

MEAT CONSUMPTION AND COLORECTAL CANCER –

MECHANISMS AND MITIGATION

Stefaan De Smet, 1/2/2017, Workshop Sustainable Beef Quality for Europe, Milan





Laboratory of Animal Nutrition and Animal Product Quality

STRENGTH OF THE EVIDENCES FOR CRC

| | Red meat | |
|--------------------------------------|---|----|
| Human data | Limited | |
| Animal data | Inadequate | 35 |
| Mechanistic and other data Hazard | analysis, not re Strong | |
| Overall evaluation | Group 2A: probably carcinogenic to humans | |



Bouvard et al (2015) The Lancet Oncology 16: 1599-1600



Processed meat

Sufficient sessment! Inadequate

Moderate

Group 1: carcinogenic to humans

International Agency Research on Cancer



HOW COULD RED AND PROCESSED MEAT CAUSE CRC?

Many factors involved, hard to separate

Probably not a single factor

Factors in meat and/or during digestion

Roasting, grilling, pan-frying, boiling ...









Salt, nitrite/nitrate curing, fat, cooking, drying, smoking ...

MECHANISMS FOR THE LINK RED/PROCESSED MEAT ~ CRC



GENT

Demeyer et al (2015) Critical Reviews in Food Science and Nutrition 56: 1-20 Hammerling et al (2015) Critical Reviews in Food Science and Nutrition, doi: 10.1080/10408398.2014.972498

May contribute

- Heterocyclic aromatic amines
- **Polycyclic aromatic hydrocarbons**
 - Fat Protein

More research needed

- Salt, nitrite
- N-glycolylneuraminic acid
- Interaction with other foods and lifestyle factors



Bastide et al (2011) Cancer Prev Res 4: 177-184

HUMAN INTERVENTION STUDIES ON HIGH RED MEAT INTAKE ~ **DNA ADDUCT FORMATION**



Le Leu et al (2015) Brit J Nutr 114: 220

DNA adducts putatively derived from NOC

Lewin et al (2006) Cancer Research 66: 1859



Bastide et al (2011) Cancer Prev Res 4: 177-184

CALCIUM AND A-TOCOPHEROL PROTECT



meat 160 g/d for 4 days.

cured-meat promotion of volunteers.



DCNO = dark cooked meat with nitrite, oxidized.



- Cross-over study in 18 human volunteers given a model cured
- Calcium & tocopherol suppress
- carcinogenesis in rats and reduce
- associated biomarkers in human

Pierre et al (2013) Am J Clin Nutr 98: 1255

RED MEAT + ANTIOXIDANTS IN VITRO DIGESTION





Some antioxidants are very effective.

Van Hecke et al (2016) J Agric Food Chem doi: 10.1021/acs.jafc.5b05915

RED MEAT + ANTIOXIDANTS IN VITRO DIGESTION





... but not all, on the contrary !

Van Hecke et al (2016) J Agric Food Chem doi: 10.1021/acs.jafc.5b05915

HETEROCYCLIC **AROMATIC AMINES (HCA)**

E.g.



PhIP: 2-Amino-1-methyl-6phenylimidazo(4,5-b)pyridine

smoking









POLYCYCLIC AROMATIC HYDROCARBONS (PAH)



BaP: Benzo[a]pyrene

direct flame





Skibsted (2011) Nitric Oxide 24: 176

NO formed by nitrite during meat curing can participate in numerous reactions modifying proteins and pigments.



- Residual concentrations in
 - processed meats low.
- No evidence for carcinogenic effect, even rather a nutrient.
- Antioxidant properties.
- Presence in a meat diet
 - seems to increase
 - endogenous NOC formation.
- Reacts also with lipids.



• Widely used in curing salt

(NaCl containing 0.6% NaNO₂).

Bedale et al (2016) Meat Science 120: 85

MITIGATION OPTIONS - OVERVIEW

Processing

- \checkmark Prevent oxidation (e.g. α -tocopherol, polyphenols).
- Nitrite alternatives and Zn-Protoporphyrin.
- Meal preparation
 - Appropriate cooking practices to reduce HCA and PAH.
 - \checkmark Addition of spices to meat to reduce HCA.
- Meal composition ullet
 - \checkmark Consumption of cruciferous vegetables, yogurt, chlorophyl, wine or coffee, calcium supplements or α -tocopherol to meat diets.
 - \checkmark Alleviating effect of resistant starch.







Demeyer et al (2015) Critical Reviews in Food Science and Nutrition 56: 1-20.

FOCUS ON DIETS AND LIFESTYLES RATHER THAN ON SINGLE FOODS?

