

**EFSA Meeting on the Outcome of the Public
Consultation on Acrylamide in Food – December
2014, Brussels**

Professor Ian D. Morris,
Hull York Medical School, UK

representing
**UK Committees on Carcinogenicity and Toxicity of
Chemicals in Food, Consumer Products and the
Environment**

Harderian gland and cancer risk

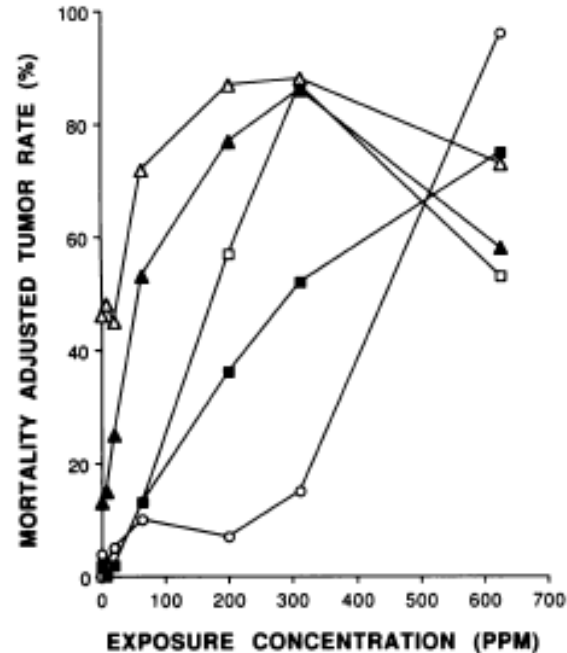
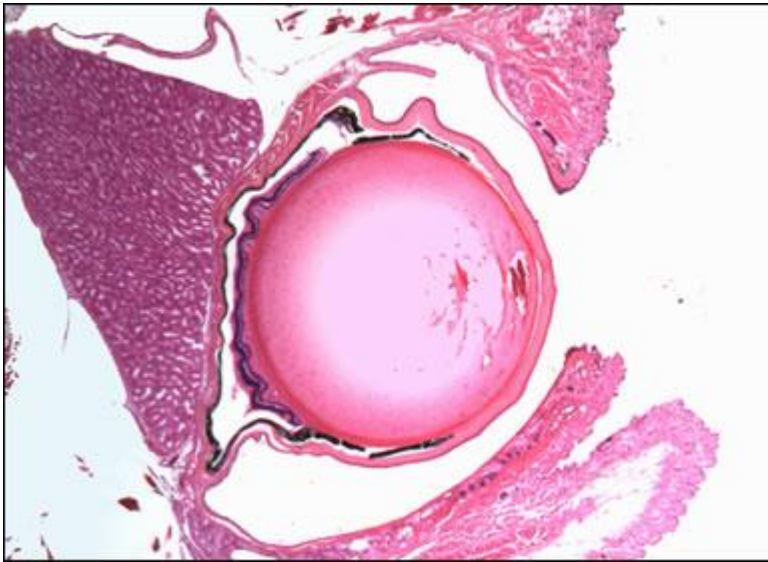


Fig. 2. Dose-response curves for lymphocytic lymphomas (○), hemangiosarcomas of the heart (□), alveolar-bronchiolar neoplasms (△), Harderian gland neoplasms (▲), and squamous cell neoplasms of the forestomach (■) in male B6C3F₁ mice exposed to 1,3-butadiene. Results from the 312-ppm, 52-wk stop-exposure group are also included, because that was the longest exposure duration of the stop-exposure groups and the incidence of lymphocytic lymphoma was not increased in that group compared with controls. Mortality-adjusted tumor rates were determined by the method of Portier and Bailer (20) using a power value equal to 3 (21).

Relevance?

Harderian gland tumours. Appx K Loglogistic data mg/kg/day

BMD is 10% extra risk, BMDL is 95% confidence

Table	Harderian gland			Mammary gland	
	BMD	BMDL		BMD	BMDL
8/9	0.37	0.15		0.41	0.006
11/12	0.37	0.17		0.55	0.3

