer

__FS #43—Breast Cancer in Men

__FS #44—Diet and Lifestyle and Survival from Breast Cancer

__FS #45—Environmental Chemicals and Breast Cancer Risk--Why is There Concern?

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