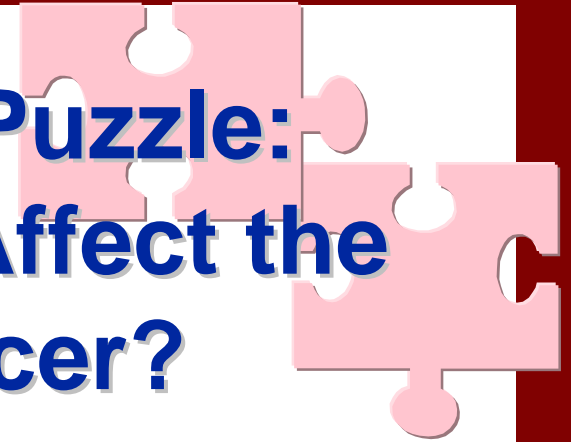




Pieces of the Puzzle: Does Atrazine Affect the Risk of Cancer?



Content developed by
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Cornell University
Program on Breast Cancer and
Environmental Risk Factors (BCERF)



Translational cancer research *– expanding your knowledge*

- **Do environmental chemicals affect the risk of cancer?**
- **1995 Cornell University Program on Breast Cancer and Environmental Risk Factors was founded to address these concerns**
- **Launched a new translational research program**



Translational cancer research **– *expanding your knowledge***

- **Address the relationships between environmental factors and cancer risk**



Translational cancer research **– *expanding your knowledge***

- **Address the relationships between environmental factors and cancer risk**
- **Critically evaluate the current scientific evidence**



Translational cancer research *– expanding your knowledge*

- **Address the relationships between environmental factors and cancer risk**
- **Critically evaluate the current scientific evidence**
- **Translate this science-based data into information individuals can use to expand their knowledge and reduce their risk of cancer**



Translational cancer research *– expanding your knowledge*

- **Address the relationships between environmental factors and cancer risk**
- **Critically evaluate the current scientific evidence**
- **Translate this science-based data into information individuals can use to expand their knowledge and reduce their risk of cancer**
- **Recommend promising avenues of new research**



Breast cancer statistics for the US **– *projections for the year 2002***

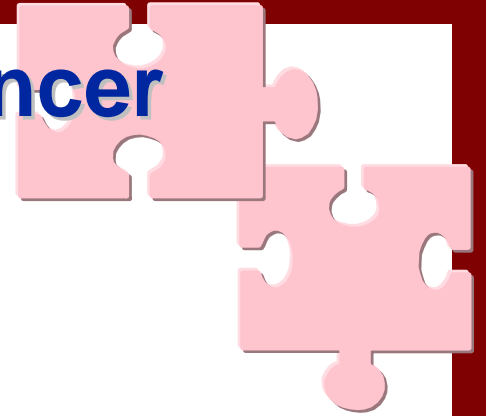
New Cases in Women: 203,500

New Cases in Men: 1,500

*** US estimates for 2002 from the American Cancer Society,
*Cancer Facts & Figures 2002***

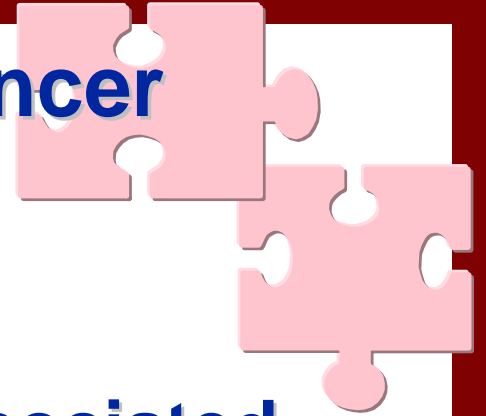


The puzzle of breast cancer



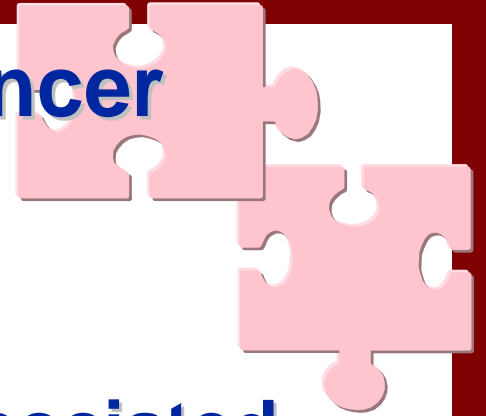
- **Very complex disease**

The puzzle of breast cancer



- **Very complex disease**
- **No one single factor associated with causing the disease**

