Pesticides and Prostate Cancer – what the literature says

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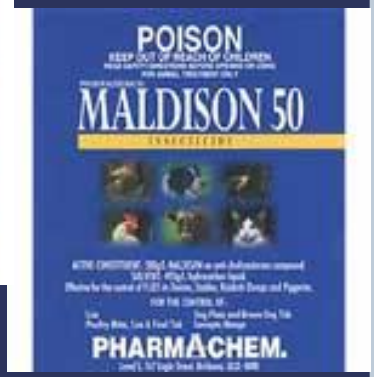
Presentation aims

- Background to literature and current research
- Cause and effect
- Prostate physiology
- Implication for farmers and general population

Faster, stronger, more effective and cheaper



Literature review

- Extensive literature review
- PubMed, and CINAHL data bases using (Prostate, pesticides and cancer)
- 220 articles
- Biomedical, health and epidemiological journals
- 20 articles drawn (10% sample)
- Referenced from 2000 onwards, extended to 20 years for studies of meta analyses

Literature scope

- Agriculture Health Study (AHS) – 57,000 applicators b/w 1993-1997. (Alavanja et el 1999)
- Boner et al 2009
- Lynch et al 2009

- Fleming et al 1999
- Parent et al 2009
- McFarlane et al 2009 (Australian)
- ***Van Maele-Fabry et al 2003 and Van Maele-Fabry and Willems 2007 meta analysis (1995-2001 and 1966-2003)***

Background

PCFA 2009 www.prostate.org.au

- Prostate Cancer in Australian Men
- In 2010 approx 22,000 men with be diagnosed with prostate cancer
- 3300 deaths per annum
- 1 in 9 lifetime risk
- For every 100 men in metro cities 121men will be die in rural areas
- 23% higher incidence in firefighters
- 53% higher incidence in Vietnam veterans

Prostate cancer

- Genetic links proven
- Higher incidence in African American populations (60% increased chance)
- Waist measure linkage Cancer Council 2006
- Where you live and Vitamin D/Sunlight exposure (PCFA 2009)
- For those diagnosed prostate cancer, high body mass, smoking, and low vegetable intake increase risk

Cause and effect

- Donham and Thelin (2006) highlight

  "pesticides are products that kill living things that are economically, socially or healthfully detrimental to us"

- There are currently some 16,000 in the US and over 8000 in Australia APVMA 2009

Physiological impacts

- Protein Tyrosine Kinase Synthesis (often in pyrethoids)
- Estrogenic Inhibition Factors (decreases cellular immunity, primarily in OP's)
- Alteration to Steroidal Metabolism (primarily chlorinated hydrocarbon insecticides, eg DDT, 2, 4-D)

1.Blair, 2005. 2.Settimi, 2001. 3.Alavanja, 2005. 4. Keller-Byrne, 1997. 5. Settimii, 2001.

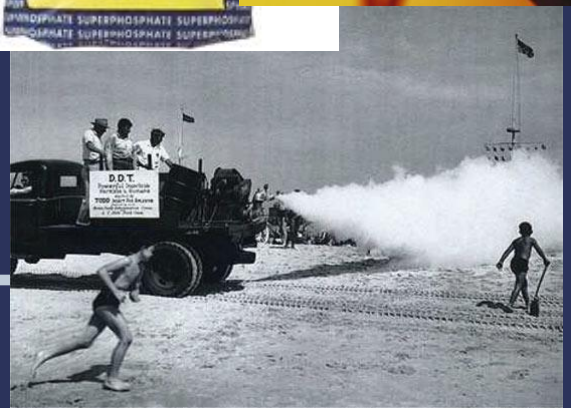
Agent	Action	Example	Physiological action
Organophosphates .[1]	Interfere with transmission of nerve impulses	Parathion Diazinon, Atrazine, endosulphan, carbendazim	Inhibit serine esterase which in turn inhibits the immune system to cancerous cells
Chlorinated hydrocarbon insecticides.[2]	Endocrine disrupters block hormonal activity	Chlorophenothaine (DDT) Aldrin telodrin etc 2, 4-D	Thought to be related to genitourinary tumour development . Accumulates in fat cells
Pyrethroids, pyrethrins[5]	Modifies sodium channels, of insects	Control of insects, long acting fly treatments, baygon, fipronil (fleas), frontline, revolution	Activates protein tyrosine kinase which is thought to promote prostate cancer cell development (Pyrethroids)
Methyl Bromide.[3]	Fumigant	Used to kill weeds, rodents and insects as a fumigant	Dose response relationship shown, alkylating agent. Proven carcinogen promoter
Dioxins.[4]	Found within grain dust	Dioxins accumulate in fat stores therefore having a persistent effect , agent orange , paper production	Estrogen inhibitor. Estrogen is known to be a prostate protective hormone. Inhibition may promote prostate cancer development

