







Slide-Script and Interactive CD



# Pieces of the Puzzle: Does Atrazine Affect the Risk of Cancer?

Improving your knowledge of pesticides and health

Cornell University Program on Breast Cancer and Environmental Risk Factors

CORNELI

# Pieces of the Puzzle: Does Atrazine Affect the Risk of Cancer?



Pesticide Applied Learning Series

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### ACKNOWLEDGEMENTS:

The inspiration for this module came from a series of workshops I conducted at the 1999 National Pesticide Certification & Training Workshop in Portland, Maine, on the cancer risk of several widely used herbicides. These talks were based on translational research conducted in the BCERF program. The critical assessment of the scientific literature on the cancer risk, environmental fate, and potential for human exposure to atrazine was published as a BCERF Critical Evaluation and was translated into a consumer-oriented fact sheet in 1999. Both documents are available on the BCERF web site at <http://www.cfe.cornell.edu/bcerf>. I am indebted to Heather Clark who helped develop the usage sections of the original Atrazine Critical Evaluation and fact sheet manuscripts, to the technical reviewers of these manuscripts, John Bucher and James Huff at the National Institute of Environmental Health Sciences (NIEHS), and Ruthann Rudel at the Silent Spring Institute. This learning module on the cancer risk of atrazine has been updated to reflect the most recent information available in Environmental Protection Agency's risk assessment of this herbicide.

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S. Snedeker



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### **INTRODUCTION:**

There is concern that certain widely used pesticides may affect the health of humans and wildlife. New emerging research is investigating how pesticides can affect cancer risk and reproduction by acting as hormonally active agents. While these are topics of interest to the scientific and regulatory community, others, including those in agriculture, and who use and consume agricultural products, are not always aware of these ongoing scientific discussions and evaluations. Nor do they have access to easy to understand scientific information on emerging research or on risk assessments conducted by federal agencies such as the Environmental Protection Agency (EPA).

We hope the PALS modules will fulfill several needs. This includes making current scientific topics on agriculture, the environment and health available to pesticide educators and applicators and to others who are interested in improving their knowledge about the health effects of pesticides.

The PALS Atrazine module is designed to improve the knowledge level of the user/audience on the current scientific evidence of whether atrazine affects the risk of cancer. This is an evolving area of research where scientists are still seeking more answers. The module also gives information on exposures of concern identified by the Environmental Protection Agency.

This module is provided in three different formats to increase the availability and accessibility of this information to a variety of audiences:

### Guidebook/Traditional Slide-Script Version - for group presentations

The Guidebook includes 35 mm slides and a hard copy of the slides and script. The presenter has the option of reading the script during the group presentation. The Guidebook also includes a handout with a mini-version of all slides.

#### Interactive Version - for individualized self-study

The Interactive Version is meant to be viewed by an individual at a computer workstation. You can hear an audio version of the script, as well as view the text of the script. The presentation has animation, including a mini-movie on how breast cancer develops.

#### Adaptable PowerPoint Version - for electronic group presentations

This version can be modified and tailored to meet the needs of your audience. Slides can be deleted or edited.



### LEARNING OBJECTIVES for: Pieces of the Puzzle; Does Atrazine Affect the Risk of Cancer?

Participants will:

- Gain an awareness of breast cancer risk factors and the complexity of the disease.
- Be able to identify the primary crop and non-cropland uses of atrazine.
- Increase their knowledge of the human and animal studies that have evaluated the cancer risk of atrazine.
- Be able to identify exposures of concern to atrazine in the workplace and residential settings.
- Increase their knowledge of trends in levels of atrazine in water supplies.
- Increase their knowledge of how atrazine may affect the sexual development of wildlife.

### INSTRUCTIONS for the SLIDE-SCRIPT VERSION:

This module is provided in a traditional slide-script format.

This includes a Guidebook Binder with:

- a set of numbered 35 mm slides
- a hard copy version of each slide with the facing page containing the script
- a handout master, with three slides per page and areas for note taking
- a suggested pre-post test

A PDF version of the Guidebook is also available on the CD in the folder "PDF Guidebook".

Equipment needed:

- 35 mm slide projector
- Movie/slide projection screen
- Podium (optional) for script
- Flip-chart, pad and markers if you wish to write out questions after the presentation

#### Hints for presenters:

Familiarize yourself with the slides and script by reading the script to yourself and aloud in a conversational tone several times. You can then decide if you want to use all of the slides "as is" or select a sub-set of slides to individualize the presentation to meet the needs of your audience.

Anticipate the number of attendees, and make sure you have made a sufficient number of the handouts as well as the pre-post tests.

The summary slides are meant to help you "wrap up" the presentation, and review the major points of the presentations. These summary points are good jumping off points that can be used as a lead-in to any post-presentation question and answer period.

The slides on additional BCERF materials are optional, but do provide added resources for attendees that want more information on the cancer risks of pesticides and cancer risk reduction strategies. An index of the slides by title is contained in Appendix C.



### **INSTRUCTIONS for the INTERACTIVE VERSION**

What you need:

• A computer capable of reading a CD-ROM disk

• A web browser

- Browser versions for **PC users**: Internet Explorer 4.0 or higher, Netscape 4.0 or higher.

- Browser versions for **Mac users**: Internet Explorer 5.1 or higher, Netscape 7.0 or higher.

Known incompatibilities with certain browsers are listed in Appendix D.

• Macromedia Flash plug-in installed on your computer. This is a free plug-in available from Macromedia at: <u>http://www.macromedia.com/shockwave/download/</u>

<u>index.cgi?P1\_Prod\_Version=Shockwave</u> It provides the sound and animation for the module

• A printer if you wish to make hard copies of any printed text, the manual, instructions, etc.

Overview:

- The self-directed Interactive Version can be used for individualized self-study
- This version of the module has animation and sound (audio of script)
- An audio version of the script is played for each slide
- The text of the audio can be viewed by scrolling to the bottom of the slide
- The Interactive Version can be viewed with either Netscape Navigator or Internet





Explorer

How to Access the Interactive Version:

• On the CD, click the "START\_HERE.html" icon, then select the Interactive Module

### OR

• You can open the folder called "Interactive\_Module" and select the "START.html" icon. This method will bypass the overall start screen which provide access to other features on the CD.

### **INSTRUCTIONS for the INTERACTIVE VERSION (continued)**



# Navigation and Layout of the Interactive Version:

Navigating the Interactive Version is easy. The page always includes a graphic, which is usually on the left-hand side, and a text area for the main points of the slide.

The audio plays automatically when you first see a slide. An area of text below the main window provides the script of the spoken information. You may have to scroll down the screen to see the whole of the script.

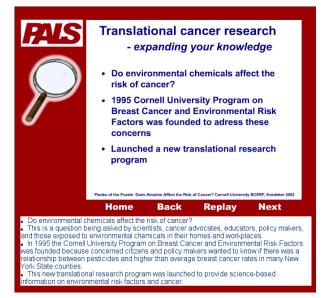
Navigation buttons are located directly underneath the main information area. Two buttons are always available: Home and Back. These allow the reader to retrace their steps in case they missed something.

Back Button Goes to the previous slide.

**Home Button** Returns to the main screen at the start of the presentation. The HOME screen provides a link to the Table of Contents with a list of all slides.

After the audio for the slide has played two more options become available. The buttons called Replay and Next appear.

- **Replay Button** This button will allow you to listen to the audio of the slide again.
- Next Button The Next button will take you to the next slide in the series.





### INSTRUCTIONS for the ADAPTABLE POWERPOINT VERSION

What you need:

- A computer capable of reading a CD-ROM disk
- A web browser, either Internet Explorer (version 4.0 or higher) or Netscape (version 4.0 or higher)

• PowerPoint software (version 6.0 or higher) needs to be installed on your computer if you wish to view or edit the PowerPoint version of this module. You must purchase this software separately from Microsoft

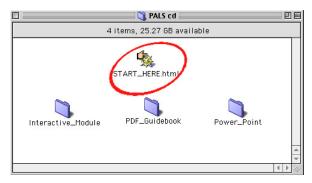
• A printer if you wish to make hard copies of any printed text, instruction, overheads, handout master, or customized handouts, etc.

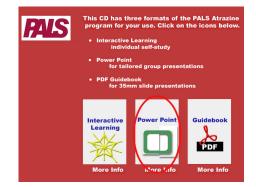
The PowerPoint version with electronic slides and notes can be:

- Played directly on your computer from the CD-ROM using PowerPoint software
- · Downloaded onto your computer for use with PowerPoint software
- · Edited by you or other users to develop individualized presentations

How to Access the PowerPoint Version:

• On the CD, click the "START\_HERE.html" icon then select the PowerPoint Version





### OR

• You can open the folder called "Power\_Point" and select the "START.html" icon. This method will bypass the overall start screen which provides access to other features on the CD

### To Edit the PowerPoint Version:

• On the CD, open the "Power\_Point" folder. Save the file named "PALS\_Atrazine.ppt" to your computer's hard drive or desktop

• You can make and save changes to this copy

• You cannot make or save changes to the PowerPoint version of the CD

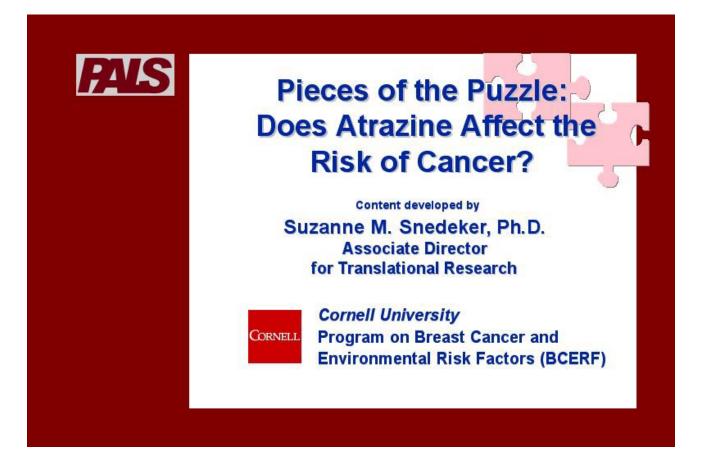
Slide Notes:

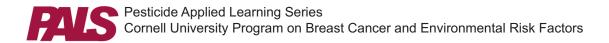
• Notes for each slide can be viewed by choosing the "**View : Notes**" option in the PowerPoint Version

PALS Pesticide Applied Learning Series Cornell University Program on Breast Cancer and Environmental Risk Factors

### Notes







- Pieces of the Puzzle: Does Atrazine Affect the Risk of Cancer? by Suzanne M. Snedeker, Ph.D., Associate Director for Translational Research at the Cornell University Program on Breast Cancer and Environmental Risk Factors (BCERF)
- This module is part of PALS, the Pesticide Applied Learning Series.

