Recent Results from the IARC Monographs:
Carcinogenicity of Consuming Red & Processed Meat, Coffee and Very Hot Beverages

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Conflict of Interest Statement

I declare no financial interests related to the subject matter of my presentation.
The IARC Monographs

Launched in 1971 by request of participating states to identify carcinogens

- The “encyclopaedia of carcinogens”

Almost 1000 “agents” have been evaluated, including:

- Chemical and physical exposures
- Biological agents
- Foods, drugs and personal habits (tobacco smoking)

National and international health agencies use the Monographs

- To control exposure to known or suspected carcinogens
- As a basis for cancer prevention policy
- To formulate health guidelines
How are Evaluations Conducted?

Published guidelines & procedures

- Participant selection
- Conflict of interest
- Data eligibility
- Review of evidence
- Decision process for overall evaluations
- Public participation

[Image of IARC Monographs on the Evaluation of Carcinogenic Risks to Humans]

http://monographs.iarc.fr/ENG/Preamble/index.php
Who does the evaluation?

IARC Secretariat
Coordinates all aspects of the evaluation

Working Group
Independent scientists without conflict of interest
Review science and develop evaluations

Invited Specialists
Scientists with relevant knowledge but a competing interest

Representatives
of governments and health agencies

Observers
Scientists with a competing interest: observe but do not influence outcomes

Attend meetings but do not write reviews or contribute to evaluations
What evidence is considered?

Publicly available scientific data
- Peer reviewed papers
- Government reports
- Available in enough detail for critical review

Overall Evaluation

- Cancer in Humans
- Cancer in Animals
- Mechanisms

Center international de Recherche sur le Cancer
Organisation mondiale de la Santé
What are the IARC classifications?

<table>
<thead>
<tr>
<th>Classification</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinogenic to humans</td>
<td>Group 1</td>
</tr>
<tr>
<td>Probably carcinogenic to humans</td>
<td>Group 2A</td>
</tr>
<tr>
<td>Possibly carcinogenic to humans</td>
<td>Group 2B</td>
</tr>
<tr>
<td>Not classifiable as to carcinogenicity</td>
<td>Group 3</td>
</tr>
<tr>
<td>Probably not carcinogenic to humans</td>
<td>Group 4</td>
</tr>
</tbody>
</table>

- IARC classifications refer to the strength of scientific evidence (the level of certainty that the agent causes cancer)
- They DO NOT reflect the level of carcinogenic risk
How are the data evaluated?

- **Cancer in humans**
  - Preamble Part B, Section 6(a)

- **Cancer in experimental animals**

- **Mechanistic and other relevant data**

- **Sufficient evidence**
  - Causal relationship has been established
  - Chance, bias, and confounding could be ruled out with reasonable confidence

- **Limited evidence**
  - Causal interpretation is credible
  - Chance, bias, or confounding could not be ruled out

- **Inadequate evidence**
  - Studies permit no conclusion about a causal association

- **Evidence suggesting lack of carcinogenicity**
  - Adequate studies covering the full range of exposure are consistent in not showing a positive association at any level of exposure
How are overall evaluations determined?

**EVIDENCE IN EXPERIMENTAL ANIMALS**

- **Sufficient**
- **Limited**
- **Inadequate**

- **Sufficient**
  - Carcinogenic to humans (Group 1)

**EVIDENCE IN HUMANS**

- **Sufficient**
- **Limited**
- **Inadequate**

**Examples Group 1**
- Asbestos
- Tobacco smoking
How are overall evaluations determined?

**EVIDENCE IN EXPERIMENTAL ANIMALS**

- **Sufficient**
- **Limited**
- **Inadequate**

**Sufficient**

**Limited**

**Inadequate**

**Probably carcinogenic** (Group 2A)

**Examples Group 2A**
- DDT
- Tetrachloroethylene
How are overall evaluations determined?

**EVIDENCE IN EXPERIMENTAL ANIMALS**

- **Sufficient**
- **Limited**
- **Inadequate**

**EVIDENCE IN HUMANS**

- **Sufficient**
- **Limited**
- **Inadequate**

**Possibly carcinogenic** (Group 2B)

Examples Group 2B
- Chloroform
- Styrene
How are overall evaluations determined?

EVIDENCE IN EXPERIMENTAL ANIMALS

- Sufficient
- Limited
- Inadequate

EVIDENCE IN HUMANS

- Sufficient
- Limited
- Inadequate

Not classifiable (Group 3)
How are overall evaluations determined? Mechanistic Modifications

Evidence in Experimental Animals

- Sufficient
- Limited
- Inadequate

Group 1 (carcinogenic to humans)

Group 2A (probably carcinogenic) (exceptionally, Group 2A)

Group 2B (possibly carcinogenic)

Group 2B (possibly carcinogenic)

Group 3 (not classifiable)

Strong evidence in exposed humans
Results

Consumption of processed meat is carcinogenic to humans (Group 1)

• Sufficient evidence in humans for colorectal cancer

Consumption of red meat is probably carcinogenic to humans (Group 2A)

• Limited evidence in humans for colorectal cancer
**Exposures**

**Red meat**
Unprocessed mammalian muscle meat (beef, veal, pork, lamb, etc) – including minced or frozen

**Processed meat**
Meat transformed through salting, curing, fermentation, smoking or other processes (ham, sausage, bacon, etc)

**Related exposures**

**HAA.** From high-temperature cooking (frying, grilling, BBQing)

**PAH.** From high-temperature cooking and meat processing

**Nitrates/ nitrites.** Additives used in meat processing

**Haem** (from haemoglobin). Mediates formation of NOC
The Scientific Data

> 2300 studies reviewed!