Choice and Uncertainty

(Male) germ cell mutagens

Lesions

Adducts and UDS; *Segal 1990, Maniere et al 2005*

Big Blue; *Wange 2010*

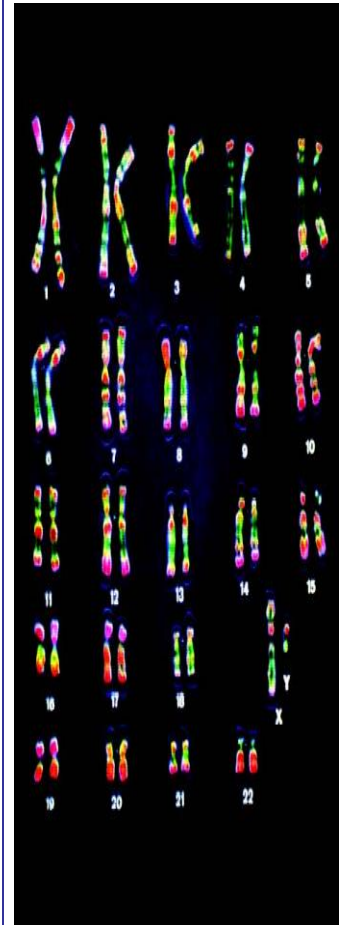
Comet; -0.001mg/Kg *Nixon 2012/13,*

Germ and somatic equal. *Hansel et al;*

Outcome

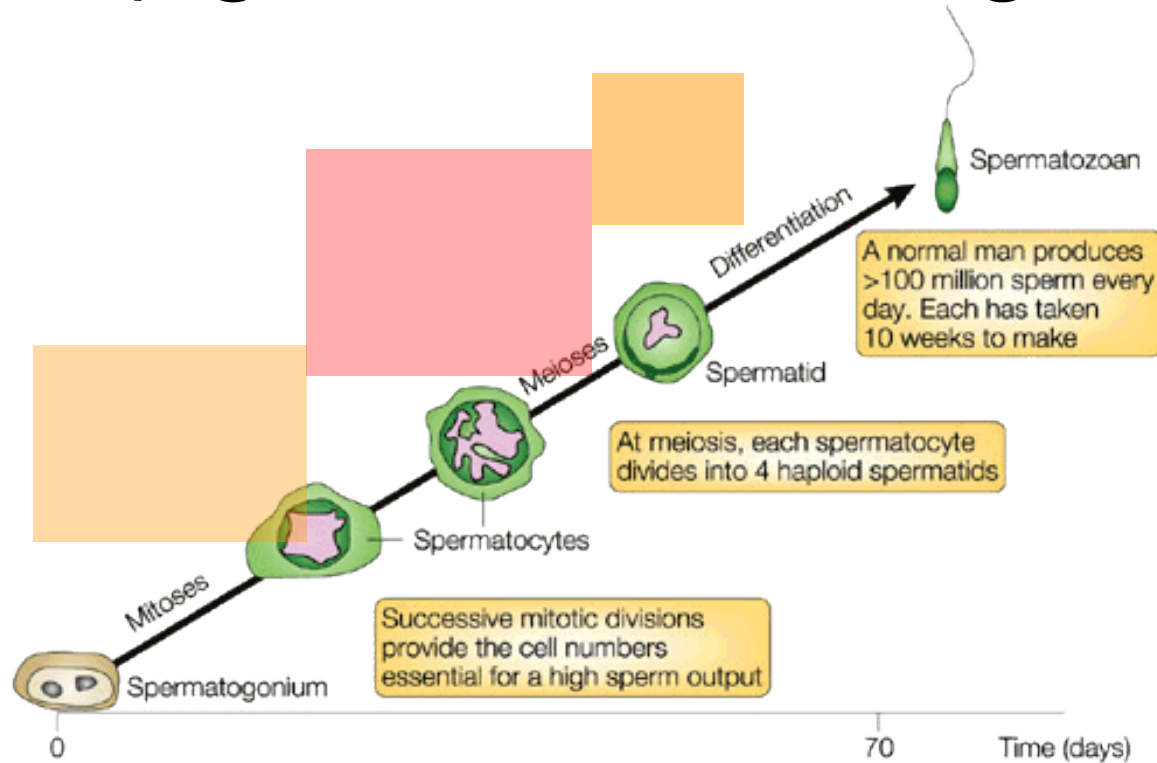
Embryo morbidity and lethality; *Marchetti et al 2009*

Dominant lethal mutations, specific locus mutations;



Heritable reciprocal translocations; *Shelby 2005*

(Male) germ cell mutagens



Nature Reviews | **Genetics**

Health of the surviving offspring?