The puzzle of breast cancer



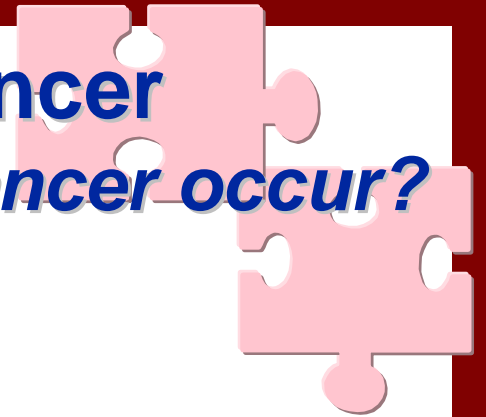
- **Very complex disease**
- **No one single factor associated with causing the disease**
- **Breast cancer develops over a long period of time, usually 10 to 30 years**



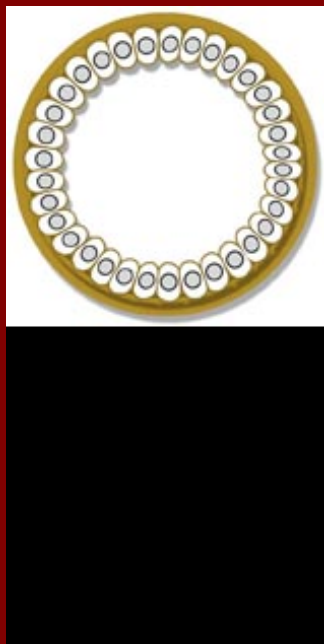
The puzzle of breast cancer

– *how does breast cancer occur?*

- There are many steps



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The puzzle of breast cancer – *how does breast cancer occur?*

- There are many steps
- Occurs as a result of a cell accumulating changes in key genes that control the cell's ability to divide, mature and die

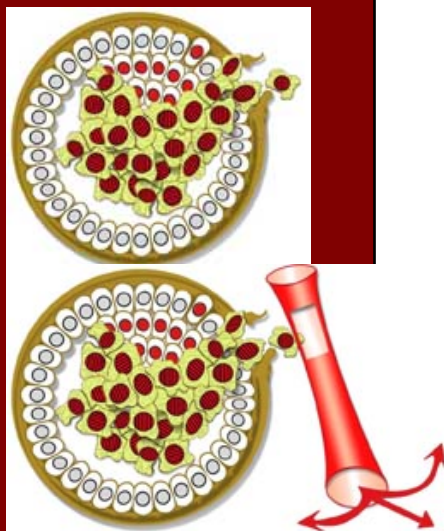


The puzzle of breast cancer **– *how does breast cancer occur?***

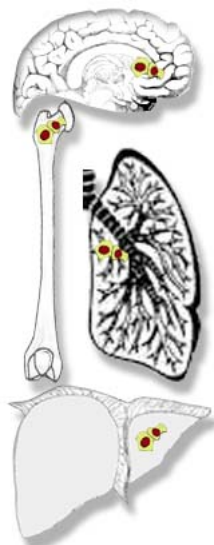
- **There are many steps**
- **Occurs as a result of a cell accumulating changes in key genes that control the cell's ability to divide, mature and die**
- **The result is an abnormal cell that divides out of control and forms a tumor**

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The puzzle of breast cancer *– how does breast cancer occur?*

