Glyphosate use at Murramarang Community Gardens: a quick review of the scientific literature on health risks from glyphosate use.

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1. Introduction

Glyphosate is the active ingredient in broad spectrum herbicides used to control unwanted plant matter. Use has spread rapidly in the last few decades and it is now one of the most commonly used agrochemicals worldwide. Glyphosate deters plant growth by inhibiting an aromatic amino acid pathway that produces certain proteins in plants and its disruption stops production of these proteins essential to plant growth. The amino acid pathway is apparently present only in plants, microorganisms and fungi; not animals. In spite of this, evidence is emerging of detrimental impacts of formulations of glyphosate used as herbicides on insects, aquatic environments, amphibians and possibly mammals.

Several countries have banned the use of glyphosate and GBH products including Sri Lanka (the first country to issue a nation-wide ban), France, Belgium, El Salvador & Bermuda. A number of other countries are moving towards phasing it out to some extent. In other countries states, cities, counties or sales outlets have also chosen to ban or restrict its use (Baum Hedund Aristei Goldman PC 2018). In Australia, this source reports:

> Numerous municipalities and school districts throughout the country are currently testing alternative herbicides in an effort to curtail or eliminate glyphosate use. Many use steam technology for weed control on streets and in other public areas.

This review seeks to present findings from some key reports and studies to assist us in decision-making about the use, hazards and risks of glyphosate-based herbicides (GBH). After reviewing the risks and hazards associated with glyphosate, the MCG committee may decide to investigate alternative weed management options.

Assessing the literature

There are several differences to consider in the complexity of arguments used in the debate and it's important to understand the scope of each investigation. The scope gives us the 'limitations' of each report. Also, what are the issues for us at MCG? There appear to be two main considerations: glyphosate levels in food produced and eaten, and exposure to glyphosate of those using it at the gardens.

Under what circumstances is it toxic, environmentally problematic or a potential human carcinogen?

- Is glyphosate carcinogenic to humans i) who handle or apply it or ii) through the food chain (ie who eat it)?
- Is it carcinogenic at any dose, or doses used when applying it or in levels commonly present in food eaten?
- Is it carcinogenic when ingested or inhaled?
- Does it bioaccumulate in animal tissue including human tissue?
- What evidence is there that it causes cancers in humans?
- How does glyphosate toxicity compare with other chemical weed control methods on the market?
- What are the risks or hazards of glyphosate alone, and how does it change when combined with other chemicals such as surfactants in products such as Zero or Roundup?

- Does it have an effect on bees?

2. WHO reports

IARC report 2015

In 2015 the International Agency for Research on Cancer of WHO based in Lyon, France classified glyphosate as "probably carcinogenic to humans". This was based on "limited evidence" for the carcinogenicity of glyphosate in humans and "sufficient" evidence in experimental animals. IARC also took into account "strong evidence" that "glyphosate or glyphosate-based formulations" can be genotoxic, which means it can damage genes. This damage *may* then lead to cancer. This study used only published experimental findings, and their conclusion aimed to identify any *potential cancer hazard* glyphosate may pose to humans at *some level of exposure* (Guyton et al 2015).

From the IARC report the following excerpts are perhaps most relevant:
In mice studies:

- Glyphosate induced a positive trend in the incidence of a rare tumour, renal tubule carcinoma.
- A second study reported a positive trend for haemangiosarcoma in male mice.[15]
- Glyphosate increased pancreatic islet-cell adenoma in male rats in two studies.
- A glyphosate formulation promoted skin tumours in an initiation-promotion study in mice.

Studies of humans in the agriculture industry:

- There was limited evidence in humans for the carcinogenicity of glyphosate.
- Case-control studies of occupational exposure in the USA,[14] Canada,[6] and Sweden[7] reported increased risks for non-Hodgkin lymphoma that persisted after adjustment for other pesticides. The AHS cohort did not show a significantly increased risk of non-Hodgkin lymphoma.
- Glyphosate has been detected in the blood and urine of agricultural workers, indicating absorption.
- Soil microbes degrade glyphosate to aminomethylphosphoric acid (AMPA). Blood AMPA detection after poisonings suggests intestinal microbial metabolism in humans.
- Glyphosate and glyphosate formulations induced DNA and chromosomal damage in mammals, and in human and animal cells in vitro.
- One study reported increases in blood markers of chromosomal damage (micronuclei) in residents of several communities after spraying of glyphosate formulations.

From these findings the Working Group classified glyphosate as "probably carcinogenic to humans" (Group 2A).