• This module examines whether atrazine affects the risk of different cancers, including breast cancer. Information in this module comes from research studies. This includes studies of people exposed to atrazine and from studies using laboratory animals.

- It also includes information on situations where atrazine exposure may be a concern, and reviews information on atrazine levels in water supplies.
- This module recommends areas where more research is needed to provide additional information on the cancer risk of atrazine.







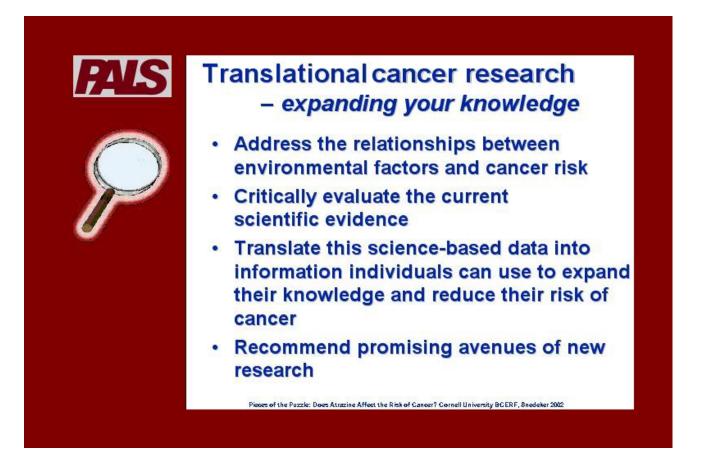
• Do environmental chemicals affect the risk of cancer?

• This is a question being asked by scientists, cancer advocates, educators, policy makers, and those exposed to environmental chemicals in their homes and work-places.

• In 1995 the Cornell University Program on Breast Cancer and Environmental Risk Factors was founded because concerned citizens and policy makers wanted to know if there was a relationship between pesticides and higher than average breast cancer rates in many New York State counties.

• This new translational research program was launched to provide science-based information on environmental risk factors and cancer.







In this approach we:

- Address the relationships between environmental factors and cancer risk.
- Critically evaluate the current scientific evidence using a strength of evidence approach.
- Translate this science-based data into information individuals can use to expand their knowledge and reduce their risk of cancer.
- However, we do not always have clear answers. So, we also recommend promising avenues of new research to help clarify any uncertainties.
- In this module we will explore why consumers are concerned about pesticides and cancer risk. This will include learning more about how cancers, in this case, breast cancer develops. We will also explore the Environmental Protection Agency's cancer risk assessment of the herbicide atrazine and the types of exposures that may be of concern for both pesticide applicators and the general consumer.
- First, let's talk about breast cancer risk and ways pesticides can affect the risk of breast and other cancers.



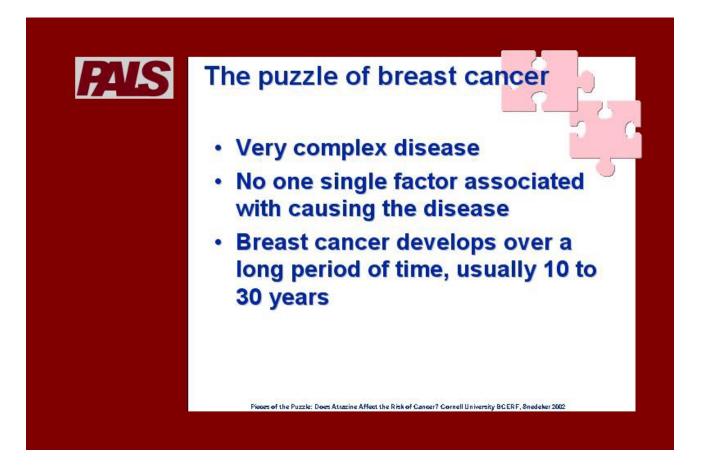




• The American Cancer Society has estimated that in the year 2002, 203,500 new cases of breast cancer will be diagnosed in American women, and 1,500 new cases will be diagnosed in men.

• Over one-fifth of the women and one-third of the men diagnosed with breast cancer will die of the disease.







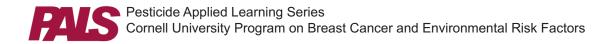
The puzzle of breast cancer

- Breast cancer is a very complex disease.
- There is no one single factor associated with causing the disease.

• Breast cancer develops over a long period of time. It can take 10 to 30 years for a normal cell to develop into a detectable tumor.





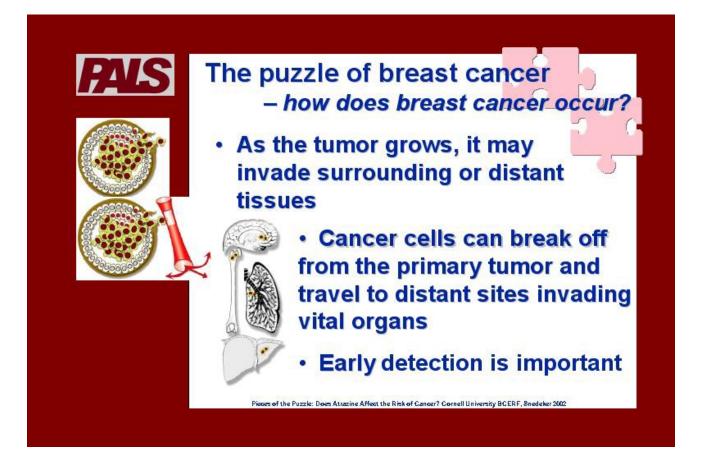


• How does breast cancer occur? The development of breast cancer is a long process that has many steps.

• Breast cancer occurs as a result of accumulating changes in key genes that control a cell's ability to divide, mature and die.

• These changes can result in an abnormal cancer cell that divides out of control and forms a tumor.





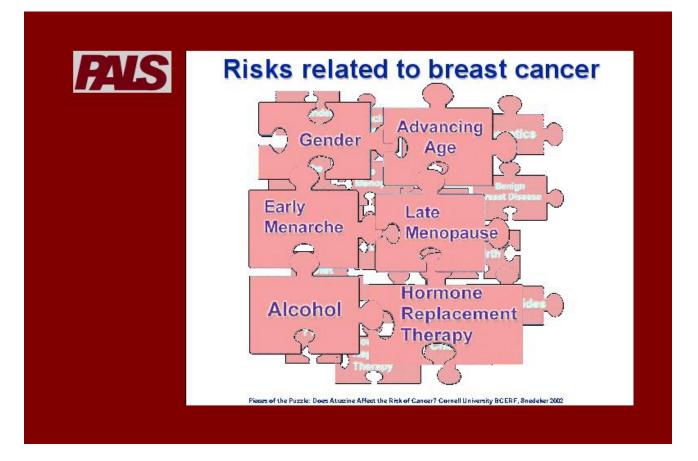


• As the tumor grows in size, it may invade surrounding or distant tissues.

• If cancer cells break off from the primary tumor they may travel to distant sites in the body, invading vital organs such as the brain, bone, liver or lung, and establish new tumors. When these vital organs fail, it can be fatal.

• That is why early detection and treatment are so important. It increases the chances of removing the tumor when it is small, before it has grown and invaded other tissues.







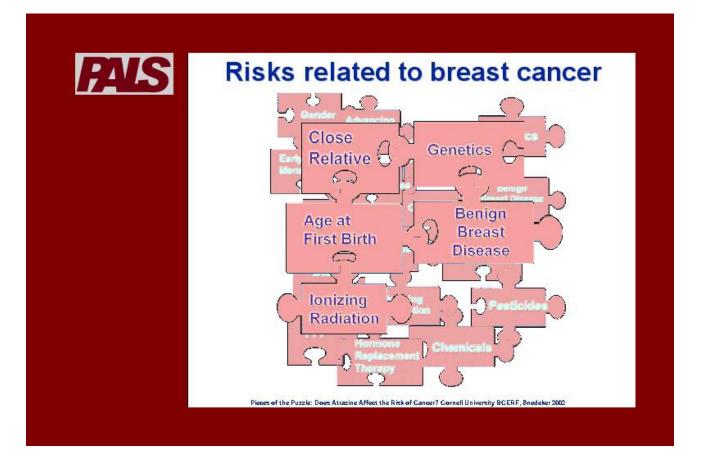
• What affects a person's risk of breast cancer? Breast cancer risk factors are like puzzle pieces. We know how some of the puzzle pieces fit together and affect risk. For other risk factors, we are just learning about the role they may play.

• Gender is the main factor that affects risk. Women have higher breast cancer rates than men.

• Advancing age, the age when a girl gets her first period, the age when a woman stops menstruating, a higher consumption of alcohol, and the use of hormone replacement therapy also affects breast cancer risk. These factors may increase exposure to certain reproductive hormones, such as estrogen and progesterone, which can stimulate breast cells to divide and grow.

• A dividing cell is more prone to making mistakes when copying its genetic material, leading to a higher rate of "by chance" or spontaneous mutations. A mutation can also be induced by an environmental chemical. Normally, our cells are very efficient at repairing these damaging mutations. However, a spontaneous or an induced mutation can be made permanent and be passed on to new daughter cells during cell division.