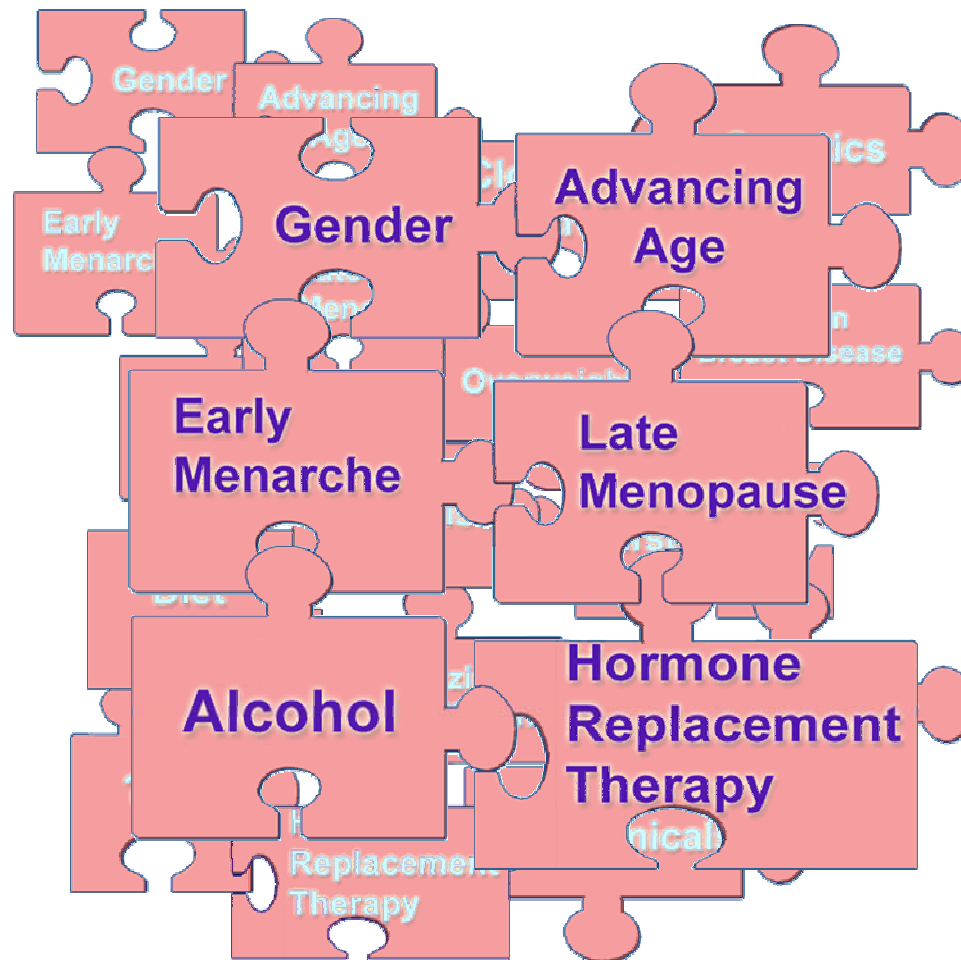


- **As the tumor grows, it may invade surrounding or distant tissues**

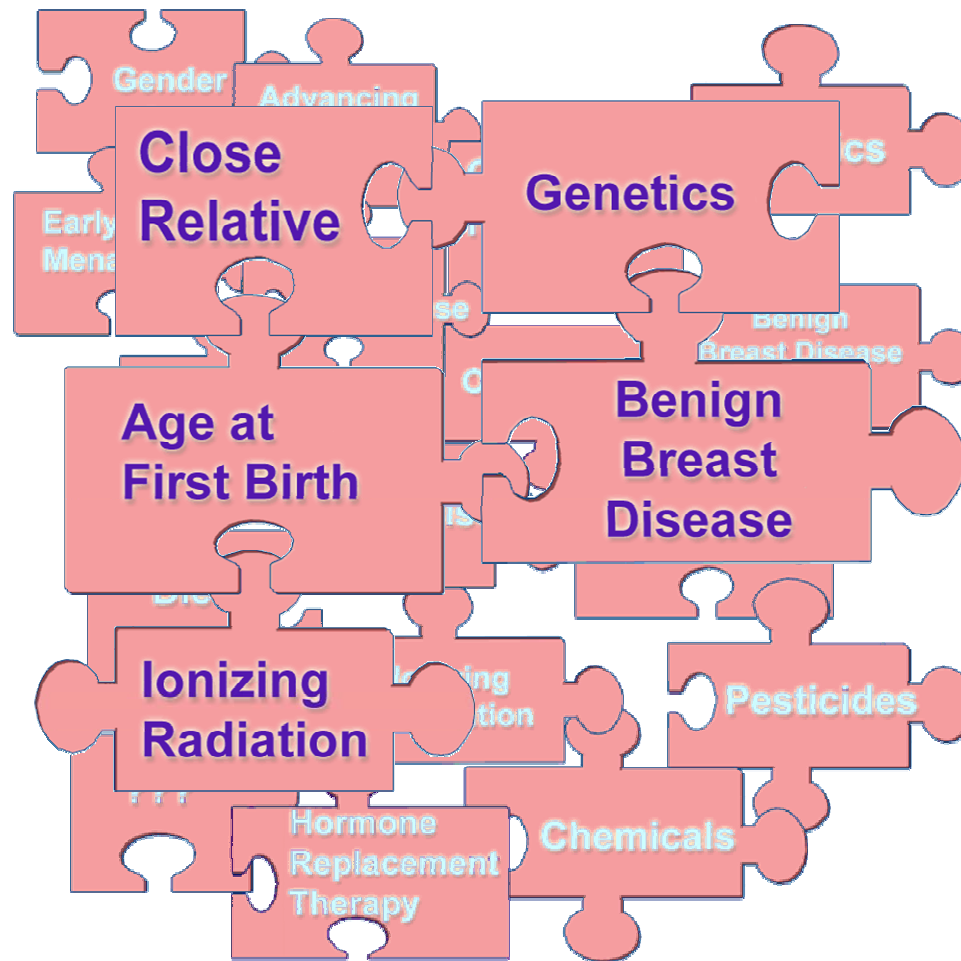


- **Cancer cells can break off from the primary tumor and travel to distant sites invading vital organs**
- **Early detection is important**