WHO & UN Pesticides Residues Experts report 2016

In 2016, a group of pesticides residues experts at the WHO and UN concluded that glyphosate is "unlikely to pose a carcinogenic risk to humans" through their diets. These researchers noted that there's conflicting evidence on whether glyphosate leads to non-Hodgkin lymphoma, a cancer of the lymph nodes, in workers who handled the herbicide. They also pointed out that the "overall weight of evidence indicates" glyphosate isn't genotoxic in mammals at doses and routes "relevant to human dietary exposure." These scientists used unpublished data in addition to the published findings (and there were different findings about cancer links in these data sets); and they assessed the *actual cancer risk* the herbicide poses to consumers at a *specific level of exposure*, namely *the level commonly found in foods*.

In summary, the IARC aimed to identify any potential cancer hazard to humans at some level of exposure; the pesticide residue experts assessed the actual cancer risk to consumers at specific level of exposure, namely the level commonly found in food. This means that glyphosate may have different effects at different rates, via different routes of exposure, depending on how much a person is exposed to. Similar really to fluoride and many other chemicals, including those we regularly consume.

Other agencies have conducted their own reviews of the risk of glyphosate. The German Federal Institute for Occupational Safety and Health (BAuA) proposed to add a classification for specific organ toxicity after repeated exposure (Yasenov 2016). The European Chemicals Agency who classify and label hazardous chemicals investigated Germany's proposal and concluded in March 2017 that 'the available scientific evidence did not meet the criteria to classify glyphosate as a carcinogen, as a mutagen, or as toxic for reproduction.' (ECHA/PR/17/6). The ECA continues to classify glyphosate as causing serious, irreversible eye damage (presumably if splashed into the eyes) and toxic to aquatic life, with long lasting effects (ECHA 2017). The role of the RAC (ECHA Committee for Risk Assessment) is to harmonise labelling of any products that contain a particular chemical.

> The classification is based solely on the hazardous properties of the substance. It does not take into account risk or exposure because the assessment does not evaluate the quantities used, nor the way in which it is used. Such aspects are considered later on, as part of further risk management measures when assessing if a certain use can be authorised. For example, the use of glyphosate as a pesticide is covered by the Plant Protection Products Regulation, which is managed by the European Food Safety Authority (EFSA). (Yasenov 2016)

As in all reports we review to understand the risks and hazards of a chemical, we need to know which aspects of the chemical are considered in the study, so we can understand how to interpret and apply the results. The limitations of the EFSA review may be that it doesn't look at how the impact of glyphosate on human health may be altered when it is combined with other chemicals, such as in herbicide products.

3. Risks from consuming food contaminated with glyphosate

The most conservative acceptable level of glyphosate in food eaten set by the European Food Safety Authority is 0.5 mg per kg body weight, per day. i.e. a 60 kg person can 'safely' consume 30 mg in food or water consumed per day without a risk of developing cancer. WHO advise food and water are the main routes of exposure for the general population (not those applying the chemical). The main source is food given the way the chemical interacts with solids and liquids.

Glyphosate is the active ingredient in many herbicide formulations and most manufacturers keep their 'recipes' to themselves making independent research into health and environmental effects difficult. One chemical in particular used in formulations, POEA (polyoxyethylene tallow amine) as a surfactant and also present in degreasers and cleaning products has been tested and found harmful to aquatic wildlife. The US EPA lists POEA as an 'inert' ingredient in GBHs. While low levels of glyphosate in food have been found not to cause cancer, low levels of products such as Roundup have not been tested. Monsanto, manufacturer of Roundup has admitted this omission. They have not tested done the necessary testing on Roundup to make the statement that Roundup does not cause cancer (Schipani 2017).

4. Risks to those using glyphosate

The long-term Agriculture Health Study (AHS) and findings

The National Institutes of Health, USA are conducting a long-term study (enrolment into the study began in 1993-1997) looking at cancer prevalence and other health issues in over 89,000 farmers and their spouses in North Carolina and Iowa (Schipani, 2017) & (Andreotti et al, 2018) Some key findings of the long-term Agriculture Health Study (AHS 2018) include:

- Farmers have lower rates of many disease compared to the rest of the population, perhaps because they are less likely to smoke and are more physically active
- Farmers have a higher risk for developing some cancers, including prostate cancer
- Gloves matter. Use of chemically resistant gloves can reduce pesticide exposure 50 to 80%
- Rotenone and paraquat are linked to increased use of developing Parkinson's disease
- Allergic asthma in men and women may be associated with use of some organophosphate insecticides
- Accidental high pesticide exposure events may affect health later in life
- Diabetes and thyroid disease risk may increase for users of some organochlorine chemicals

Glyphosate and cancer

The AHS study of glyphosate use and cancer incidence by 54 251 licensed pesticide applicators from North Carolina and Iowa, USA, since published (Andreotti et al, 2018) found 82.8% (44 932) used glyphosate, including 79.3% of all cancer cases (5779 total cases). The results indicated glyphosate was not statistically significantly associated with cancer at any site. Among workers 'in the highest exposure quartile, there was an increased risk of acute myeloid leukemia (AML) compared with never users… though this association was not statistically significant.'