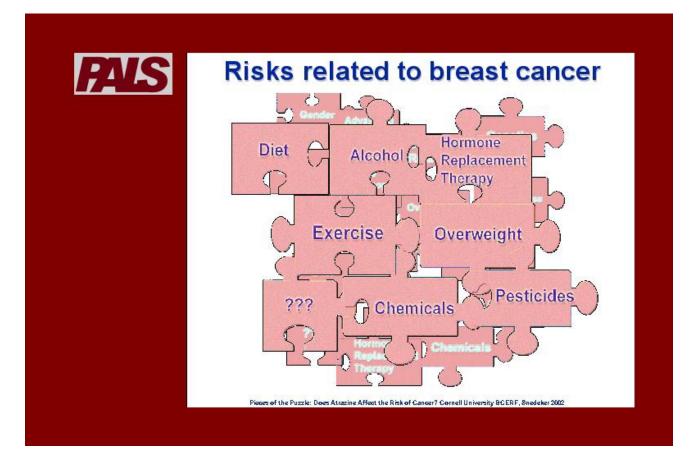


• A close relative with breast cancer (a mother, sister or grandmother), and having certain breast cancer susceptibility genes only accounts for five to seven percent of breast cancer risk. Therefore, most women who are diagnosed with breast cancer have no family history.

• The age when a woman has her first child also influences breast cancer risk. About 30% of breast cancer risk is explained by having a child late in life after 30 years of age, or never having children. Having children early in life causes immature breast cells to change and become resistant to the effects of cancer-causing chemicals.

• Other factors associated with an increased risk of breast cancer include certain types of benign breast disease, and exposure of the breast to ionizing radiation.







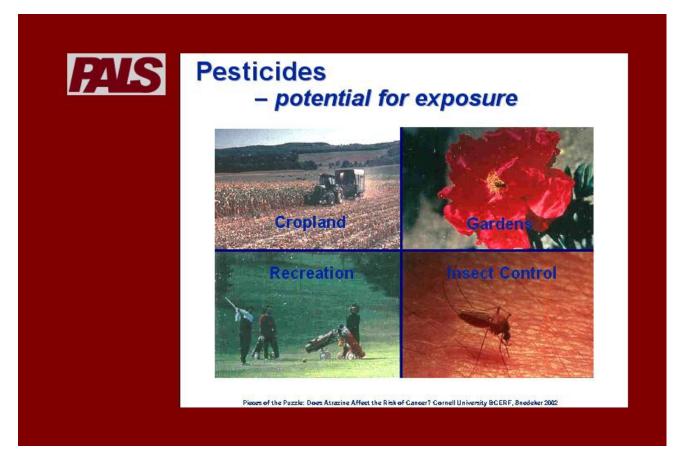
• For many other factors, we are just beginning to understand their role in breast cancer risk.

• A diet rich in fruits, vegetables and fiber may be associated with a lower risk of breast cancer. As was previously mentioned, a higher consumption of alcohol has been associated with more exposure to the hormone estrogen and a higher risk of breast cancer.

• Being overweight after menopause is associated with higher breast cancer risk. That is why regular exercise is important to help control body weight.

• There is concern that exposures to certain environmental chemicals may lead to a higher risk of breast cancer. This includes some types of dyes, flame retardants, solvents, passive cigarette smoke, certain pharmaceutical drugs and several pesticides.





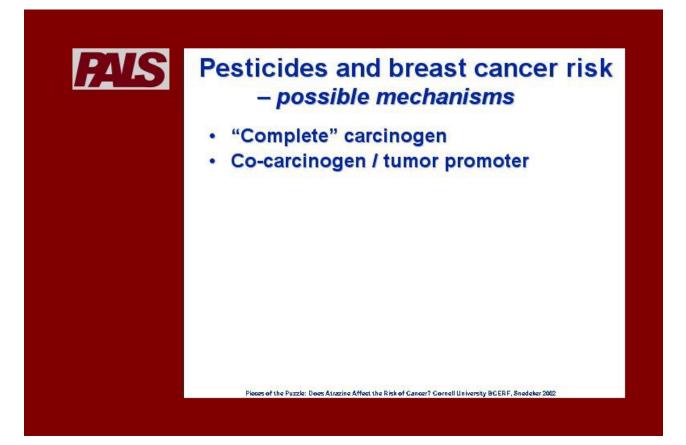


• Why is there a concern among consumers that pesticides may play a role in cancer risk? There is concern because of the potential for exposure.

- We use pesticides :
  - In agriculture to raise crops and livestock
  - In the home and garden to control weeds, structural insects and animal pests
  - To control pests in recreational areas like golf courses, parks, playgrounds and athletic fields, and
  - For large scale insect control against vector-borne diseases.

• The Environmental Protection Agency estimated that in 1997 nearly one billion pounds of pesticides were used in the United States alone. About 79% was used in agriculture, 14% for industrial, commercial and governmental use, and seven percent in the home and garden.







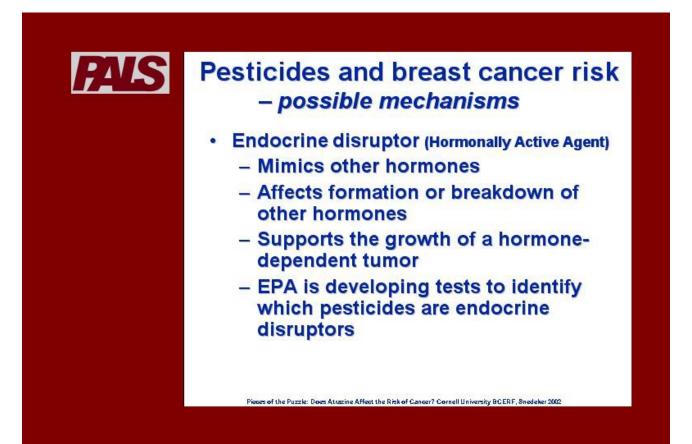
• Researchers have identified several ways that pesticides may affect breast cancer risk.

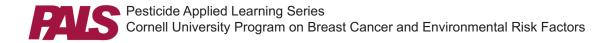
• Some pesticides may act as "complete" carcinogens. A complete carcinogen is capable of taking a normal cell through the entire multi-step process to form an invasive tumor. Only a few pesticides have been identified as "complete" carcinogens.

• Another way is to act as a tumor promoter. A tumor promoter may give an existing tumor a growth advantage, promoting its further growth and development.

• The insecticide DDT has been identified as a tumor promoter in laboratory animals. When given with or after a known cancer-causing chemical (called a carcinogen), a tumor promoter can cause a higher number or earlier appearance of breast tumors than if only the cancer-causing chemical is given.





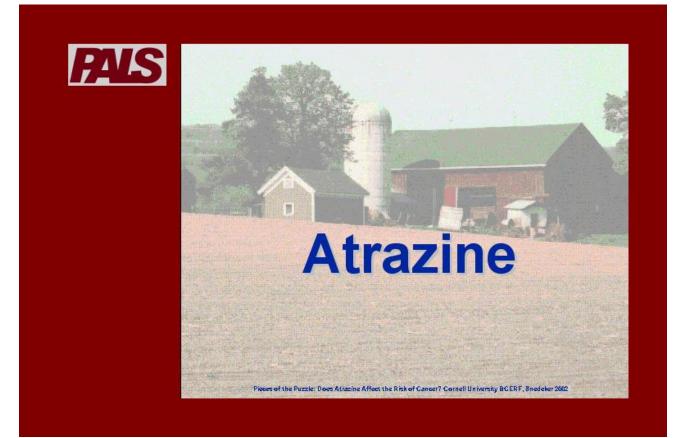


• Other pesticides may affect breast cancer risk by acting as "endocrine disruptors," also called "hormonally active agents." These chemicals may mimic a known hormone, such as estrogen, or in another way affect the formation or breakdown of hormones that regulate cell division.

• Pesticides that mimic the effect of estrogen may be able to support the growth of an existing estrogen-dependent breast tumor. We know that over half of all breast tumors depend on estrogen for growth.

• Scientists are only starting to identify which pesticides are endocrine disruptors, including estrogen mimics. The insecticides DDT and methoxychlor are weak estrogen mimics. The 1996 Food Quality and Protection Act mandates that the Environmental Protection Agency develop screening tests to identify which pesticides act as endocrine disruptors.



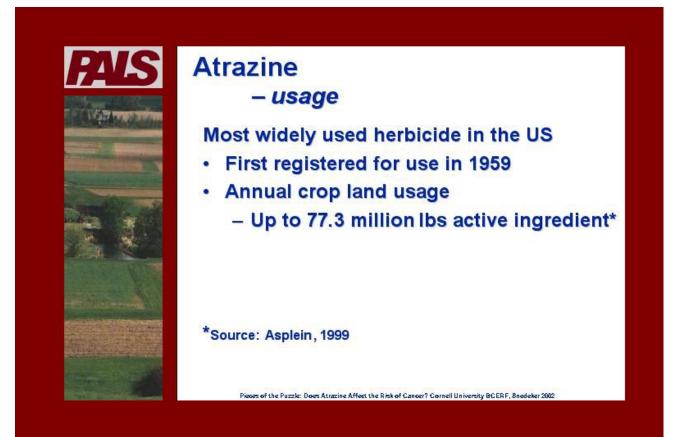




• What is the evidence that certain pesticides affect cancer risk?

• The Environmental Protection Agency has been evaluating the cancer risk of atrazine since the 1980s.







- Atrazine is one of the most widely used herbicides in the United States.
- It was first registered for use in 1959.
- Up to 77 million pounds of atrazine, as the active ingredient, were used per year during the 1990s.







- About 98% of atrazine usage is on agricultural crops.
- Its primary use is as a pre- and post-emergent herbicide on field and sweet corn, especially in the Midwestern corn-belt states.
- According to the US Department of Agriculture, about 69% of the corn crop was treated with atrazine in 1998 and about 82% of sorghum was treated with atrazine.
- Atrazine is also used for weed control on sugarcane fields.







• It is used to a lesser extent for weed control on other crops including winter wheat, guava and macadamia nuts, and on hay for animal feed and fodder, and to control weeds on fallow land.