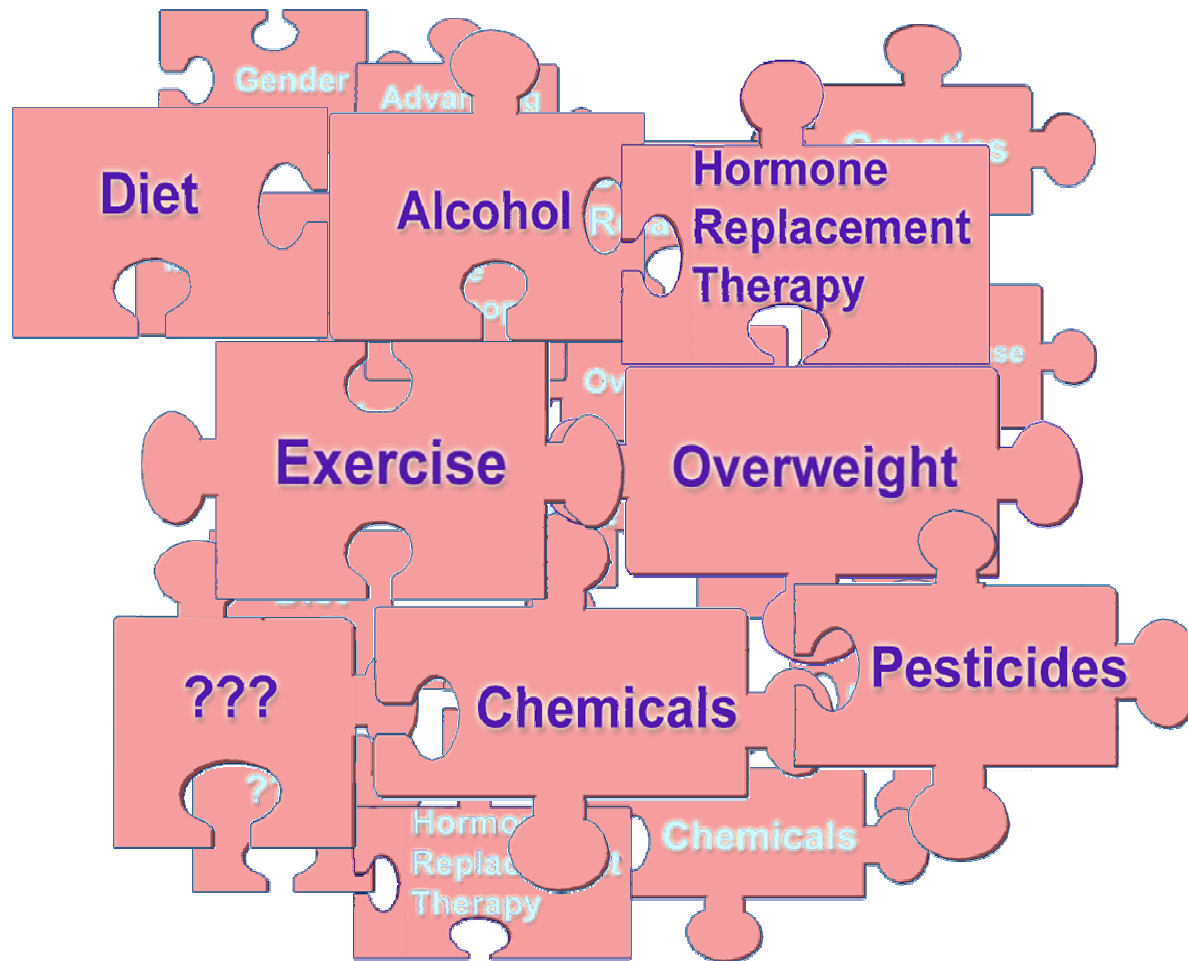
Risks related to breast cancer



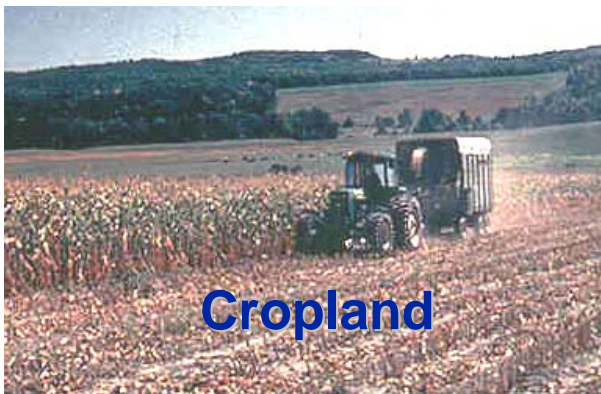
Risks related to breast cancer



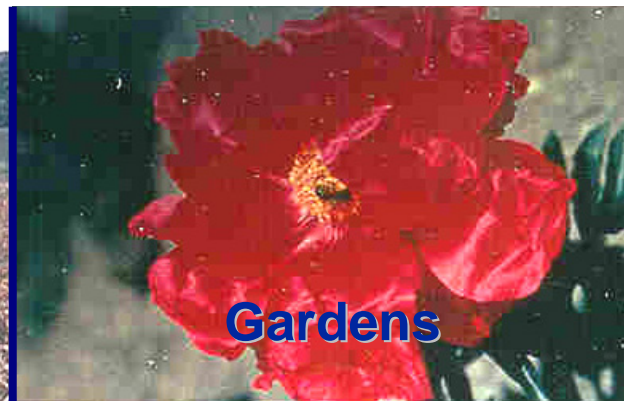
Risks related to breast cancer



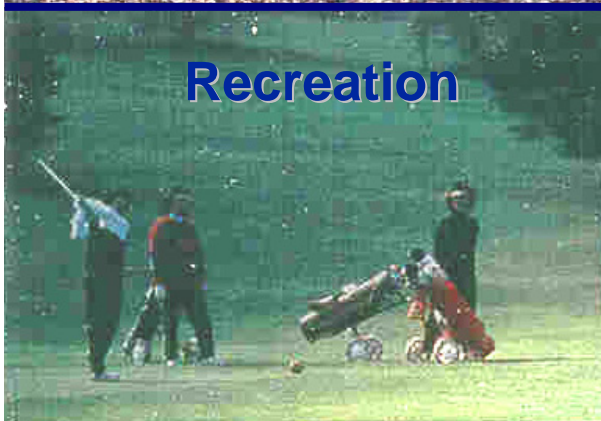
Pesticides *– potential for exposure*



Cropland



Gardens



Recreation



Insect Control



Pesticides and breast cancer risk

– *possible mechanisms*

- **“Complete” carcinogen**



Pesticides and breast cancer risk

– *possible mechanisms*

- **“Complete” carcinogen**
- **Co-carcinogen / tumor promoter**



Pesticides and breast cancer risk

– *possible mechanisms*

- **Endocrine disruptor (Hormonally Active Agent)**
 - **Mimics other hormones**
 - **Affects formation or breakdown of other hormones**
 - **Supports the growth of a hormone-dependent tumor**
 - **EPA is developing tests to identify which pesticides are endocrine disruptors**

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Atrazine

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

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Atrazine

– usage

Most widely used herbicide in the US

- **First registered for use in 1959**
- **Annual crop land usage**
 - **Up to 77.3 million lbs active ingredient***

***Source: Asplein, 1999**

Atrazine

– usage

Agricultural crops

- **Primary crops**
 - **Field and sweet corn, sorghum and sugarcane**





