Processing and Preparation of Meat and the Formation of Carcinogens

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Name of Speaker: AMANDA J CROSS

No Relevant Financial Relationship: _X________________________________________
Relevant Financial Relationship: ____________________________________________
Name of conflicting business, organization or individuals:
________________________________________________________________________
________________________________________________________________________

Nature of Conflict: NONE
Outline

• Why meat and cancer?

• Meat processing

• Meat preparation

• How can we decrease cancer risks?
Definitions

• **Red meat**: flesh from animals that have more red than white muscle fibers (beef, goat, lamb, pork)

• **Processed meat**: meat (usually red) preserved by smoking, curing, or salting, or by addition of preservatives
Eisenhower expressway in Chicago as part of an ad campaign paid for by the Physicians Committee for Responsible Medicine
“RED MEAT... SALT... BOOZE! OBVIOUSLY, THIS IS A SUICIDE!”
Variation in Red Meat Intake
Observational Studies

- Divide people into categories according to intake
- Compare the risks of cancer for individuals in the top versus those in the bottom category of intake

**Risks**

1.00 = no association (null)

0.90 = 10% lower cancer risk among those in the top vs. bottom category of intake

1.18 = 18% higher cancer risk among those in the top vs. bottom category of intake
NIH-AARP Diet and Health Study

500,000 men & women aged 50-71yrs

124-item FFQ

Meat cooking qx

1995

1996

2005

53,000 cancers

Current follow-up

500,000 men & women aged 50-71yrs
Red Meat and Cancer Risk \((Q5 \text{ vs. } Q1)\)

Cross et al., 2007
Processed Meat and Cancer Risk (Q5 vs. Q1)

Cross et al., 2007
Meat, Poultry, Fish, Eggs, & Cancer Risk

<table>
<thead>
<tr>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
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<tbody>
<tr>
<td>Exposure</td>
<td>Cancer site</td>
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<tr>
<td>Convincing</td>
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<td></td>
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<tr>
<td>Probable</td>
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<tr>
<td>Limited —</td>
<td>Fish</td>
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<tr>
<td>suggestive</td>
<td>Foods containing vitamin D(^4)</td>
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<tr>
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<td>Colorectum</td>
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WCRF / AICR, 2007
Next Steps

1) If red and processed meat increase colorectal cancer risk, they could be associated with other cancers

2) What are the mechanisms underlying this association?
Outline

• Why meat and cancer?

• Meat processing

• Meat preparation

• How can we decrease cancer risks?
Definitions

• **Red meat**: flesh from animals that have more red than white muscle fibers (beef, goat, lamb, pork)

• **Processed meat**: meat (usually red) preserved by smoking, curing, or salting, or by addition of preservatives

**Nitrate and Nitrite:**
- Helps kill bacteria
- Produce a characteristic flavor
- Gives meat a pink or red color
- Prevents lipid peroxidation
Exposure to $N$-nitroso Compounds (NOCs)

**Exogenous**
Processed meats: nitrate and nitrite added

**Endogenous**
Red meat: amines/amides + heme iron + nitrate/nitrite + bacteria
Improving Assessment of Processed Meat Intake in a FFQ

104 food codes for processed meats in US survey database

Collapsed according to ingredient (n=94 food codes)

Found and bought representative food products for 82 of the 94 meats

Analyzed additives on label

Grouped by meat type and additives

17 main questions and 22 sub-questions on processed meats

Sinha et al., 2005
Bologna Line Items in FFQ

6. In the **past year**, how often did you eat **bologna** other than turkey bologna?

<p>| | | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>NEVER</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>1-6 times per year</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>7-11 times per year</td>
<td>6</td>
</tr>
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<td>(GO TO 7, PAGE 7)</td>
<td>7</td>
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<td>10</td>
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<td>11</td>
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</tbody>
</table>
A Database to Use with a FFQ: Nitrate and Nitrite

- 10 meat items represented 90% of total mentions of processed meat in U.S.
- 23 USDA food codes
- Composite samples prepared and analyzed in collaboration with USDA
- Analyzed for nitrate and nitrite

Sinha et al., 2005
Nitrate and Nitrite Database for Most Commonly Consumed Processed Meats in U.S.
Heme Iron Database

Cross et al., 2012.
Outline

• Why meat and cancer?
  - Processed meat intake
    - More detailed questionnaire to use in conjunction with databases

• Meat processing
  - Intake of Additives
    - Nitrate
  - Nitrite resulting in NOCs
  - NOCs also formed from heme iron

• Meat preparation

• How can we decrease cancer risks?
Outline

• Why meat and cancer?