• It is also used to control weeds on Christmas tree farms.



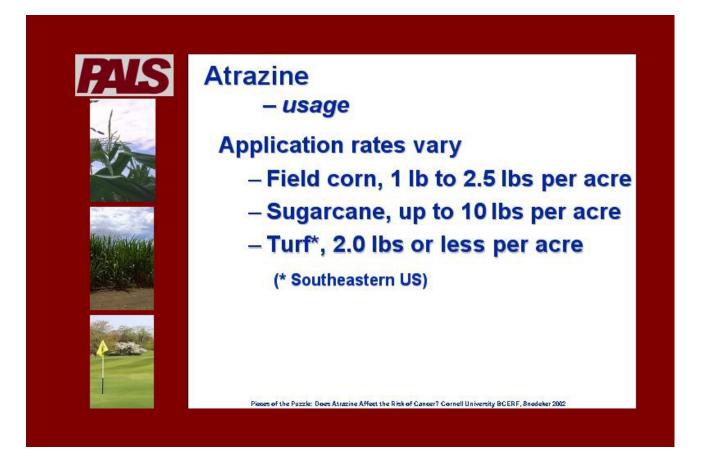


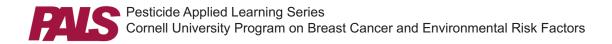


• Non-agricultural uses only make up about two percent of atrazine's usage. This includes weed control:

- On turf, including golf courses and home lawn care in the Southeastern US. Atrazine is used for weed control on St. Augustine and Bermuda grass.
- And on roadways and right-of-ways in some Midwestern and Western states.







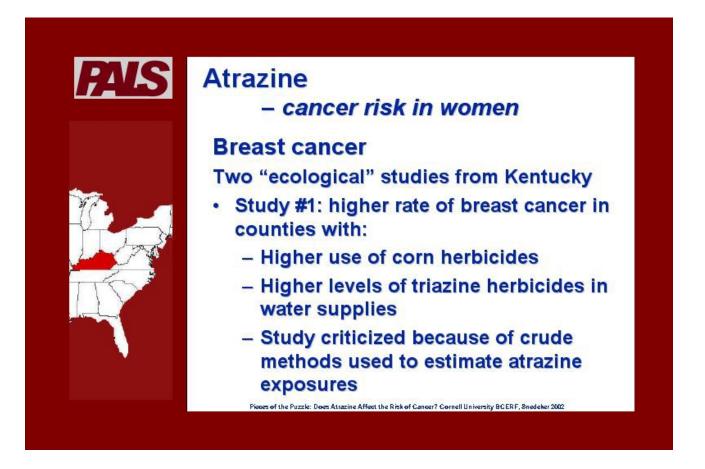
• Application rates for atrazine vary according to its use.

• In agriculture, the average field corn application rate is one pound of active ingredient per acre, while the maximum rate of application is two and a half pounds of active ingredient per acre.

• For sugarcane, the maximum application rate is ten pounds per acre, while on turf in the Southeastern US, application rates are usually two pounds or less per acre.

• Always refer to the product label for correct application rates.







• Is there evidence that atrazine exposure can affect breast cancer risk in women exposed to this herbicide? There are few studies of women that have attempted to answer this question. Unfortunately, there are no well-controlled human studies that have evaluated breast cancer risk in women exposed to atrazine compared to women not exposed to this herbicide.

• Two "ecological" studies have been conducted in Kentucky. Ecological studies approximate exposures of a population within a certain geographic area rather than evaluating exposures of individuals.

• In the first study researchers found higher breast cancer rates in women living in counties with:

- A higher use of corn herbicides and
- Higher levels of triazine herbicides in water supplies.

• This study did not estimate actual exposures to atrazine, but used surrogate measures, like number of acres of corn grown, to estimate atrazine exposure.

• This may have introduced inaccuracies, since many herbicides besides atrazine are used as corn herbicides.





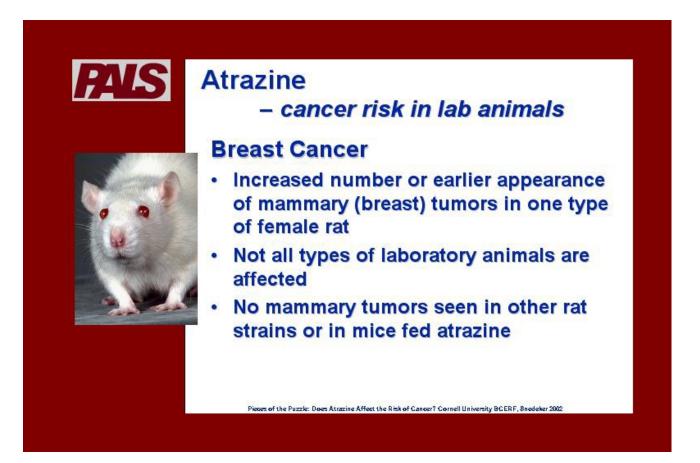


• In a recently published five-year follow-up study, breast cancer risk was not associated with:

- Number of acres of corn planted
- Atrazine sales
- Atrazine levels in the water supplies.

• But, this begs the question, what is the best way to estimate exposure to atrazine? For instance, what is sold in one county may be applied in another county. This study did not use more accurate, direct measures of exposure to atrazine, such as skin exposures, estimates of drift, or actual levels of atrazine in the air or dust of farm homes. Unfortunately, ecological studies can only give us very limited information.





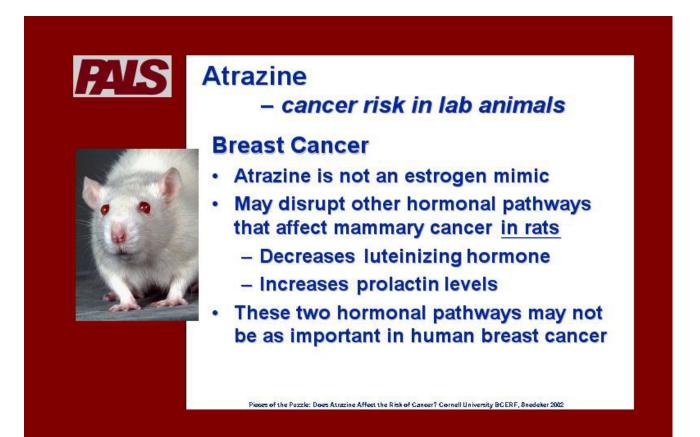


• What is the evidence that atrazine affects the risk of mammary cancer in experimental animal studies?

• Atrazine was fed at high levels over long periods of time to female rats in several studies. Atrazine caused a higher number or earlier appearance of mammary tumors in one type of female rat.

- But not all types of laboratory animals were affected.
- In other strains of rats and in mice, atrazine treatment did not induce breast tumors.







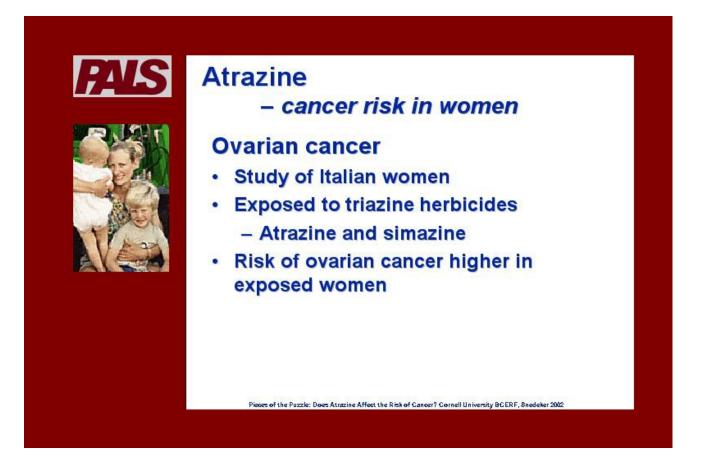
• While atrazine is not an estrogen mimic, the results of some studies suggest that atrazine may affect breast cancer risk by disrupting certain hormonal pathways in susceptible laboratory animals.

• We do know there are two hormonal pathways that are affected. Atrazine can decrease levels of luteinizing hormone, and increase levels of a hormone called prolactin. Both of these hormones are important for reproduction in laboratory animals.

• Disruption of these two pathways can lead to hormonal changes that increase the number of breast tumors in certain strains of atrazine-treated female rats.

• However, many scientists feel that these two hormonal pathways may not be as important in human breast cancer. For instance, elevated prolactin levels are known to increase the number of mammary tumors in rats. However, prolactin levels have little influence on the development of human breast cancer.







• What about other types of cancer?

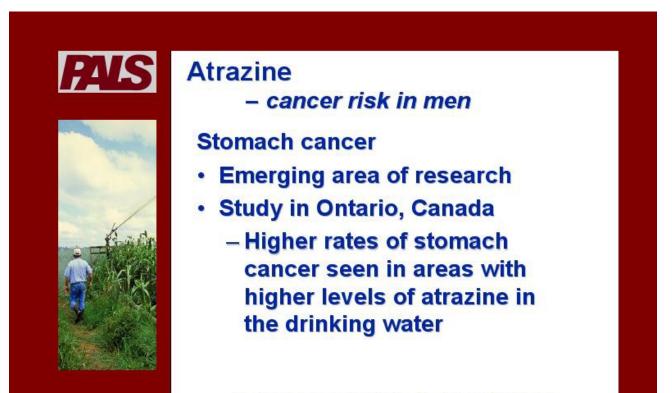
• The results from a study of Italian women suggests that women exposed to the triazine herbicides atrazine and simazine had a higher risk of ovarian cancer than women with little or no exposure.

• No other studies have been done to see if ovarian cancer rates are higher in American women exposed to atrazine.

• So, we do not have strong evidence that atrazine causes breast or ovarian cancer in women. But, it should be pointed out that this is based on very few studies.

• While there are other studies of cancer rates in farm women and female farm workers, they usually have not measured exposures to specific pesticides.