Research Article

Heme Iron Intake, <u>Dietary Antioxidant Capacity</u>, and Risk of Colorectal Adenomas in a Large Cohort Study of French Women

Nadia Bastide^{1,2}, Sophie Morois^{1,2}, Claire Cadeau^{1,2}, Suvi Kangas^{1,2}, Mauro Serafini³, Gaëlle Gusto^{1,2}, Laure Dossus^{1,2}, Fabrice H. Pierre⁴, Françoise Clavel-Chapelon^{1,2}, and Marie-Christine Boutron-Ruault^{1,2}

Conclusion: In this prospective cohort study, the association between heme iron and colorectal adenoma risk was found to depend on site, nitrosylation or not, and the ratio with the NEAC. Impact: These results emphasize the need for a global assessment of diet when considering nutritional prevention of colorectal carcinogenesis. *Cancer Epidemiol Biomarkers Prev; 25(4);* 1–8. ©2016 AACR.







DIETARY AND LIFESTYLE RECOMMENDATIONS?



RECOMMENDATION 5

ANIMAL FOODS

Limit intake of red meat¹ and avoid processed meat²



CANCERS OF THE COLON AND THE RECTUM

INCREASES RISK

- Red meat³⁴
- Processed meat⁴⁵
- Alcoholic drinks (men)6
- **Body fatness**
- Abdominal fatness
- Adult attained height⁷
- Alcoholic drinks (women)6

FINAL THOUGHTS

- High consumption of red and/or processed meat ~ small increase in risk for colorectal cancer.
- There are mitigation options.
- Meat consumed in moderate amounts fits well into

balanced diets.



THANK YOU FOR YOUR ATTENTION



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ADDITIONAL SLIDES



IT IS NOT ONLY ABOUT COLORECTAL CANCER...

| Epidemiology | Wall of colon Wall of colon Cancer | | |
|---|--|---|-----------------------------------|
| | Colorectal cancer | Cardiovascular disease | Diabetes type II |
| Relative risk per 100g red meat / day | + 17% | + 0% | + 19% |
| Relative risk per 50g processed meat / day | + 18% | + 42% | + 51% |
| Meta-analyses | Chan et al (2011) N = 13 and 14 | Micha et al (2010, 2012) N = 4 and 5 | Micha et al (2012) N = 9 and 8 |
| <u>IIII</u> UNIVERSITEIT GENT | | | |

IN COMPARISON ...



330 mL soda / day



+ 20% RR Diabetes

Greenwood et al (2014) Brit J Nutr 112: 725-734



One portion of fruit / day



Heart disease

Dauchet et al (2006) J Nutr 136: 2588-2593





10-19 cigarettes / day



+ 276% RR Lung cancer

Gandini et al (2008) Int J Cancer 122: 155-164 REUTERS http://www.reuters.com/investigates/special-report/health-who-iarc/

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WELL GRILLED: After assessing processed meat, the WHO's cancer agency ranked it in its top category of carcinogens. But the WHO also says that, in moderation, meat can be part of a healthy diet. REUTERS/Rick Wilking

How the World Health Organization's cancer agency confuses consumers

By Kate Kelland Filed April 18, 2016, 7:40 a.m. GMT

Processed meat, such as bacon, ranks alongside plutonium as a carcinogen, according to an arm of the WHO. Here's how such assessments happen – and what they mean Richard Sullivan, a professor of cancer policy and global health at King's College London, says any confusion is due to a widespread misunderstanding of IARC's role.

"IARC is purely there to do the science. And the science is absolutely fine," he told Reuters. "But there is a disjunction between the pure science and the policy and public health messaging. That's where problems arise."

HOW TO INTERPRET RELATIVE RISK VALUES?

GLOBAL CANCER OBSERVATORY ŚĊÒ,

http://gco.iarc.fr/

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| | Colorectal cancer, both sexes, 2012 | Europe |
|---------------|--|----------|
| | Incidence cases | 447 136 |
| | Cum. risk 0-75 y | 3.5 % |
| per 100 g/d | Deaths | 214 866 |
| + 17% RR | Cum. risk 0-75 y | 1.4 % |
| | Incidence risk | 4.1 % |
| Consumption ↑ | \rightarrow Not relevant at individual | |
| | | |
| | New cases / v | - 65 000 |





 \rightarrow Relevant at population level







COMPLEX INTERPLAY WITH INFLAMMATION AND GUT MICROBIOTA



Johan Gagnière, Jennifer Raisch, Julie Veziant, Nicolas Barnich, Richard Bonnet, Emmanuel Buc, Marie-Agnès Bringer, Denis Pezet, Mathilde Bonnet

- Dietary heme alters microbiota and mucosa of mouse colon ...
- ljssennagger et al (2012) PLOS ONE, 7:e49868
- Dietary heme induces acute oxidative stress ... in mouse colon
- Ijssennagger et al (2013) Carcinogenesis 34: 1628
- Gut microbiota facilitates dietary hemeinduced epithelial hyperproliferation by opening the mucus barrier in colon
- Ijssennagger et al (2015) P Natl Acad Sci USA 112:10038