• Meat processing

• Meat preparation

• How can we decrease cancer risks?
Heterocyclic Amines (HCAs) and Polycyclic Aromatic Hydrocarbons (PAHs)

- Formation dependent on
  - Meat type
  - Temperature (cooking method)
  - Time (doneness)

- HCAs: MeIQx, DiMeIQx, PhIP
- PAH: BaP

Problem:
FFQs lump meats with widely dissimilar cooking methods
Effect of Time and Temperature on HCA Formation

www.charred.cancer.gov
BaP Content of Steak and Hamburger

[Graph showing the BaP content of cooked meat, comparing cooked meat by doneness and cooking method.]
Assessment of HCA and PAH Intake

15. In the past year, how often did you eat steaks (beef, such as round, sirloin, tenderloin, porterhouse, or rib steaks)? (Include steaks in sandwiches.)

- NEVER (GO TO 16)
- 1-6 times per year
- 7-11 times per year
- 1 time per month
- 2-3 times per month
- 1 time per week
- 2 times per week
- 3-4 times per week
- 5-6 times per week
- 1 time per day
- 2 or more times per day

15a. How were the steaks you ate usually cooked? (Refer to the Cooking Methods Definitions on the first page of the Meats Card.)

- Pan-fried
- Grilled/Barbecued
- Oven-broiled
- Baked
- Boiled
- Microwaved
- Stir-fried
- DON'T KNOW (GO TO 15c)

15c. Which picture on the Meats Card most closely resembles the way you eat your steaks?

- Steak Picture A
- Steak Picture B
- Steak Picture C
- Steak Picture D
- DON'T KNOW
Outline

• Why meat and cancer?
• Meat processing
  Meat cooking method and doneness levels determine:
    - Intake of HCAs
      - MeIQx
      - DiMeIQx
      - PhIP
    - Intake of PAHs
      - Benzo[a]pyrene
• Meat preparation
• How can we decrease cancer risks?
**Food Frequency Questionnaire**

*Standard:*
- Meat type
- Frequency
- Portion size

**Meat Intake**

- Total meat
- Red meat
- White meat

**Meat-Related Exposures**

- Processed meat
- Nitrate
- Nitrite
- Heme iron
- *Heterocyclic amines:*
  - DiMeIQx
  - MeIQx
  - PhIP
- *Polycyclic aromatic hydrocarbons:*
  - BaP

**Detailed Meat Qx:**
- Cooking method
- Doneness level

*Apply quantitative databases to estimate intake*
# Meat Mechanisms and Colorectal Cancer (n=2,719)

<table>
<thead>
<tr>
<th>Substance</th>
<th>HR (95% CI) for Q5 vs. Q1</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrate</td>
<td>1.16 (1.02-1.32)</td>
<td>0.001</td>
</tr>
<tr>
<td>Nitrite</td>
<td>1.11 (0.97-1.25)</td>
<td>0.055</td>
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*Cross et al., 2010*
Summary: Nitrate, Nitrite, Iron and All Cancers

<table>
<thead>
<tr>
<th>Nitrate/Nitrite</th>
<th>Increased risk</th>
<th>Decreased risk</th>
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<tbody>
<tr>
<td>Bladder</td>
<td></td>
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<tr>
<td>Colorectal</td>
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<tr>
<td>Glioma</td>
<td></td>
<td></td>
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<tr>
<td>Prostate</td>
<td></td>
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</table>
# Summary: HCAs, PAHs, and All Cancers

<table>
<thead>
<tr>
<th></th>
<th>Increased risk</th>
<th>Decreased risk</th>
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</thead>
<tbody>
<tr>
<td><strong>HCAs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DiMeIQx</td>
<td>Colorectal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastric (cardia)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pancreas</td>
<td></td>
</tr>
<tr>
<td>MeIQx</td>
<td>Colorectal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lung</td>
<td></td>
</tr>
<tr>
<td>PhIP</td>
<td>Prostate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Renal</td>
<td></td>
</tr>
</tbody>
</table>
Outline

• Why meat and cancer?