Pieces of the Puzzle: Does Atrazine Affect the Risk of Cancer? Cornell University BCERF, Snedeker 2002

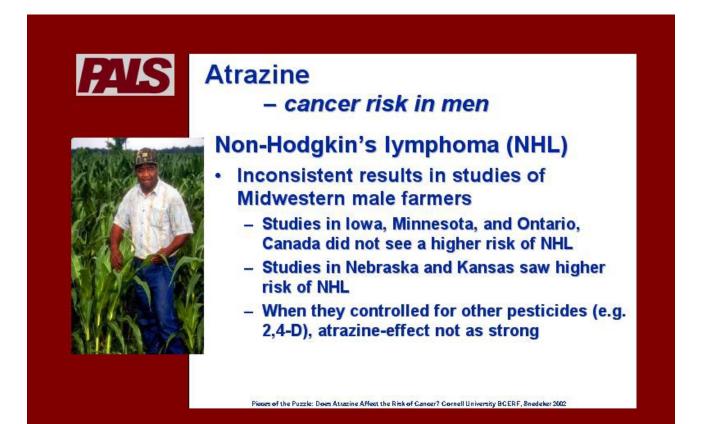


• What about cancer risk in men?

• There is emerging research from Ontario, Canada, suggesting higher rates of stomach cancer in agricultural regions where there were higher levels of atrazine in the drinking water.

• More research is needed to confirm this study's findings.







• Can atrazine exposure affect the risk of non-Hodgkin's lymphoma (NHL) in men?

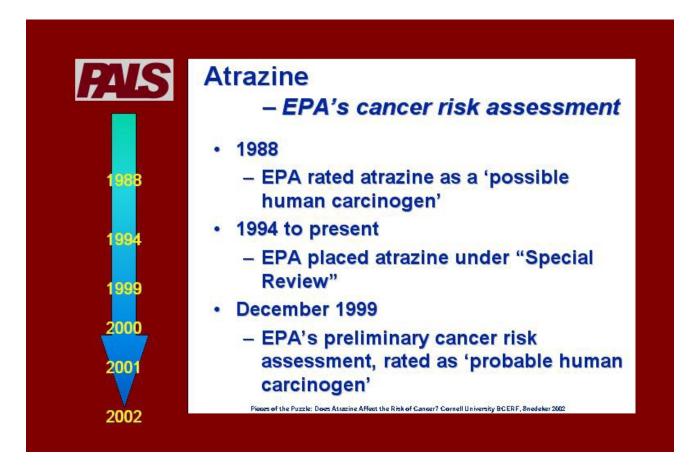
• The results have not been consistent. Some have and other studies have not observed a higher risk of non-Hodgkin's lymphoma in atrazine-exposed Midwestern male farmers.

• Studies conducted in Iowa, Minnesota and a recent study from Ontario, Canada did not see a higher risk of non-Hodgkin's lymphoma in atrazine-exposed men.

• While studies conducted in Nebraska and Kansas did see a higher risk of non-Hodgkin's lymphoma in male farmers exposed to this herbicide.

• The researchers then looked at the other pesticides the men were exposed to, and controlled for exposures to these other pesticides. When they did this, the atrazine-effect on non-Hodgkin's lymphoma was not as strong and only a small risk was observed from atrazine exposure.





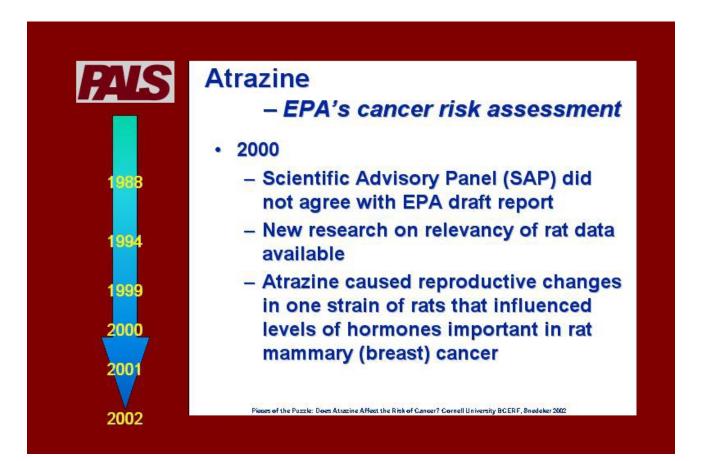


• The Environmental Protection Agency first rated atrazine as a possible human carcinogen in 1988 based on evidence of mammary (breast tumors) in female laboratory rats fed high levels of atrazine for most of their lives.

• In 1994 atrazine and two other triazine herbicides simazine and cyanazine were placed under "Special Review" by the Environmental Protection Agency because of concerns about their potential cancer-causing effects. The Environmental Protection Agency also expressed concern because of risks resulting from exposure through contaminated water and food, and exposures in workers during mixing, loading and application of this herbicide.

• In December 1999, the Environmental Protection Agency released a preliminary cancer risk assessment, rating atrazine as a 'probable human carcinogen'.



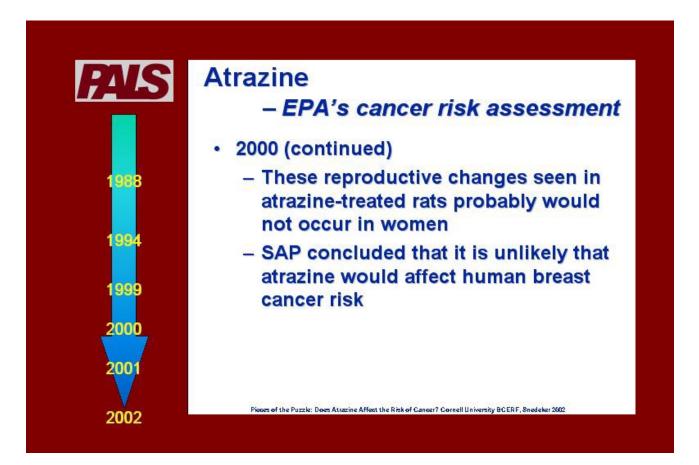




• A panel of scientists did not agree with the Environmental Protection Agency's draft report.

- At this time new research was emerging on the way atrazine induced breast tumors in rats and whether this was relevant to human breast cancer.
- Atrazine caused reproductive changes in one strain of rats that influenced levels of hormones important in rat mammary (breast) cancer.







• The advisory panel concluded that the types of reproductive changes seen in atrazine-treated rats probably do not occur in women, because of species differences.

• Therefore, the Scientific Advisory Panel concluded that it is unlikely that atrazine would affect human breast cancer risk.





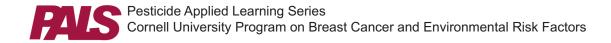


• In June of 2000, based on the Scientific Advisory Panel's recommendations, the Environmental Protection Agency changed atrazine's cancer classification to: "not likely to be a carcinogen in humans".

• The Environmental Protection Agency's reregistration decision is expected in 2003.







• There is some emerging data that has identified an effect of atrazine in wildlife that may be linked to hormone disruption. A study from the University of California at Berkeley has shown that atrazine can affect the sexual development of African clawed frogs.

• The male tadpoles were exposed to a wide range of atrazine levels from very low to high. All of the atrazine-exposed tadpoles had abnormal sexual development.

• There were no abnormalities in the control frogs that were not exposed to atrazine.

• In the atrazine-exposed male frogs, up to 20% had both testes, the male sex organ, and ovaries, the female sex organ. These frogs are called "inter-sex" or hermaphrodite frogs.

• Also, the male frogs were more like female frogs. Atrazine had a demasculinizing effect on the male frogs.

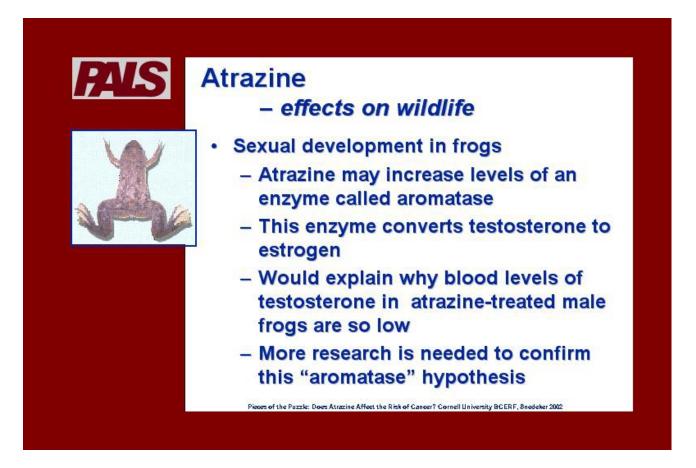
• Female frogs were not affected.

• These effects occurred at very low levels of atrazine, levels commonly seen in lakes, rivers and streams in agricultural areas where atrazine is used for crop protection.

• The effects were seen as low as 0.1 part per billion. This is 30 times lower than the maximum level for atrazine allowed by the Environmental Protection Agency in public drinking water supplies, which is 3.0 parts per billion.

• The researchers also measured levels of sex hormones in adult frogs. They found that adult male frogs that had been exposed to atrazine had very low levels of the male hormone testosterone.





• What could be the explanation?

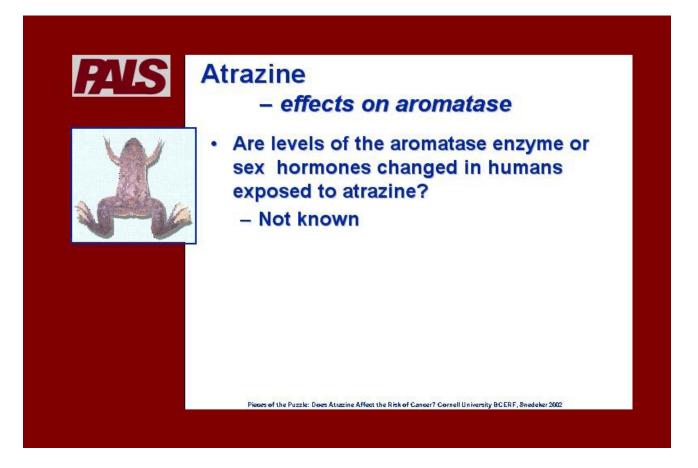
• The researchers' theory is that atrazine may increase the levels of an enzyme called aromatase. This enzyme converts testosterone, the male sex hormone, to estrogen, the female sex hormone.