Atrazine

– usage

Agricultural crops

- **Primary crops**
 - **Field and sweet corn, sorghum and sugarcane**
- **Other crops**
 - **Winter wheat, guava and macadamia nuts**
 - **Hay for animal fodder**
 - **Fallow land**
 - **Christmas tree farms**

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Atrazine

– usage

Other weed control uses

- **Turf – golf courses, home lawn care (Southeastern US, St. Augustine and Bermuda grass)**
- **Right-of-ways**

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Atrazine

– usage

Application rates vary

- Field corn, 1 lb to 2.5 lbs per acre**
- Sugarcane, up to 10 lbs per acre**
- Turf*, 2.0 lbs or less per acre**

(* Southeastern US)



Atrazine

– *cancer risk in women*

Breast cancer

Two “ecological” studies from Kentucky

- **Study #1: higher rate of breast cancer in counties with:**
 - Higher use of corn herbicides
 - Higher levels of triazine herbicides in water supplies
 - Study criticized because of crude methods used to estimate atrazine exposures



Atrazine

– *cancer risk in women*

Breast cancer

Two “ecological” studies from Kentucky

- **Study #2, a 5-year follow-up study:**
 - **Breast cancer risk not associated with**
 - Acres of corn planted
 - Atrazine sales
 - Atrazine levels in water supplies
 - **But, study did not measure skin exposures, drift, or levels inside farm homes**