> 700 epidemiologic studies on red meat

> 400 studies on processed meat

> 400 studies on mechanisms

- The largest number of epidemiologic studies concern colorectal cancer (CRC)
Cancer in Humans

Colorectal Cancer

- Greatest weight given to prospective cohort studies
- Supporting evidence from high-quality population case-control studies

Processed meat

- Positive associations in 12 of the 18 cohort studies in Europe, Japan and USA
- Supporting positive associations in 6 of 9 informative case-control studies

Red meat

- Positive associations in half of 14 cohort studies, including a cohort from 10 European countries & cohorts in Sweden and Australia
- 15 informative case-control studies, 7 with positive associations for high versus low consumption
Cancer in experimental animals

- Increased occurrence of colonic preneoplastic lesions in rats treated with colon cancer initiators and promoted with low calcium diets containing either *red meat* (3 studies) or *processed meat* (4 studies)

Mechanisms related to carcinogenicity

- Modest association with human colorectal polyps in observational studies (red & processed meat)
- Moderate evidence of genotoxicity in humans
- Changes in oxidative stress markers in human intervention studies
Summary of the Evidence

Cancer in humans

Processed meat
• *Sufficient evidence* for colorectal cancer
• Positive association with stomach cancer

Red meat
• *Limited evidence* for colorectal cancer

Cancer in experimental animals
• *Inadequate evidence* for red meat & processed meat

Mechanisms related to carcinogenesis
• *Strong* for red meat
• *Moderate* for processed meat
Results

Consumption of coffee is not classifiable as to carcinogenicity (Group 3)

Consumption of very hot beverages (>65°C) is probably carcinogenic to humans (Group 2A)

- Limited evidence in humans for oesophageal cancer
- Limited evidence in experimental animals
Mate

• An infusion of *ilex paraguayiensis* consumed mainly in South America

• Traditionally drunk very hot (>70° C) but may also be drunk warm or cold

Other very hot beverages

• In some areas (e.g. Central Asia, East Africa, China, Japan), tea may also be consumed very hot (>70° C)

• Coffee, and tea in other regions, is usually drunk at <65° C
Geographic correlations have been observed between high oesophageal cancer incidence and use of very hot beverages.
Previous Evaluations (1991)

**Coffee:** Possibly carcinogenic (Group 2B)
- *Limited* evidence for bladder cancer
- *Evidence suggesting lack of carcinogenicity* for breast & colon
- *Inadequate evidence* in experimental animals

**Hot mate drinking:** Probably carcinogenic (Group 2A)
- *Limited* evidence for oesophageal cancer
- *Inadequate evidence* in experimental animals

**Mate:** Not classifiable (Group 3)
The Scientific Data

>2000 studies reviewed

For coffee

- > 500 epidemiologic studies
- Data for > 20 cancer sites
- >500 mechanistic studies

For very hot beverages, including mate

- ~ 40 epidemiologic studies
- Most data for oesophageal cancer
Bladder Cancer

• ~80 studies in total: mostly hospital-based case-control studies
• Greatest weight given to cohort studies; population-based case-control studies seen as supportive
• 9 cohort studies in Japan, USA & European countries had inconsistent results and no evidence of dose-response
• 15 population case-control studies also inconsistent
• Positive associations observed more often in men than in women
• Inadequate control for smoking and occupational exposure in many studies
• Confounding by smoking judged likely in some studies
Coffee: Cancer in Humans

Endometrial cancer & liver cancer
- *Inverse associations* (decreased risk) in most cohort and case-control studies and in meta-analyses

Breast cancer
- *No association* or modest *inverse association* in >40 studies and a meta-analysis with >1 M women

Prostate and pancreatic cancer
- Consistent evidence of *no association* in >60 studies of these cancers

Other cancer sites (>20)
- Inconsistent results, potential bias or few studies
Coffee: Other Data

Cancer in experimental animals

- Tested in 4 chronic carcinogenicity studies and >10 initiation-promotion studies
- No significant increase in total tumours in any study
- Reduced tumour incidence in some studies

Mechanisms related to carcinogenicity

- *Strong* antioxidant effects in humans
- *Moderate* evidence of reduced colorectal polyps in humans
- *Weak* evidence of genotoxicity
Coffee: Conclusions

Cancer in humans

- *Inadequate* evidence of carcinogenicity for coffee drinking
- *Evidence suggesting lack of carcinogenicity* for cancers of the liver, uterus (endometrium), breast, prostate & pancreas

Cancer in experimental animals

- *Inadequate* evidence of carcinogenicity for coffee
Very Hot Beverages: Cancer in Humans

Oesophageal cancer

- Increased risks observed only for drinking mate or tea “hot” or “very hot”
- For mate, independent effects of temperature and quantity
- Similar RRs ≈2 for hot mate and other very hot beverages, excluding mate
Very Hot Beverages
Other Data

Cancer in Experimental Animals

• In 2 co-carcinogenicity studies, instilled water at 65-70°C promoted nitrosamine-induced tumours in mice and rats
• Drinking cold mate reduced tumour incidence

Mechanisms related to carcinogenicity

• Sparse data on relevant mechanisms
• Weak evidence for all tested characteristics of carcinogens for mate and for very hot beverages
Very Hot Beverages: Conclusions

Cancer in humans

• *Limited* evidence for drinking very hot beverages
• *Inadequate* evidence for drinking mate, not very hot

Cancer in experimental animals

• *Limited* evidence for hot water $\geq 65{^\circ}C$
• *Inadequate* evidence for drinking mate
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- American Cancer Society

**Thank you!**