Research Gaps in Evaluating the Relationship of Meat and Health

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Relative Gut Volume (%)

Half the Day’s Protein Plus Micronutrients from Beef...

100 g cooked Lean Tenderloin

- Calories
- Protein
- Fat
- Iron
- Zinc
- Selenium
- Vitamin B12
- Niacin

Percent Daily Reference Intake
Sources of the world's meat supply in 2012

- Cattle + Buffalo: 36.3%
- Sheep + Goat: 22.2%
- Pig: 4.6%
- Poultry: 1.7%
- Other: 35.2%

From: www.fao.org
Meat Consumption, 2010 or 2012

US

- Beef/Veal
- Pork
- Chicken
- Turkey

125 kg total/capita/year


EU-27

- Beef/Veal
- Pork
- Poultry
- Others

87 kg total/capita/year

From: DG AGRI, European Commission
U.S. per capita availability of beef, pork, and chicken, 1909-2012

Limitations of Observational Evidence

- We eat foods as part of a diet pattern
  - Mediterranean pattern
  - “Western” pattern
  - Diet correlates with other lifestyle factors
- Nutrient interactions
- Nutrient interactions with host factors (genetics, epigenetics)
Limitations of Observational Evidence

- **Confounding**
  - High meat intake associated with high fat intake, low fruit/veggies
  - Is it simply inadequate fiber, folate, other nutrients or a change in intestinal bacteria?
- **Other lifestyle factors**
  - Weight, exercise, tobacco, alcohol, pollution, pharmaceuticals, stress
  - Coffee and CHD ... until explained by cigarettes
  - Diet soda intake associated with obesity
- Socioeconomic status, education
Limitations of Evidence

- Can we rely on epidemiology?
  - Accuracy of diet instruments
    - 7-day food diary vs. FFQ for sat. fat & breast Ca
    - Diary RR=1.22 (p=0.005); FFQ RR 1.10 (p=0.23)
  - Variability and accuracy of food composition
  - Changes in diet over time

- Few interventions
  - Endpoints usually not cancer
Women’s Health Initiative (N=48,835)
Invasive Colorectal Cancer (n = 469)

“Failure” of Intervention

- Polyp Prevention Trial
- ~950 subjects/group, 3 yr follow-up
- Significant increases in total F/V, whole grains, legumes, cruciferous vegetables
- Significant decrease in total fat, red and processed meat
- RR of recurrent polyps: 1.00 (0.90-1.12)

NIH-AARP Diet & Health Study of 500,000 Americans aged 50-71, 8.2 y follow-up - 53,396 incident cancers

5th vs 1st Quintile of Processed Meat Intake and Cancer Risk

Aj Cross et al, PLoS Medicine, 4:e325 (Dec 2007)
NIH-AARP Questionnaires

- 1995-6 mailed 3.5 million questionnaires; 0.5 million returned
- 26 questions on diet during the past year
- Supplemental Risk Factor Questionnaire focused on meat and cooking methods
  - Six questions on meat over past year
  - One question on diet 10 years ago – 37 foods
  - One question on diet at age 12-13 years
Meat Intake and Mortality
NIH-AARP Study

71,000 deaths in 500,000 people  R. Sinha et al, Arch Intern Med 169:562 (2009)
Open Questions...

• Is high red meat intake a risk factor?
• Is charred/smoked meat a problem?
• Is low intake of fruits/veggies/fiber the problem?
• Are inadequate vitamins/minerals the problem?
• Are only some genetically susceptible people affected?
• ...Or is high red/processed meat intake a marker for a set of lifestyle characteristics that increase cancer risk?
  – Need to know mechanism(s) of contribution to disease
NIH OPEN Study

- NCI FFQ – 124 food items and 3 portion sizes
- Used biomarkers for energy and protein intake
- “the FFQ cannot be recommended as an instrument for evaluating the absolute intakes of energy and protein in relation to disease.”
What do Epidemiologists Say about Relative Risk?

- “In adequately designed studies we can be reasonably confident about big relative risks, sometimes; we can be only guardedly confident about relative risks estimates of the order of 2.0, occasionally; **we can hardly ever be confident about estimates of less than 2.0**, and when estimates are much below 2.0, we are simply out of business. Epidemiologists have only primitive tools, which for small relative risks are too crude to enable us to distinguish between bias, confounding and causation.”

“Epidemiology is particularly prone to the generation of false-positive results... Further exacerbating the problem in epidemiological studies is the search for and reporting of weak associations, among which the potential for the distorting influences of bias, confounding, and chance is further enhanced.”

Multiple Comparisons in Epidemiology

- 100 food items x 40 food constituents x 50 disease/risk factor outcomes
  - 120,000 outcomes
    - 6,000 false positives expected
- U.S. studies: 125 x 65 x 50 = 406,250 outcomes
  - 20,312 likely false positives at p≤0.05
Hill Considerations for Causation

- Strength – by far, the most important
- Consistency – in the same direction?
- Specificity
- Temporality – exposure before disease
- Biological gradient – dose-response
- Plausibility
- Coherence
- Experiment
- Analogy

Observational Studies

• “In terms of prevention, you should discount all claims about effects discovered in observational studies. Consider them hypotheses to be evaluated.”

• “90% of the work in an observational study lies with ruling out competing explanations. This is the key.”

  — J. Michael Oakes, U Minnesota, presentation at IOM workshop on obesity prevention, Jan 8, 2009
Figure 1. Correlation between Countries' Annual Per Capita Chocolate Consumption and the Number of Nobel Laureates per 10 Million Population.

Lifespan analyzed by first letter of first name

Male athletes, doctors and lawyers (n=10,000)

EL Abel & ML Kruger, Death Studies, 34:71-81, 2010
“...there is always an easy solution to every human problem – neat, plausible, and wrong.”

- H. L. Mencken (1880-1956)