Evidence

Study	Type of study	Results	Conclusion
Parent, et al (2009) 1980's study in Montreal of 4000 cancer sufferers	Population based control study of men exposed to 10 agricultural chemicals including **diesel, gasoline, hydrocarbons and pesticides**	Based on a model adjusting for age, ethnicity and education a 2 fold increased risk was found for prostate cancer. OR 2.3 and CI 1.1-5.1 compared to unexposed farmers	Noteworthy results yet large scope of variants and trends appeared with wide range of chemicals.
Bonner, et al A (2009) study assessing terbofos, and cancer	Review of the Agricultural Health Study in the USA prospective cohort study of 57,310 pesticide applicators	Overall cancer incidence was higher in terbofos applicators and highest incidence for prostate cancer noted	Suggestive association of cancer of the prostate and terbofos use. Study highlights risk of interpretation of risk associated with terbofos
Lynch et al. (2009) using AHS data	Use of the AHS to assess the association between butylate and cancer risk	Lifetime days exposure and intensity weight lifetime exposure was used and compared to non exposed and minimal users	Prostate cancer risk was significantly elevated among applicators with the highest lifetime days exposure
Fleming et al (1999)	Retrospective cohort study of licensed pesticide applicators in Florida total number (33658)	Prostate cancer mortality was noted to be significantly higher in the cohort with CI 1.83 to 3.04 or 95%	Cancer of the prostate was significantly elevated in pesticide applicators.

Parent et al (2009)

- 4000 farmers
- Looked at 10 agricultural chemicals
- Included diesel, gasoline, hydrocarbons and pesticides
- 2 fold increase of prostate ca
- OR 1.1-5.1 compared to non farmers
- Metal working , solvents, hydraulic fluids, liquid fuel, emissions
- Cadmium exposure – rodent Prostate cancer development
- Also some association b/w heavy diesel engine emissions (OR 5.7 CI 1.2-26.5)



Bonner et al 2009

- Using data from the AHS study
- Study of terbufos and cancer incidence
- Systemic insecticide
- Applicators v's non applicators
- Suggestive linkage of NHL, Prostate, lung and leukeamia
- More experimental evidence required for terbufos as a carcinogen required

Fleming et al 1999

- Retrospective study 33,000 applicators in Florida USA
- Primarily organochlorines
- Private to commercial use comparison
- Prostate cancer rates Standard Mortality Rate 2.38 (CI 1.83-3.04)
- Interesting fact of male alligators in the Florida region (reproductively incompetent)

Alavanja et al

- 55,000 male pesticide applicators
- Iowa and North Carolina (AHS study)
- Stratified exposure to chemicals and linked family history
- Use of chlorinated pesticides DDT, 2,4,5-T and methyl bromide
- Significant risk in males >50
- 45 pesticide exposure study

Meta Analyses

Study	Type of study	Results	Conclusion
Van Maele-Fabry and Willems (2007)	Meta analysis 1966-2003	Higher estimated of RR and confidence interval than previous meta analyses	Provides additional evidence for a possible relationship between exposure and prostate cancer
Van Maele-Fabry et al 2003	Meta analysis of studies undertaken between 1995 -2001	22 epidemiological studies, stratified analysis carried out significant increase in rate ratio was observed for occupational exposure	Although not identifying sole use of pesticides and prostate cancer incidence this study supports 3 previous meta-analyses for exposure as a possible risk factor

Where is the real risk?

t Orange on foliage in Vietnam
(Archive Photos)

Research Implications

- Chemical development speed
- Regulatory control – APVMA
- PPE- little evidence of use and management (<50% use)
- Research rigor-need more time exposure studies
- Now versus the future (RISK or Rationale)

Re the evidence

- Support of a clinical linkage
- Exposure, dose, multiple agents, not in isolation
- Chemical linkage to disease development
- Occupational questions need to be raised
- Need of rigor in research
- PPE mandate for all users
- This is more than just a farmer issue

Quick and easy!