Atrazine

– cancer risk in lab animals

Breast Cancer

- **Increased number or earlier appearance of mammary (breast) tumors in one type of female rat**
- **Not all types of laboratory animals are affected**
- **No mammary tumors seen in other rat strains or in mice fed atrazine**





Atrazine

– *cancer risk in lab animals*

Breast Cancer

- Atrazine is not an estrogen mimic
- May disrupt other hormonal pathways that affect mammary cancer in rats
 - Decreases luteinizing hormone
 - Increases prolactin levels



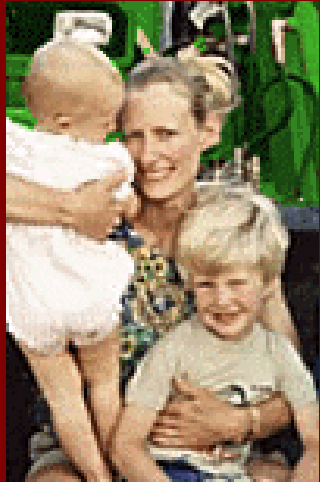
Atrazine

– cancer risk in lab animals

Breast Cancer

- **Atrazine is not an estrogen mimic**
- **May disrupt other hormonal pathways that affect mammary cancer in rats**
 - **Decreases luteinizing hormone**
 - **Increases prolactin levels**
- **These two hormonal pathways may not be as important in human breast cancer**





Atrazine

– *cancer risk in women*

Ovarian cancer

- Study of Italian women
- Exposed to triazine herbicides
 - Atrazine and simazine
- Risk of ovarian cancer higher in exposed women

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Atrazine

– cancer risk in men

Stomach cancer

- **Emerging area of research**
- **Study in Ontario, Canada**
 - **Higher rates of stomach cancer seen in areas with higher levels of atrazine in the drinking water**



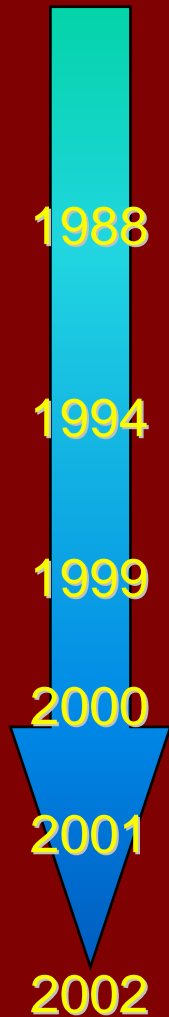
Atrazine

– *cancer risk in men*

Non-Hodgkin's lymphoma (NHL)

- Inconsistent results in studies of Midwestern male farmers
 - Studies in Iowa, Minnesota, and Ontario, Canada did not see a higher risk of NHL
 - Studies in Nebraska and Kansas saw higher risk of NHL
 - When they controlled for other pesticides (e.g. 2,4-D), atrazine-effect not as strong

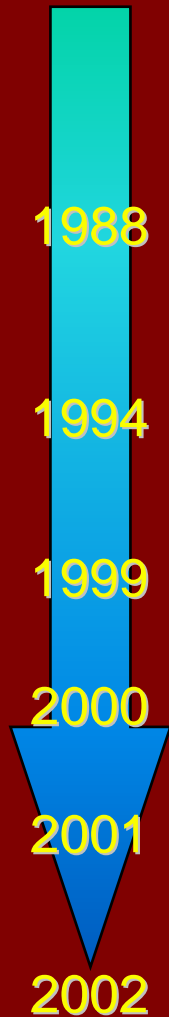




Atrazine

– *EPA's cancer risk assessment*

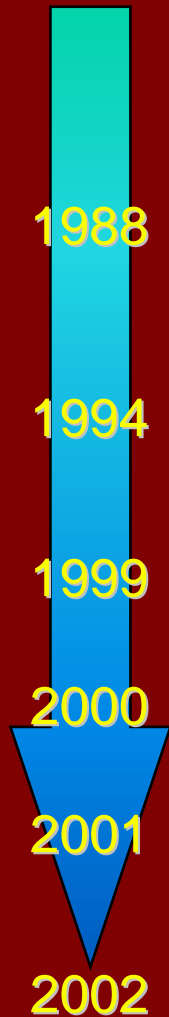
- 1988
 - EPA rated atrazine as a 'possible human carcinogen'
- 1994 to present
 - EPA placed atrazine under "Special Review"
- December 1999
 - EPA's preliminary cancer risk assessment, rated as 'probable human carcinogen'



Atrazine

– *EPA's cancer risk assessment*

- 2000
 - Scientific Advisory Panel (SAP) did not agree with EPA draft report
 - New research on relevancy of rat data available
 - Atrazine caused reproductive changes in one strain of rats that influenced levels of hormones important in rat mammary (breast) cancer

