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Glyphosate Kills Rat Testis Cells

Another link between Roundup and infertility Dr. Eva Sirinathsinghji

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A new study finds that Monsanto's glyphosate-based herbicide Roundup Bioforce® as well as glyphosate alone reduced testosterone levels in testicular cells at very low concentrations; and at higher concentrations - still 10 times below agricultural use – the cells died in 24-48 hours.

The study, carried out by Gilles-Éric Séralini and his colleagues at the Université de Caen Basse-Normandie in France [1], was published just ahead of reports on glyphosate contamination of groundwater in Catalonia, Spain [2], and the presence of glyphosate in urine samples of Berlin city residents at 4-20 times the level allowed in drinking water (0.1 micrograms per litre, or 0.1 parts per billion (ppb)) [3]. American consumers exposed to glyphosate through residual levels in genetically modified (GM) foods are likely to have even higher levels in their system; although no studies appear to have been done.

These studies are emerging amid growing concern for the effects of environmental contaminants on decreasing levels of male fertility in humans and animals in industrialised nations [4], and there are already indications that glyphosate herbicide is linked to infertility and other reproductive problems.

Endocrine dysfunction at very low doses

Endocrine disruption can impact a wide range of physiological functions that includemetabolism, growth and development, tissue function, behaviour, mood and reproduction. Healthy levels of testosterone in men are necessary for sperm production among other things. With previous links of pesticides to infertility, the researchers were interested in whether glyphosate and its formulations can induce endocrine disruption in testicular cells.

The effects of Roundup Bioforce® and glyphosate alone were tested on three types of rat testicular cell: Leydig cells that produce testosterone, Sertoli cells that nurture germ cells through spermatogenesis, and germ cells that mature into sperm.

Doses of 1ppm (0.0001%) of both glyphosate and Roundup Bioforce® reduced testosterone levels in Leydig cells by as much as 35 %, and a significant increase in expression of aromatase was found within 24 hours. Aromatase is an enzyme that converts testosterone to oestrogens, and its activity is important for maintaining a healthy balance between the two hormones. These effects of supposedly 'non-toxic' dilutions of the herbicide underlie glyphosate's ability to disrupt the endocrine system.

These results build on a long list of previous findings. Male prepubescent rats exposed to glyphosate showed reduced testosterone levels as well as disruption of testicular morphology and a delay in the onset of puberty [5]. The male offspring of rat mothers exposed to glyphosate during gestation exhibited abnormal sexual behaviour and abnormal levels of testosterone and estradiol, early puberty, and increased sperm count [6]. Glyphosate exposure reduced testosterone levels in mouse Leydig cells [7], and depressed aromatase activity in human placental cell lines [8]. The effects were more pronounced when commercial formulations were used.

Hormonal disruption and/or reproductive problems occurred in both humans and animals followed environmental exposure to sprayed herbicides or herbicide residues in GM feed [9] (see [10] Ban Glyphosate Herbicides Now, *SiS* 43, [11] Lab Study Establishes Glyphosate Link to Birth Defects,*SiS*48) Regions of high glyphosate use in Argentina have seen rises in birth defects, infertility and cancers, to the point that Argentinean doctors are calling for a complete ban of pesticide use near residential areas and a complete ban of aerial spraying (see [12] Argentina's Roundup Human Tragedy, *SiS* 48 [13] and Pesticide Illnesses and GM Soybeans, SiS 53). Livestock consuming large amounts of GM feed have shown increased infertility, still births, and pseudo-pregnancies, thought to be due, at least in part, to direct endocrine-disrupting effects of glyphosate (see [14] USDA Scientist Reveals All, SiS 53).

Higher doses kill cells

Séralini and colleagues also tested whether Roundup and/or glyphosate kill testicular cells, and whether this occurs through inducing necrosis (premature cell death caused by external stimuli such as toxins, inflammation, infection or trauma) or apoptosis (programmed cell death). Necrosis is first marked by a loss of cell membrane integrity, while apoptosis is a tightly regulated process that is marked by morphological changes such as cytoplasmic shrinkage, chromatin condensation (the compaction and fragmentation of nuclear chromatin, with chromatin being the native organisation of DNA wrapped around histone proteins in the nucleus), as well as biochemical changes such as the activation of caspase 3/7 enzymes and the release of cytochrome c from the mitochondria. In addition, there are variations of cell death that can include necrosis-like programmed cell death, apoptosis-like programmed cell death that lacks caspase 3/7 activation, as well as secondary necrosis where apoptotic cells eventually also lose membrane integrity.