• This would explain why blood levels of testosterone in atrazine-treated male frogs are so low.

• But, this hypothesis needs to be tested to see if aromatase levels are actually higher in atrazine-treated frogs.

• Does this potential hormone disruption have any implication for humans?







• In humans, testosterone can be converted to estrogen by the same aromatase pathway.

• Do we know if atrazine can affect levels of sex hormones or the aromatase enzyme in humans?

• This is not known. However, it is important to determine if atrazine can affect the levels of aromatase in other non-frog species, including humans.







• Are there any exposures of concern that have been identified by the Environmental Protection Agency?

• During the Special Review of atrazine, the Environmental Protection Agency has identified several exposures of concern.

• While there is little concern for short-term exposures of workers with proper protective clothing, there are concerns for those who have higher exposures from handling large amounts of this herbicide.

• The highest potential for exposure to atrazine occurs in those who handle, mix, load or apply atrazine to large acreage of crops. Decreased application rates and the use of closed cabs has reduced exposure during agricultural applications. Many uses of atrazine to control weeds on right-of-ways have been eliminated over the years. However, in recent studies, the Environmental Protection Agency found exposures of concern in 30% of the applicators who used the proper personal protective equipment.

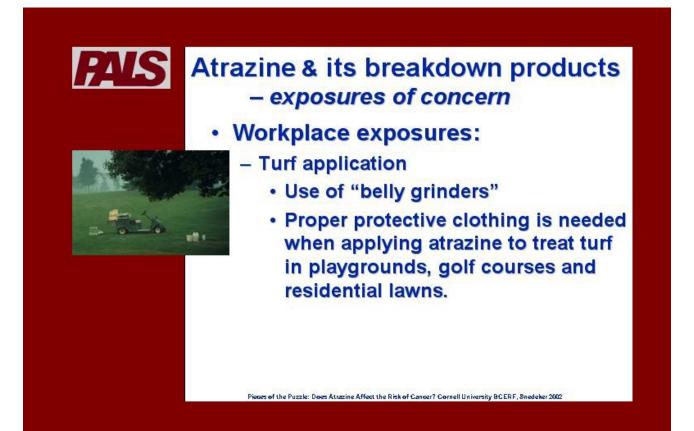
• Those who enter treated fields after atrazine has been applied also have the potential for exposure. The Environmental Protection Agency has expressed concern for exposures of workers who reenter atrazine-treated fields to scout sugarcane.

• Those who are involved with aerial application and hand spraying activities, or who are flaggers for aerial applicators potentially also have higher exposures to atrazine.





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• Application of atrazine to turf, especially by the use of "belly grinders" (hand-held broadcast spreaders) was another type of exposure of concern identified by the Environmental Protection Agency.

• Those who apply atrazine to turf in the Southeastern US (playgrounds, golf courses, residential lawns) may have potential exposures of concern if proper protective clothing is not worn. In this situation, exposure is possible by breathing mists, sprays or powder, or by exposure to unprotected skin on the face, neck and hands.







• Rural families also have the potential for higher exposures to this pesticide. This includes exposure to atrazine as drift from treated fields.

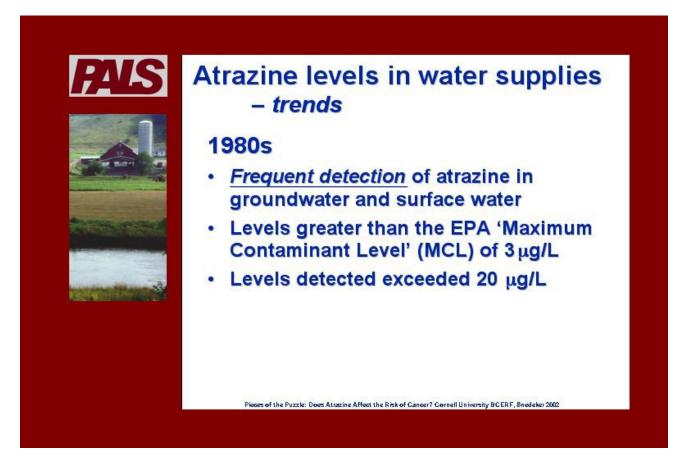
• Tracking atrazine into living and food preparation areas of their homes. Atrazine does not breakdown easily without exposure to sunlight or bacteria.

• Through the handling of soiled work clothes, when removing or while laundering the clothes.

• Or by drinking water from contaminated wells or contaminated community water supplies.

• When drinking contaminated water, exposure may be to atrazine as well as to its breakdown products. Two of the most commonly detected atrazine breakdown products are deethylatrazine (DEA) and deisopropylatrazine (DIA).







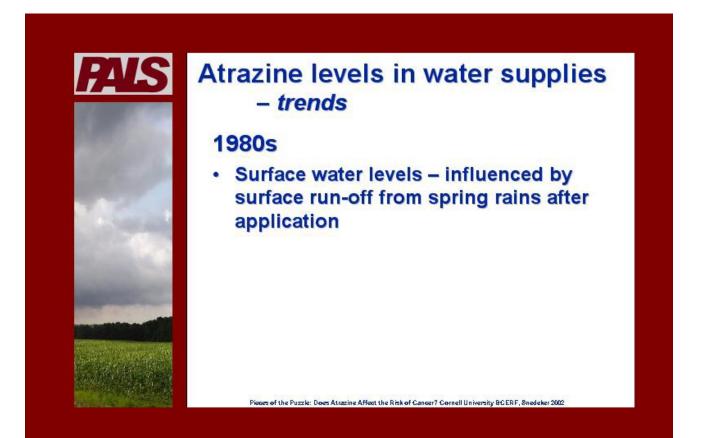
• What have been the trends in the levels of atrazine in water supplies?

• During the 1980s, atrazine was frequently detected in groundwater and especially in surface water in Midwestern, Western, and Eastern states and in Florida.

• Levels of atrazine frequently exceeded the Maximum Contaminant Level (MCL) of 3 micrograms per liter allowed in public water supplies. This level is set by the Environmental Protection Agency. It is the highest level of a contaminant allowed in public drinking water.

• Levels of atrazine detected often exceeded 20 micrograms per liter. The Environmental Protection Agency, in their most recent risk assessment for atrazine, stated that the greatest concern in water supplies for human or ecological health is when concentrations were 10 to 20 micrograms per liter or greater.

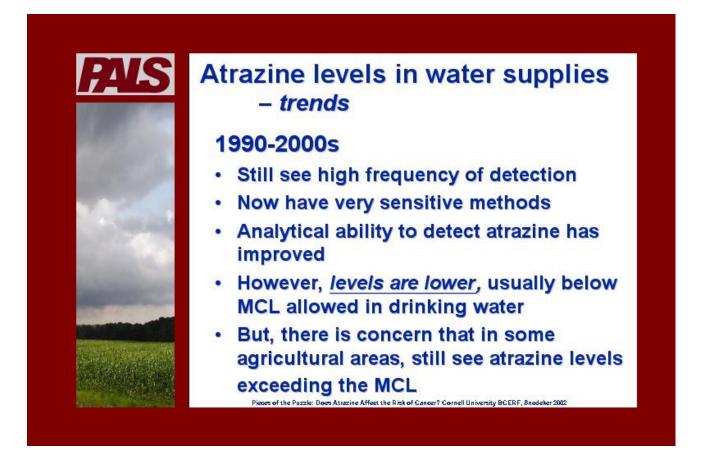






• Levels in surface water are influenced by surface run-off from spring rains after application. This can result in transient levels that "spike" after a heavy rainfall in the late spring and early summer.







• While atrazine remains one of the most frequently detected herbicides in water supplies in the US, the high frequency of detection is partially attributed to an increase in the sensitivity of analytical methods used to detect atrazine.

• The levels detected in the last ten years have usually been lower than the Maximum Contaminant Level (MCL) allowed in drinking water.

• But, there is concern that atrazine levels in water of some areas, especially agricultural areas, is still in the 10-20 microgram per liter range. In a recent study over five percent of the water samples from agricultural areas had atrazine levels that exceeded the 3.0 micrograms per liter, the Maximum Contaminant Level for atrazine in drinking water. Levels as high as 120 micrograms of atrazine per liter were detected in this study.



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• In Southeastern states, especially Florida, atrazine is used for weed control on St. Augustine and Bermuda grass.

• Some situations where adults can come into contact with atrazine include when they mix or apply atrazine to turf, or

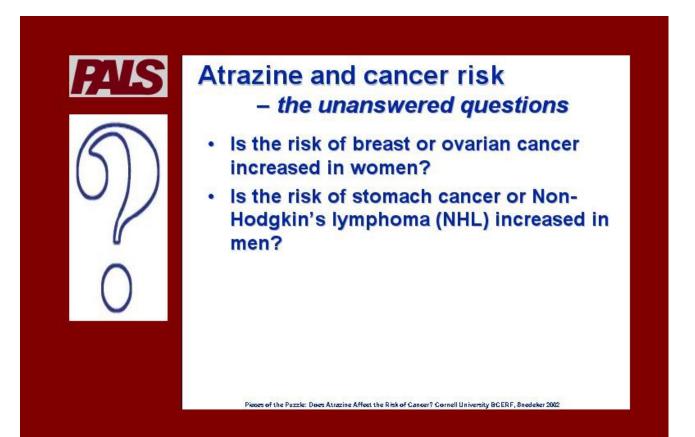
• When they come into contact with recently treated turf from walking, playing on or mowing residential lawns, or using golf courses or parks.

• Tracking atrazine on shoes and clothes into living and food preparation areas of the home is also of concern.

• Of special concern is the exposure of children to atrazine. This includes exposures when playing on treated turf at home, in playgrounds and in parks.