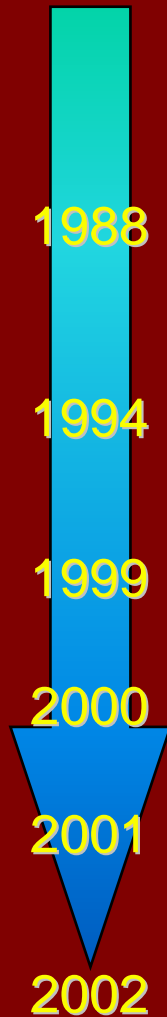


Atrazine

– *EPA's cancer risk assessment*

- 2000 (continued)
 - These reproductive changes seen in atrazine-treated rats probably would not occur in women
 - SAP concluded that it is unlikely that atrazine would affect human breast cancer risk

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Atrazine

– *EPA’s cancer risk assessment*

- **June 2000**
 - **Based on SAP recommendations the EPA changed atrazine’s cancer classification to:
“not likely to be a carcinogen in humans”**
- **EPA’s reregistration decision expected in 2003**

Atrazine

– effects on wildlife



- **Sexual development in frogs**
- **Male tadpoles exposed to atrazine**
 - **All had abnormal sexual development**
 - **Up to 20% had both testes and ovaries**
 - **Males were more like females**

Atrazine

– effects on wildlife



- **Sexual development in frogs**
- **Male tadpoles exposed to atrazine**
 - **All had abnormal sexual development**
 - **Up to 20% had both testes and ovaries**
 - **Males were more like females**
 - **Occurred at very low levels of atrazine**

Atrazine

– effects on wildlife



- **Sexual development in frogs**
- **Male tadpoles exposed to atrazine**
 - **All had abnormal sexual development**
 - **Up to 20% had both testes and ovaries**
 - **Males were more like females**
 - **Occurred at very low levels of atrazine**
 - **Adult frogs had low levels of the male hormone testosterone**

Atrazine

– effects on wildlife



- **Sexual development in frogs**
 - **Atrazine may increase levels of an enzyme called aromatase**
 - **This enzyme converts testosterone to estrogen**
 - **Would explain why blood levels of testosterone in atrazine-treated male frogs are so low**
 - **More research is needed to confirm this “aromatase” hypothesis**

Atrazine

– effects on aromatase



- **Are levels of the aromatase enzyme or sex hormones changed in humans exposed to atrazine?**
 - **Not known**

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Atrazine & its breakdown products **– *exposures of concern***

- **Workplace exposures:**
 - Handling, mixing, loading or applying to row crops or right-of-ways

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Atrazine & its breakdown products **– *exposures of concern***

- **Workplace exposures:**
 - Handling, mixing, loading or applying to row crops or right-of-ways
 - Post-application field work (sugarcane)



Atrazine & its breakdown products

– *exposures of concern*



- **Workplace exposures:**
 - Handling, mixing, loading or applying to row crops or right-of-ways
 - Post-application field work (sugarcane)
 - Aerial application or hand spraying



Atrazine & its breakdown products – *exposures of concern*

- **Workplace exposures:**
 - Turf application
 - Use of “belly grinders”
 - Proper protective clothing is needed when applying atrazine to treat turf in playgrounds, golf courses and residential lawns.





Atrazine & its breakdown products

– *exposures of concern*

- **Rural families**
 - **Drift from treated fields**





Atrazine & its breakdown products

– *exposures of concern*

- **Rural families**
 - Drift from treated fields
 - Tracking into homes





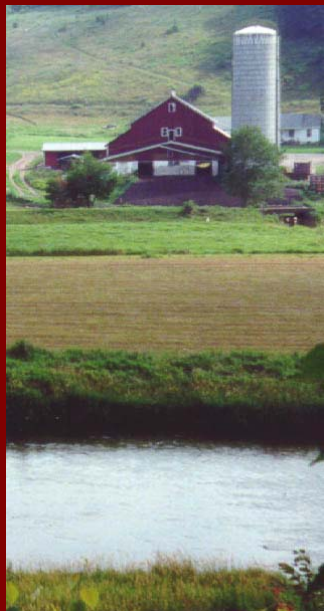
Atrazine & its breakdown products

– *exposures of concern*

- **Rural families**
 - Drift from treated fields
 - Tracking into living & food preparation areas
 - Handling soiled work clothes