The report conclusions state:

> In this large, prospective cohort study, no association was apparent between glyphosate and any solid tumors or lymphoid malignancies overall, including non-Hodgkin lymphoma (NHL) and its subtypes. There was some evidence of increased risk of AML among the highest exposed group that requires confirmation.

Use of chemicals and aggressive prostate cancer

Other than certain skin cancers, prostate cancer is the most common cancer in men in the United States. Farmers are more likely than other men to develop prostate cancer. The AHS published a report in 2014 following analysis of 2 000 men from the AHS study who had developed prostate cancer. The report found:

- Some evidence of an association between some pesticides and prostate cancer
- The strongest evidence was for a link between a few specific insecticides and a subtype of prostate cancer that is fast-growing or aggressive
- Frequent users of the insecticides malathion and terbufos were more likely to develop aggressive prostate cancer, compared with participants who didn't use either insecticide.
- Fonofos and aldrin, insecticides that are no longer registered for use in the U.S., were also associated with an increased risk of aggressive prostate cancer.

Recent work on prostate cancer (Schumacher et al, 2018) is looking at genetic susceptibility to this form of cancer to improve risk prediction and understanding of the underlying biology of the disease.

5. Use of glyphosate and the environment

Glyphosate binds tightly to soil and can persist in the soil for up to six months and is broken down by bacteria (Henderson et al 2015). This source did not specify if this is glyphosate in a

herbicide formulation and if soil type affected this process (clay soils are more reactive than say sandy soils).

Glyphosate resistant plants, bioaccumulation and glyphosate-based herbicides (GBH)

Development of glyphosate resistance has led to increased use of the herbicide, including the practice of spraying crops genetically modified to resist glyphosate with the herbicide prior to harvest (to remove weeds). Peterson Myers et al (2016) expressed a statement of seven concerns about glyphosate-based herbicides and their increased use, calling for the need for

> 'new investments in epidemiological studies, biomonitoring, and toxicology studies that draw on the principles of endocrinology to determine whether the effects of GBHs (glyphosate-based herbicides) are due to endocrine disrupting activities. We suggest that *common commercial formulations of GBHs* should be prioritized for inclusion in government-led toxicology testing programs such as the U.S. National Toxicology Program, as well as for biomonitoring as conducted by the U.S. Centers for Disease Control and Prevention.'

This call to action includes studying the changes in toxicity that may result from glyphosate being combined with other chemicals in herbicide products; 'current data suggest that chemicals in combination can have effects that are not predicted from tests of single compounds'.

This finding is supported by another study of earthworms subjected to glyphosate and Roundup Ultra. The formulation Roundup Ultra was found to be more ecotoxicological effective than glyphosate on its own (Contardo-Jara et al 2009).

The surfactant used to get glyphosate into leaves, by dissolving the waxy cuticle also damages the skin of amphibious animals, such as frogs. This explains why hazard descriptions of glyphosate chemical can be described as non-toxic to animals, yet in practice (formulated with other chemicals including surfactants) it is found to be harmful to amphibians.

Another study of risks associated with glyphosate use in planted forests drew on research from Canada and New Zealand. This study found no evidence of bioaccumulation in fish or mammals (Rolando et al 2017). Glyphosate use was described as 'infrequent', used within legal label recommendations by trained staff. From the literature cited one factor we can consider at MCG is the *amount* of herbicide being used in various applications worldwide and the method of application (clearly aerial spraying has potential to cause the most environmental and health damage).

Bees

Along with our interest in diversifying honey and native bees on the site at MCG, reduction of chemicals that may interrupt these ecological servicers would seem to be a good strategy to implement. Liao et al (2017) report 'exposure to glyphosate reduces sensitivity to sucrose and interferes with learning performance and navigation ability'. In their testing of various chemicals, the researchers found

> Of pesticides eliciting a response, bees displayed a preference at specific concentrations for glyphosate and chlorothalonil. This paradoxical preference may account for the frequency with which these pesticides occur as hive contaminants and suggests that they present a greater risk factor for honey bee health than previously suspected.

Regarding navigational ability in honey bees, a study by (Balbuena et al 2015) found

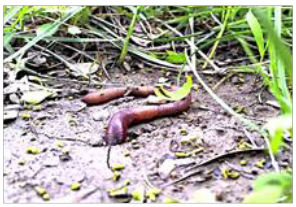
> exposure to levels of glyphosate commonly found in agricultural settings impairs the cognitive capacities needed to retrieve and integrate spatial information for a successful

return to the hive. Therefore, honeybee navigation is affected by ingesting traces of the most widely used herbicide worldwide, with potential long-term negative consequences for colony foraging success.