• Children can easily get residues from the treated grass on their hands. Children often lick their fingers or exhibit other "hand to mouth" behavior, including putting toys or other objects into their mouths or even eating dirt.

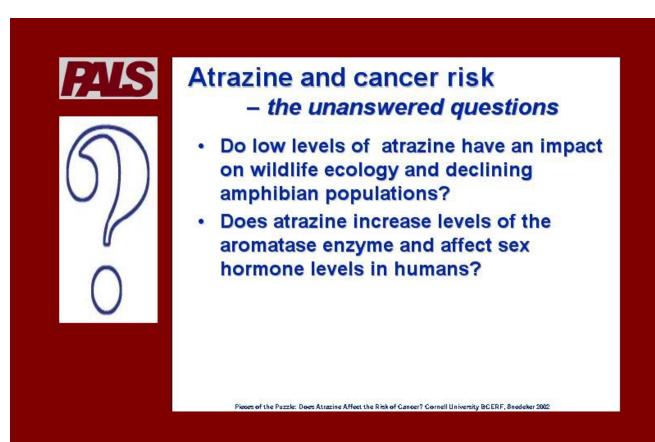






- What are some of our unanswered questions?
- We still lack human studies evaluating the cancer-causing potential of atrazine.
- We still need more information on whether the risk of breast or ovarian cancer is increased in women, or whether the risk of stomach cancer or non-Hodgkin's lymphoma is increased in men exposed to atrazine.







• We need more information on whether low levels of atrazine commonly found in surface and groundwater can have an impact on wildlife ecology and declining amphibian populations.

• Whether atrazine can increase levels of the aromatase enzyme and affect sex hormone levels in humans is still an unanswered question. Whether this has implications for human breast cancer risk is not known at this time.





#### Atrazine and cancer risk - the unanswered questions

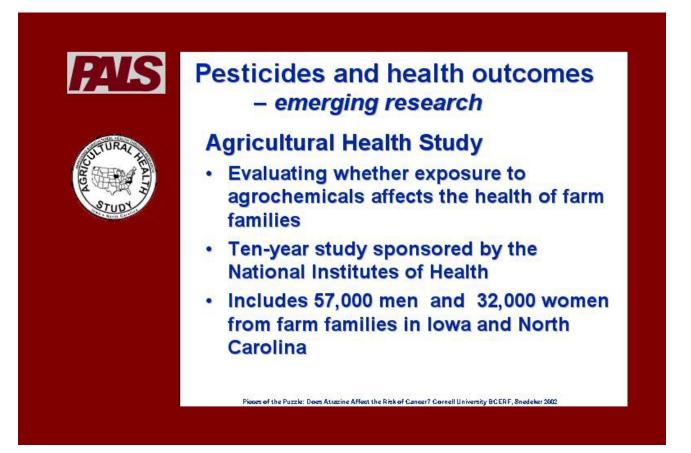
- What are the trends in levels of atrazine and its breakdown products in surface water, rural drinking water wells and rainfall?
- Can atrazine breakdown products affect human health?
- Can exposure to atrazine affect sensitive populations such as children or developing wildlife?

Pieces of the Puzzle: Does Atrazine Affect the Risk of Cancer? Cornell University BCERF, Snedeker 2002



- What are the trends in water levels of atrazine and its breakdown products?
- We need to continue to monitor water supplies for atrazine and its breakdown products in surface water, rural drinking water wells, and rainfall.
- One of the needs that still has not been adequately addressed is whether atrazine breakdown products can affect human health. No Maximum Contaminant Levels in drinking water have been set for atrazine breakdown products.
- There is still concern that seasonably high levels of atrazine in water supplies could affect sensitive populations, including children and developing wildlife.





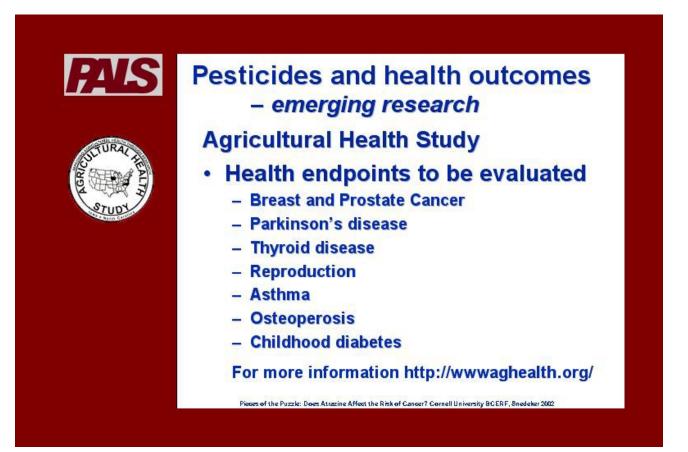


• Where will we be able to find more answers?

• The Agricultural Health study is one of the largest studies ever designed to evaluate whether exposure to agrochemicals, including pesticides, diesel exhaust, etc. affects the health of farm families.

• This long-term ten-year study, sponsored by the National Institutes of Health, has over 57,000 men and 32,000 farm women enrolled from the states of Iowa and North Carolina.



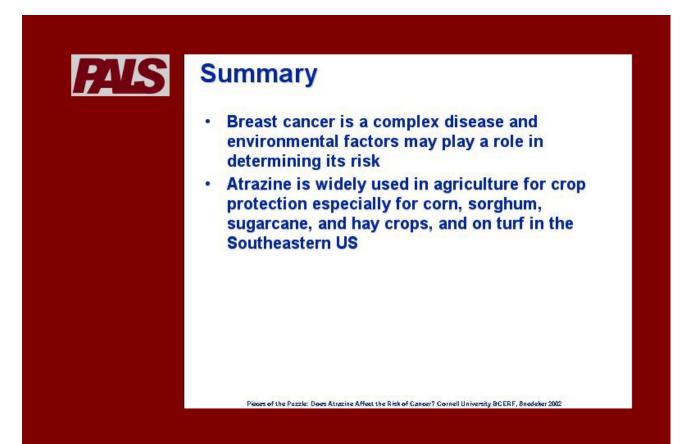




• A variety of health endpoints, including whether exposure to pesticides affect breast and prostate cancer risk, Parkinson's disease, thyroid disease, reproduction, asthma, osteoperosis or childhood diabetes, will be evaluated.

• For more information on this study you can go to http://www.aghealth.org/



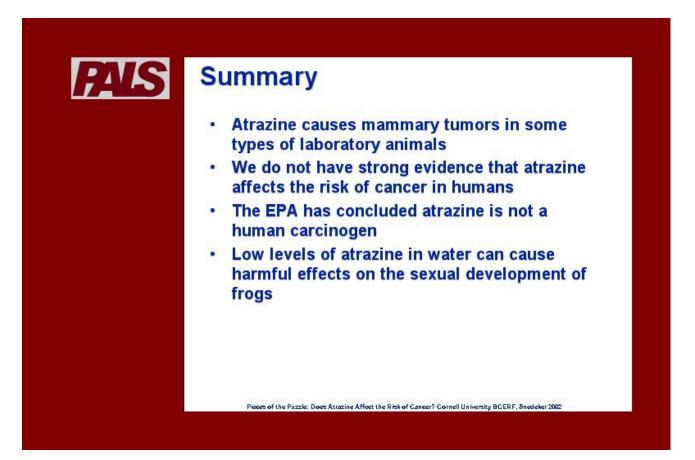


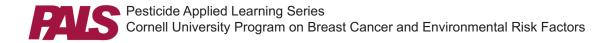


• Breast cancer is a complex disease and environmental factors may play a role in determining its risk.

• Atrazine is widely used in agriculture for crop protection especially for corn, sorghum, sugarcane, and hay crops, and on turf in the Southeastern US.



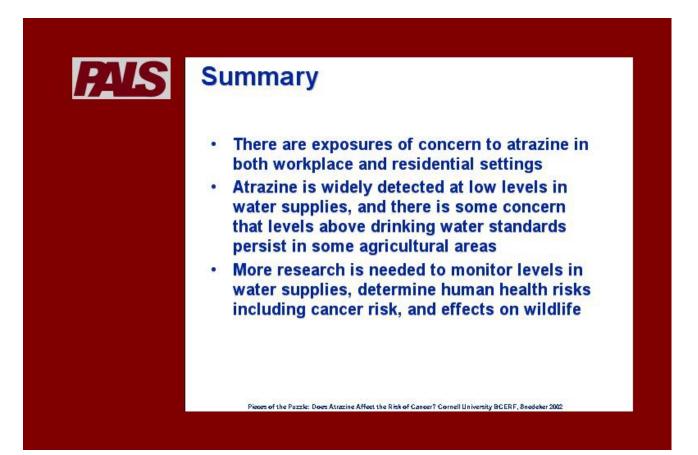


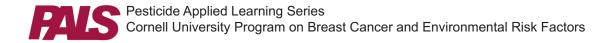


- Atrazine causes mammary tumors in some types of laboratory animals.
- We do not have strong evidence that atrazine affects the risk of cancer in humans.
- The Environmental Protection Agency has concluded that atrazine is not a human carcinogen.

• Low levels of atrazine in water can cause harmful effects on the sexual development of frogs.





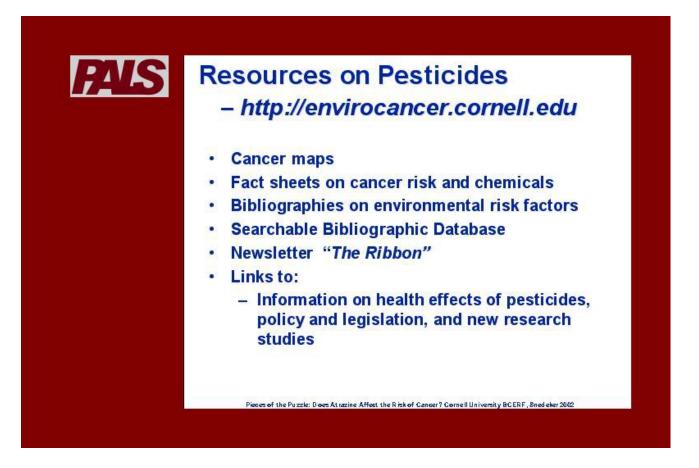


• There are exposures of concern to atrazine in both workplace and residential settings.

