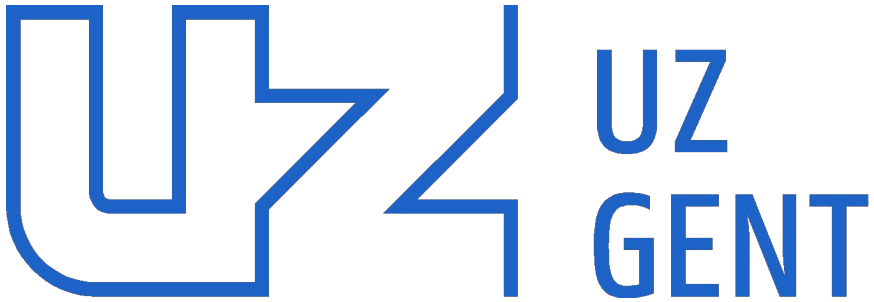

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GLYPHOSATE AND HUMAN HEALTH:

A COMPLEX RELATIONSHIP

Fraeyman

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1. Brief introduction about glyphosate

- First use: early seventies, USA
- Target enzyme in plants: **EPSPS**
- **Exponential increase of the use** of glyphosate after 1996
- First use in **EU in 2002**
- IARC classify glyphosate as “**probably carcinogenic**” (2015)
- EFSA permits the use of glyphosate for **10 years in 2023**
- Absence of acute toxicity

- Probably the most efficient pesticide ever

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2. Health in lower organisms, animals

- Lower monocellular structures are sensitive to glyphosate (Gill et al., 2018)

- Rats, mice…
  experiments with rats and mice needed for approval of the use of glyphosate;
  There is clear evidence for toxicity, dose dependent

- Honey bees are sensitive to glyphosate in relevant concentrations
  Social behaviour is disturbed
  Disorientation between feeding ground and hive
  Effects at the microbiome of honey bees
  Acute toxic effect of roundup is probably due to tallowamine

3. Health in humans (1)

Carcinogenicity (1)

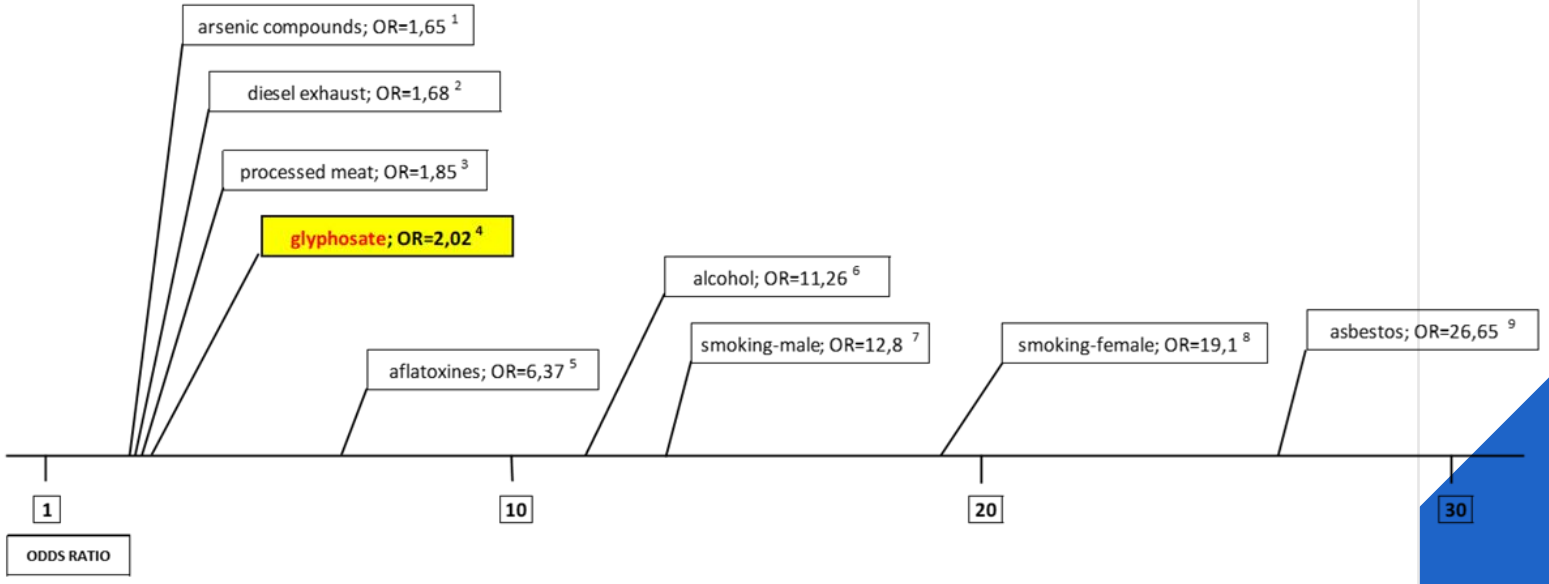
- Glyphosate is carcinogenic in in vitro experiments (different cell lines)
- Biological mechanism for carcinogenicity has been demonstrated
- Human carcinogenicity is difficult to prove (epidemiology – see further)

  IARC: probably carcinogenic to humans (2015),

  EPA, EFSA, ECCA: glyphosate is not carcinogenic
- **Glyphosate is likely to be carcinogenic to humans but not to the same extent as e.g. smoking cigarettes or asbestos**

3. Health in humans (1)

Carcinogenicity (2)



1 : lung cancer; t'Mannetje, 2011
2 : large cell lung carcinoma; Villeneuve, 2011
3 : gastric cancer; Ferro, 2019
4 : non-hodgkin lymphoma; Eriksson, 2008
5 : hepatocellular cancer; Liu, 2012
6 : hypopharyngeal cancer; Zeng, 2019
7 : lung cancer; Stapelfeld, 2019
8 : lung cancer; Stapelfeld, 2019
9 : parenchymal diseases; West, 2019

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3. Health in humans (1)

Carcinogenicity (3)

- The carcinogenicity of glyphosate is comparable to the carcinogenicity of e.g. diesel exhaust or processed meat but lower than the carcinogenicity of smoking (lung cancer) or asbestos (mesothelioma).