• Meat processing

• Meat preparation

• How can we decrease cancer risk?
Minimizing Exposure to Potential Carcinogens in Meat

• Limit processed meat intake

• Limit meat cooked well-done at high temperatures

• Some evidence for decreased HCA formation:
  – Marinating
  – Pre-heating meat in microwave
RECOMMENDATION 5

ANIMAL FOODS

Limit intake of red meat\(^1\) and avoid processed meat\(^2\)

PUBLIC HEALTH GOAL

Population average consumption of red meat to be no more than 300 g (11 oz) a week, very little if any of which to be processed

PERSONAL RECOMMENDATION

People who eat red meat\(^1\) to consume less than 500 g (18 oz) a week, very little if any to be processed\(^2\)
Acknowledgments

• Rashmi Sinha
  Division of Cancer Epidemiology and Genetics, NCI

• Leah Ferrucci
  Associate Research Scientist, Yale School of Public Health

• Carrie Daniel
  MD Anderson Cancer Center

• Sheila Bingham
  Mar 7, 1947 -- Jun 16, 2009

• Arthur Schatzkin
  Feb 11, 1948 – Jan 20, 2011
Five Hypotheses on Processed Meat & Cancer

- **H1** - Red meat contains myoglobin with **heme iron**:
  - Heme promotes polyunsaturated fat peroxidation
  - In cured meat heme is nitrosylated
  - (Nitroso-)heme promotes nitrosation of amines

- **H2** - Cured meat contains nitrite =>
  carcinogenic **N-nitrosated compounds**

- **H3** - Cooking = **Heterocyclic Aromatic Amines**

- **H4** - Meat is **fat** => excessive calories & bile acids

- **H5** - Meat lacks protecting agents (Ca++, phytochem)
Methods of Curing: Salt and Sugar

Salt: 
- Flavor
  - Growth of spoilage-causing microorganisms
  - Beneficial bacteria (e.g. *Lactobacillus*)
  - Acidic environment (around 4.5 pH)
    - Extracts salt soluble protein (emulsions)

Sugar: Energy source for *Lactobacilli*
- Fermentation
- Spoilage bacteria to grow
- Tangy flavor of some cured products
  - Browning agent
Problems with Previous Studies

- Self-reported diet → Biomarkers of intake
Other Additives Found in Processed Meats During Label Checks

- Benzoic acid
- Sodium diacetate
- Butylated hydroxyanisole
- Mono-, di-sodium phosphate
- Butylated hydroxytoluene (BHT)
- Sodium erythorbate, Erythorbic acid
- Citric acid
- Sorbic acid, Sodium sorbate, Calcium sorbate

- Sodium lactate
- Lactic acid starter culture
- Sodium nitrate
- Sodium nitrite
- Mono-, di-potassium phosphate
- Sodium tripolyphosphate
- Sodium ascorbate, Ascorbic acid
Meat Intake and Mortality

Adjusted for age, race, education, marital status, family hx cancer, BMI, smoking, physical activity, alcohol, vitamin use, energy, fruit & veg, HRT

Sinha et al., 2009
Meat and Colorectal Cancer

• Meta-analysis: 34 case-control & 14 cohort studies (Norat et al., 2002)
  – Red meat = 1.35 (CI: 1.21-1.51) for top category
  – Processed meat = 1.31 (CI: 1.13-1.51)

• Meta-analysis of 15 cohort studies (Larrson et al., 2006)
  – Red meat = 1.28 (1.15-1.42) for top category
  – Processed meat = 1.20 (1.11-1.31)

• Meta-analysis of 9 cohorts (WCRF/AICR Continuous Update, 2010)
  – Red meat = 1.17 (1.05-1.31) for 100g/d
  – Processed meat = 1.18 (1.10-1.28) for 50g/d
Effect of Red Meat and Iron on Endogenous N-nitrosation

MAY NOT BE RELEVANT – CONSIDER DELETING

Cross et al., 2003
## Incident Cases

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Meat module</th>
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<tbody>
<tr>
<td>Colorectal</td>
<td>6,000</td>
<td>2,719</td>
</tr>
<tr>
<td>Lung</td>
<td>9,100</td>
<td>6,361</td>
</tr>
<tr>
<td>Breast</td>
<td>7,845</td>
<td>3,818</td>
</tr>
<tr>
<td>Prostate</td>
<td>17,451</td>
<td>10,313 (1,102 adv)</td>
</tr>
</tbody>
</table>