• Atrazine is widely detected at low levels in water supplies, and there is some concern that levels above drinking water standards persist in some agricultural areas.

• More research is needed to monitor levels in water supplies, determine human health risks including cancer risk, and effects on wildlife.







• Where can you find other resources on the health risks of pesticides and cancer risk from environmental chemicals?

- Visit our web site at http://envirocancer.cornell.edu
- We provide:
  - Color-coded breast cancer maps
  - Fact sheets on the cancer risk of agrochemicals and other environmental chemicals
  - Detailed bibliographies on environmental risk factors
  - A searchable on-line bibliography
  - An electronic version of our newsletter, "The Ribbon"
  - And extensive links to information on pesticides, policy and legislation,
  - and new research studies



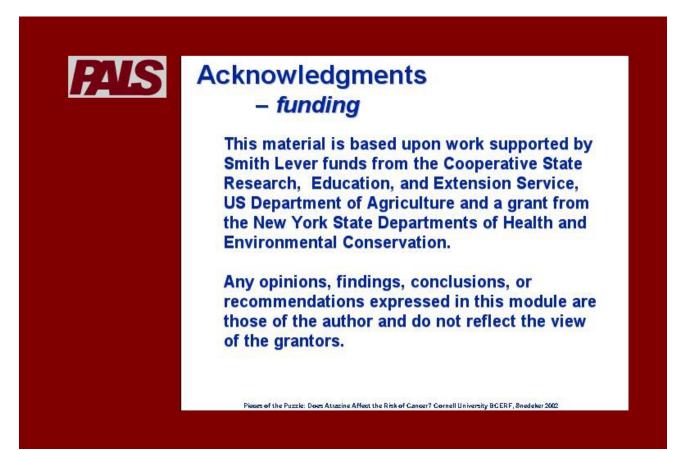




You can find BCERF on the web at http://envirocancer.cornell.edu



PALS Pesticide Applied Learning Series Cornell University Program on Breast Cancer and Environmental Risk Factors

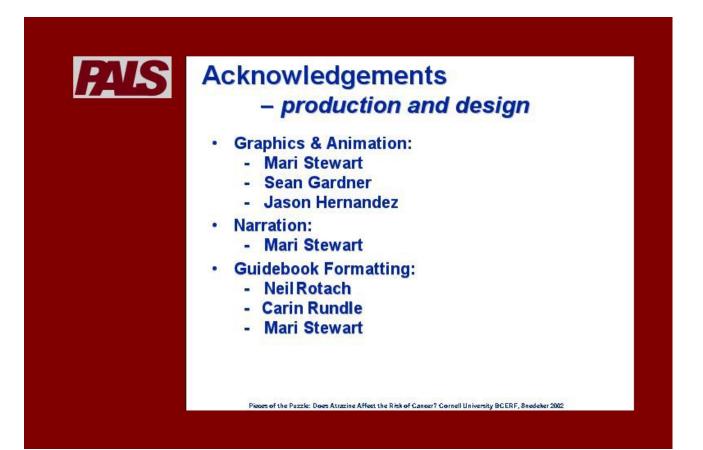


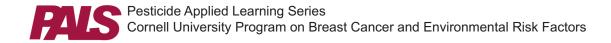


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Any opinions, findings, conclusions, or recommendations expressed in this module are those of the author and do not reflect the view of the grantors.







Graphics & Animation: Mari Stewart Sean Gardner and Jason Hernandez Narration: Mari Stewart Guidebook Formatting: Neil Rotach Carin Rundle and Mari Stewart



### Appendix A: PowerPoint Handout Master

The slide set for this module is accompanied by a set of handouts. Each page of the handout features three slides and an area for notes. You may choose to provide copies of this handout to participants in the presentation. You can also print out another master of the handout whenever needed from the PowerPoint presentation on the CD. Consult your PowerPoint manual for instructions.



Appendix B: Evaluation Tools



### Appendix C: 35 mm Slide / Script Index

slide 01 Titlepage slide 02 Translational cancer research 1 slide 03 Translational cancer research 2 slide 04 Breast cancer statistics slide 05 Puzzle of breast cancer - introduction slide 06 Steps in breast cancer 1 slide 07 Steps in breast cancer 2 slide 08 Steps in breast cancer 3 slide 09 Metastasis/Early detection Steps in breast cancer - animation slide 10 Puzzle - risk factors 1 slide 11 Puzzle - risk factors 2 slide 12 Puzzle - risk factors 3 slide 13 Four major uses of pesticides slide 14 Pesticides and breast cancer risk 1 slide 15 Pesticides and breast cancer risk 2 slide 16 Atrazine slide 17 Atrazine - usage 1 slide 18 Atrazine - usage 2 slide 19 Atrazine - usage 3 slide 20 Atrazine - usage 4 slide 21 Atrazine - usage 5 slide 22 Atrazine - ecological studies 1 slide 23 Atrazine - ecological studies 2 slide 24 Atrazine - cancer risk in lab animals 1 slide 25 Atrazine - cancer risk in lab animals 2 slide 26 Atrazine - cancer risk in women slide 27 Atrazine - cancer risk in men 1 slide 28 Atrazine - cancer risk in men 2 slide 29 EPA's cancer risk assessment 1 slide 30 EPA's cancer risk assessment 2 slide 31 EPA's cancer risk assessment 3 slide 32 EPA's cancer risk assessment 4 slide 33 Atrazine - African clawed frogs slide 34 Atrazine - aromatase theory slide 35 Atrazine - effects on aromatase slide 36 Atrazine & breakdown products - workplace 1 slide 37 Atrazine & breakdown products - workplace 2 slide 38 Atrazine & breakdown products - workplace 3 slide 39 Atrazine & breakdown products - workplace 4



slide 40 Atrazine & breakdown products - families 1 slide 41 Atrazine & breakdown products - families 2 slide 42 Atrazine & breakdown products - families 3 slide 43 Atrazine in water supplies - trends 1 slide 44 Atrazine in water supplies - trends 2 slide 45 Atrazine in water supplies - trends 3 slide 46 Atrazine exposures of concern slide 47 Atrazine and cancer risks - unanswered questions 1 slide 48 Atrazine and cancer risks - unanswered questions 2 slide 49 Atrazine and cancer risks - unanswered questions 3 slide 50 Agricultural Health Study - structure slide 51 Agricultural Health Study - endpoints slide 52 Summary - atrazine risk? 1 slide 53 Summary - atrazine risk? 2 slide 54 Summary - atrazine risk? 3 slide 55 Resources on pesticides slide 56 BCERF on the web slide 57 Acknowledgments - funding slide 58 Acknowledgments - production and design



### Appendix D: Troubleshooting and Known Incompatabilities for Interactive Module

We have done our best to insure that the PALS Interactive Module is a self-contained program and free of technical problems. However, we have discovered in our testing that some problems can occur and we offer you these pathways for solving the problems if you should encounter them.

#### 1. The program won't play.

A. Make sure you have the required software. The only software you will need on your computer in order to view the interactive module is a web browser (like Netscape or Explorer) and the Macromedia Flash Player.

The Interactive Module will play using Netscape or Microsoft Explorer as your browser. There is no preference for which browser to use. Certain versions of browsers work best. PC users should use either Netscape 4.0+ or Explorer 4.0+. For Mac users, PALS will work best when using Explorer 5.1+ or Netscape 7.0+. See Section 6.0 for known incompatibilities with lower versions of browsers.

If you cannot read the files labeled "Start\_Here.html" check to make sure that your computer has either web browser correctly installed. Help to install and configure your choice of web browser can be found at either support.microsoft.com or help.netscape.com.

The free media player can be downloaded to your computer from the Macromedia website. www.macromedia.com/downloads/. The program is installed to your computer by the download. If you need additional help installing or configuring the Macromedia Flash Player visit the Macromedia web site for support. (www.macromedia.com/support/)

### 2. The sound won't play.

A. The presence of sound is an integral part of the PALS Interactive Module. If the sound will not play, check that your computer's sound card is installed correctly and has the appropriate drivers. If you need further assistance with your sound card contact Apple.com.

# 3. The slide does not advance when the next button is pushed, but a new window opens to play the same slide.

A. This problem is another manifestation of the incorrect installation and designation of a sound card. This problem has only been reported on MacIntosh systems running OS 9.0. Check that your computer's sound card is installed correctly and that the appropriate drivers are in place. If you need further assistance with your sound card contact Apple.com.

### 4. My computer has frozen while playing the Interactive Module. (Mac Only)

A. Reboot your computer and make sure that no other applications are running. If the problem persists increase the amount of memory to the network browser you are using to run the module.

#### 5. I can't edit the Interactive Module.

A. The Interactive Module does not allow edits. If you want to increase the flexibility of your presentation or edit the presentation those edits can only be made in the PowerPoint version of PALS. Refer to your PowerPoint manual if you need assistance in editing.

#### 6. Known browser and Operating System (OS) incompatabilities

We have tested the PALS Interactive Module on many combinations of common web browsers and operating systems. However, testing every combination was impossible. Here is a list of the known incompatible OS and brower combinations and the symptoms you may encounter. The best thing to do if you encounter one of these situations is to upgrade your web browsing program.

Browser	<u>Mac/PC</u>	<u>OS</u>	Problem
Netscape 4.7	Mac	9.2.2	next button replays slide
Explorer 5.0	Mac	9.2.2	next button takes you to index





### **Appendix E: Photographic Credits**

Our thanks to the following people and organizations for providing photographs and illustrations for use in this module.

Photographs:

Mari Stewart - Cornell University Alexis A. Wenski-Roberts - Cornell University Water Resources Institute - Cornell University **USDA** Photography Center

Illustrations:

Suzanne Snedeker, Ph.D. - Cornell University Mari Stewart - Cornell University Sean Gardener - Cornell University