HOWEVER

- If you smoke, it is your own choice**.** If you eat processed meat every day, it is your own choice.

Whether we like it or not: we are all continuously exposed to glyphosate, probably at low concentrations that express carcinogenic properties in experimental circumstances.

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3. Health in humans (2)

Endocrine disrupting properties

- Clear endocrine toxicity in animals and in (human) cell lines in vitro. The molecular mechanism has been described involving a.o. steroid receptors
  (Gasnier et al., 2009, Thongprakaisang, 2013, Pham, 2019, Zhang, 2020, Lorenz, 2021, Maddalon, 2021……)

- Evidence for increased endocrine-related pathologies in humans related to exposure to glyphosate: altered female fertility, altered immunity
  (Romano, 2021, Kafshgiri, 2022, Ingaramo, 2020 ……)

- BUT: EFSA found no evidence for endocrine disrupting properties of glyphosate
  (EFSA journal, 2017)

3. Health in humans (3)

Enteric microbiome (1)

- The target of glyphosate (EPSPS) is not unique to plants but is present in other micro-organisms such as the micro-organisms in the microbiome.
  (Mathew, 2022, Walsh 2023, Giambo 2021)
- Glyphosate affects the microbiome of lower animal species
  (Owagboraye 2021)
- Glyphosate affects the microbiome of mice and rats
  (Del Castilo 2022, hu 2021, Lehman 2023, Mesnage 2022)

3. Health in humans (3)

Enteric microbiome (2)

- Glyphosate affects the microbiome of humans leading to dysbiosis

  (Anderson 2023 and ALS, Barnett 2022 and neuropsychiatric diseases, Madani 2022 and neurological diseases, Puigbo 2022)

- DIRECT effect: glyphosate triggers pro-inflammatory reactions
- INDIRECT effect: dysbiosis could cause endotoxemia (leaky gut) with the release of toxic compounds in the abdomen such as lipopolysaccharides

  (Izumi 2023)

3. Health in humans (4)

Link to neuronal pathologies

- Glyphosate crosses the Blood Brain Barrier
  (Winstone 2024)
- Madani 2022: glyphosate and GBHs have significant adverse effects on the brain and behavior and increase the risk of at least some serious neurological diseases.
- Costas-Ferreira 2022: it is unequivocal that exposure to glyphosate produces important alterations in the structure and function of the nervous system of humans, rodents, fish, and invertebrates.
- The mechanism is not clear yet
  (Chang 2023)

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4. What are the problems

- Proof for carcinogenicity of glyphosate
  Carcinogenicity is likely to occur for the **most exposed persons**

- Epidemiology
  Epidemiology has intrinsic difficulties in yielding proof
  There is a **RISK for developing a pathology** after exposure
  Epidemiological studies never giver proof of the individual case

- Undiliberate exposure
  we are all exposed to glyphosate, whether we like it or not
  glyphosate is part of **the exposome**: the totality of chemicals we are exposed to.

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5. What are the solutions (1) ?

- A short-term complete ban of glyphosate is unrealistic
  - No (chemical) alternative
  - Economic consequences would be devastating
  - Need to feed the world (Sustainable Development Goals)

- Need to study the (possibly deleterious) effects of glyphosate on human health

- Willingness of the relevant authorities to review decisions if new information is available

- Long term ban with mentality change
  - ¾ of the crops are use to feed animals for consumption
  - Dietary change to vegetarian diet.

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5. What are the solutions (2) ?

- Short term actions: limiting the use of glyphosate
  - No use of glyphosate by non-professionals
  - Reduce the exposure of bystanders
  - Integrated weed management
  - Promotion of biological pesticides

- Examples of some of the measures already taken:
  - France: Parkinson disease among farmers is considered as professional disease
  - Belgium, France, The Netherlands: glyphosate banned for private consumers
  - Germany: former ban is lifted till june 2024
  - Austria, Luxembourg: failure to ban glyphosate

5. What are the solutions (3) ?

HOWEVER…….

Possible solutions are counteracted by the industry
(Fraeyman, 2024)

- Before december 2023: lobbying by the Glyphosate Renewal Group
  - lobbying costs 2022: 300,000 – 399,000 EUR (i.e. what is known….)
  - Lobbying against the “farm to fork” movement

- Most recent activity of glyphosate consortium lead by Bayer
  - “Modern Ag Alliance” (USA): **Control Weeds, Not Farming** is dedicated to advocating for the availability of glyphosate to American farmers by working with policymakers, growers, and the agricultural community.

6. Conclusions (1)

1. Glyphosate is **not an innocent molecule**

2. Glyphosate can cause **several pathologies**, either directly, either indirectly by affecting the endocrine system or the microbiome

3. The ubiquitous use of glyphosate causes its omnipresence in all parts of the environment **affect everybody**. This is important in particular for the **young and unborn** probably affecting proper development at older age.

4. This is a realistic example for to apply the **precautionary principle**

5. There are sufficient reasons to consider a **gradual, well-planned ban of glyphosate**

6. Conclusions (2)

It is NOT only the carcinogenicity of glyphosate that is important

IT IS THE TOXICOLOGICAL PROFILE OF GLYPHOSATE

REQUIRING TIMELY BANNING OF THE PESTICIDE.

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