Trans generational toxicity

Human Observations

- Occupation

- Internal dose. Calleman '94. Conts 0.92, Synthesis 1.80 $\mu\text{mol AA}$
Conts 0.23, Synthesis, 19.5 Anval
nmol/gHb

- Risk assessment for **general population**.

- Diet

- confounders, age, sex, BMI, alcohol, smoking

- smoking as a source. Potato crisps 100 $\mu\text{g}/100\text{g}$, smoke 2.3 $\mu\text{g}/\text{cig}$
(Diekmann 2007)

- total exposure**, role of biomarker adducts

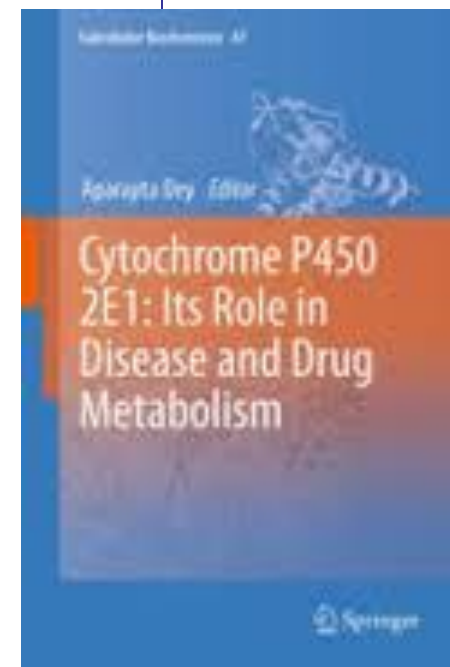
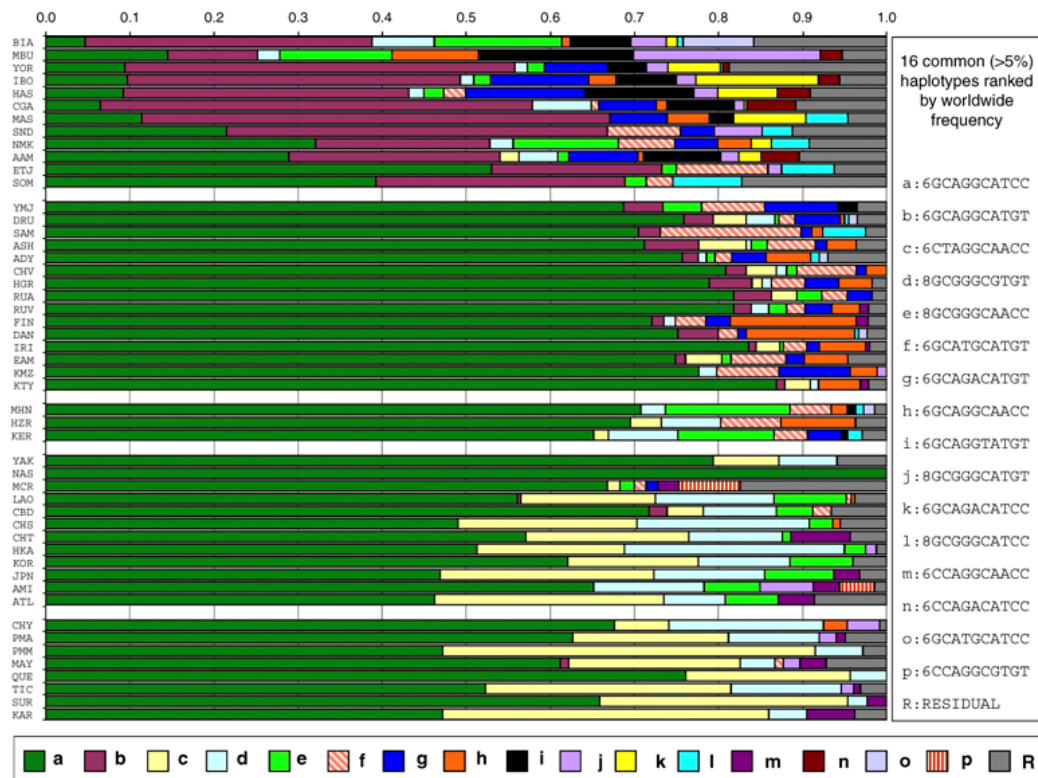
- Smoking

- AA associations with disease

- Exposure and dose, **health outcomes and risk estimates**



Metabolic activation of AA toxicity. Cytochrome p450 2E1



Induction by alcohol, expressed in variety of tissues eg lung and testis

Susceptable populations