The experiments monitored membrane integrity, caspase 3/7 activation as well as chromatin condensation. Leydig cells showed the strongest necrotic response, with significant membrane degradation after 1 hour of exposure to 0.1 % Roundup. Degradation reached 5 times that of control untreated cells at a higher concentration of 1 %, peaking at around 6 hours but remaining significant after 48 hours.

No membrane degradation was found in cells exposed to glyphosate alone. Thus, the effect may be due to adjuvants present in the commercial formulation such as polyoxyethyleneamine (POEA), which is added to allow glyphosate to penetrate plant leaves. There was no significant caspase

3/7 activation other than a small peak after 6 hours exposure. Chromatin condensation was apparent after 24 hours following application of 1% Roundup, as consistent with apoptosis.

Sertoli cells also showed signs of necrosis, with membrane degradation occurring in response to 0.1% Roundup within 24 hours, although to a lesser extent than Leydig cells. Germ cells appeared almost insensitive, with only a slight, but statistically significant membrane degradation following exposure to 1 % Roundup. In contrast to Leydig cells, germ cells as well as Sertoli cell/germ cell co-cultures showed an apoptotic response within 48 hours to 1 % glyphosate. However, there was no response to Roundup. This disparity, as speculated by the authors may be due to distinct membrane properties that allow glyphosate to enter germ cells more easily. This result may also be an *in vitro* artefact that should be investigated further in animal experiments.

The findings clearly show cell death responses in testicular cells, most notably in the Leydig cells. Further experiments are needed to clarify the type of cell death involved. As mentioned above, cell death is a complicated process.

Question of dosing

The concentration of the herbicides used in the experiments ranged from 0.0001 % (1 ppm) of Roundup Bioforce®, (corresponding to 0.366ppm of pure glyphosate) to agricultural levels of 1 % (10,000ppm). The lowest concentration shown to have an endocrine effect was within the range of a previous study published by Monsanto reporting the presence of glyphosate concentrations of up to 0.233ppm in American farmers [13]. Further, the permitted level of glyphosate residue on food or feed in the US is 400 ppm, or 400 times the lowest concentration tested by Seralini and colleagues. Thus, the concentrations used in the study are very relevant to human exposure as well as exposure of other animals. Of particular concern is the scarcity of published data regarding the possible bioaccumulation of this herbicide, leaving us only able to speculate how much is in our bodies.

With the cell death experiments, significant results were seen with doses of 0.1%, or 1000ppm. Although this concentration is relatively high, and well above permitted drinking water concentrations, it is 10 times below that used in agricultural practice, and 8 times below the maximum level of glyphosate residue permitted in GM feed. Moreover, as shown by the endocrine disruption experiments, cell death is not the only parameter of acute toxicity, so while higher doses may be necessary to kill cells, low doses can disrupt endocrine function without killing the cells, but nevertheless impact a wide range of physiological functions, resulting in disease.

Not addressed in this study is the chronic effect of glyphosate-based herbicide exposure; as only acute effects over 48 hours were assessed. Chronic exposure has not been sufficiently tested, and needs to be investigated. Furthermore, regulatory tests are usually done, not with commercial formulations, but with glyphosate alone. As demonstrated in these and other experiments, the adjuvants that enhance glyphosate's action alter the toxicity of Roundup, resulting in differing effects from those of glyphosate alone.

To conclude

Evidence linking glyphosate to birth defects and reproductive problems in both the female and male is surely more than sufficient justification for banning this herbicide [10].

The paucity of studies assessing the presence of glyphosate and its commercial formulations in humans also needs to be addressed.

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gabriel Comment left 27th February 2012 21:09:32
The respond of a friend. This is so f-c-ing terrible!! Why are they not prosecuted and sentenced to the electric chair once and for all?!

James Cooley Comment left 28th February 2012 09:09:03
This information should grab FDA scientists and politicians by the gonads. Let them have it!

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