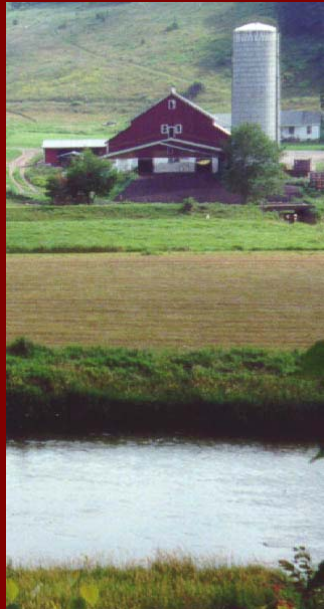
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Atrazine & its breakdown products **– exposures of concern**

- **Rural families**
 - **Drift from treated fields**
 - **Tracking into living & food preparation areas**
 - **Handling soiled work clothes**
 - **Drinking water from contaminated wells or contaminated community water supplies**

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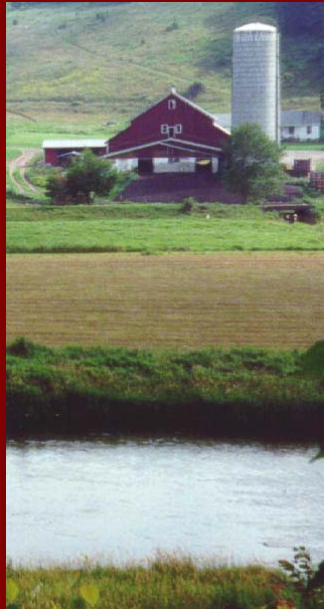


Atrazine levels in water supplies – trends

1980s

- **Frequent detection of atrazine in groundwater and surface water**

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Atrazine levels in water supplies – trends

1980s

- **Frequent detection of atrazine in groundwater and surface water**
- **Levels greater than the EPA 'Maximum Contaminant Level' (MCL) of 3 $\mu\text{g}/\text{L}$**
- **Levels detected exceeded 20 $\mu\text{g}/\text{L}$**



Atrazine levels in water supplies – trends

1980s

- **Surface water levels – influenced by surface run-off from spring rains after application**



Atrazine levels in water supplies – trends

1990-2000s

- **Still see high frequency of detection**
- **Now have very sensitive methods**
- **Analytical ability to detect atrazine has improved**
- **However, levels are lower, usually below MCL allowed in drinking water**
- **But, there is concern that in some agricultural areas, still see atrazine levels exceeding the MCL**



Atrazine & its breakdown products

– *exposures of concern*



- **Residential - Recreational Exposure**
 - **Adults**
 - Mixing and applying atrazine to turf
 - Contact with treated turf; residential lawns, mowing, golf courses and parks
 - Tracking into living & food preparation areas
 - **Children**
 - Playing on treated turf at home, playgrounds and parks
 - Hand to mouth behavior, and dirt eating

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Atrazine and cancer risk

– *the unanswered questions*

- **Is the risk of breast or ovarian cancer increased in women?**
- **Is the risk of stomach cancer or Non-Hodgkin's lymphoma (NHL) increased in men?**

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Atrazine and cancer risk **– *the unanswered questions***

- **Do low levels of atrazine have an impact on wildlife ecology and declining amphibian populations?**
- **Does atrazine increase levels of the aromatase enzyme and affect sex hormone levels in humans?**



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?**



Pesticides and health outcomes

– *emerging research*

Agricultural Health Study

- **Evaluating whether exposure to agrochemicals affects the health of farm families**
- **Ten-year study sponsored by the National Institutes of Health**
- **Includes 57,000 men and 32,000 women from farm families in Iowa and North Carolina**



Pesticides and health outcomes

– *emerging research*

Agricultural Health Study

- **Health endpoints to be evaluated**
 - **Breast and Prostate Cancer**
 - **Parkinson's disease**
 - **Thyroid disease**
 - **Reproduction**
 - **Asthma**
 - **Osteoperosis**
 - **Childhood diabetes**

For more information <http://www.aghealth.org/>



Summary

- **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**



Summary

- **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 EPA has concluded atrazine is not a human carcinogen**
- **Low levels of atrazine in water can cause harmful effects on the sexual development of frogs**



Summary

- **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**



Resources on Pesticides

– <http://envirocancer.cornell.edu>

- Cancer maps
- Fact sheets on cancer risk and chemicals
- Bibliographies on environmental risk factors
- Searchable Bibliographic Database
- Newsletter “*The Ribbon*”
- Links to:
 - Information on health effects of pesticides, policy and legislation, and new research studies



BCERF on the Web

<http://envirocancer.cornell.edu>

Cornell University
**Program on Breast Cancer and
Environmental Risk Factors
in New York State
(BCERF)**



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