The US EPA provides information to protect pollinators from pesticides and promotes best practice (US EPA 2018).

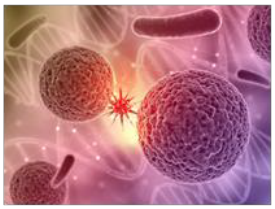
There are studies looking at the effects of GBH on ecosystem services such as earthworms and soil microbes (essential to developing healthy soils), pollinators such as bees and plant defences (Figure 1) (Pesticide Action Network Europe, 2017).

Ecosystem services and glyphosate



Earthworms: Also called "ecosystem engineers", they shred and redistribute organic material in soil, increase soil penetrability for roots through their movement, and consequently improve overall soil fertility. Glyphosate-based herbicides affect the reproduction of earthworms and cause a dramatic decline in their population[1].

Soil microbial communities: These form the basis of ecosystem services such as plant residues and litter decomposition, organic matter mineralization, carbon and nitrogen cycling among others[2]. Certain fungi and bacteria facilitate nutrient uptake in plant roots. Repeated applications of glyphosate alter the microbial community of certain soils[3] , increase soil pathogens[4] and plant nutrient uptake[5].



Pollinators: Honey bees, bumble bees, butterflies and other insects, play a key role in the pollination of the plants, and have a key role in the pollination of crops in agriculture to produce, seeds or fruits. Glyphosate being a broad spectrum herbicide, it reduces the number of flowering plants that are a food source for the pollinators but it may also impact honey bees following long-term exposure[6].

Plant defence: Plants have their own defence system to respond to infections by synthesizing and exerting specific substances to reach the site of infection (e.g. antimicrobial phytoalexins). Glyphosate acts on the pathway that many of these plant-defences are produced, making the crops more susceptible to pathogens and diseases[7].

[1]Gaupp-Berghausen et al., 2015; [2]Delgado-Baquerizo et al., 2016; [3]Lancaster et al., 2010; [4]Kremer and Means, 2009';[5]Zaller et al., 2014; [6]Herbert et al., 2014; [7]Johal and Huber, 2009.

Figure 1 ecosystem services and glyphosate

6. Alternatives

The decision to ban GBHs may be a complex one in Australia, including economic considerations such as revenue raised from sale of these products and the costs of alternative methods of weed control in commercial operations (Taylor 2016). However, it is unlikely these constraints will affect the decision-making process for MCG ☺. Stem technology has been used in Perth, replacing chemical sprays (Shurmer 2016). Burning weeds, followed up with irrigation has been

used in some bush regeneration settings and this method may also trigger germination of native colonising plants by replication of bushfire regeneration strategies.
Care of must be taken before adopting some weed and pest control strategies using soaps, salt and vinegar. These substances can also be toxic to soil, microbes, invertebrate animals, mycorrhizal fungi that benefit plants and potentially the plants we intend to grow to harvest.

7. Conclusions

It would seem in agricultural practice the use of glyphosate-based herbicides (GBH) has significantly increased, primarily with the use of genetically modified crops designed to be resistant to glyphosate. Glyphosate formulations are then used to kill other weeds amongst these crops, often prior to harvest. This may increase the glyphosate content of food, and amount of herbicide chemicals in the environment. GBHs are also used to 'kill off' or dry down crops after harvest, again increasing the chemical impact on the environment.

Direct links of glyphosate to specific cancers in humans is not widely represented in the scientific literature. Evidence of cancer-type disease responses in mice has been found under controlled experimental testing.

Studies on the effects of glyphosate in combination with other chemicals including surfactants required to make glyphosate effective are underrepresented in the discussion of the 'safety' of glyphosate use. In many cases the effects of GBH have not been tested. Some reports indicate that glyphosate in formulations with other chemicals to produce herbicides may be more toxic than test results on glyphosate alone have indicated. It is unclear whether companies such as Montana, who produce GBH formulations such as Roundup, have conducted tests on these herbicide products to determine if they cause cancer in humans or mice, or what impacts they have on the environment. (That surely seems to be a loop hole in legislation?)

At MCG, spraying glyphosate to clear grass would clearly have a greater impact on the environment and expose the user (applicator) to higher risk of ingesting or inhaling herbicides. Strategic, careful and controlled painting of target weeds such as Beach Pennywort (*Hydrocotyle bonariensis*) with glyphosate-based herbicides may still be a good use on our MCG site, to efficiently and effectively control problem weeds with minimal chemical use.

Most of the research into human and environmental effects of herbicide use are in commercial settings where large volume aerial spraying is conducted.

This review has not included alternate technologies or weed control strategies or the reasons some countries, states, cities, counties or local councils have chosen to ban or restrict glyphosate use. This also could be a useful avenue for further investigation.

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