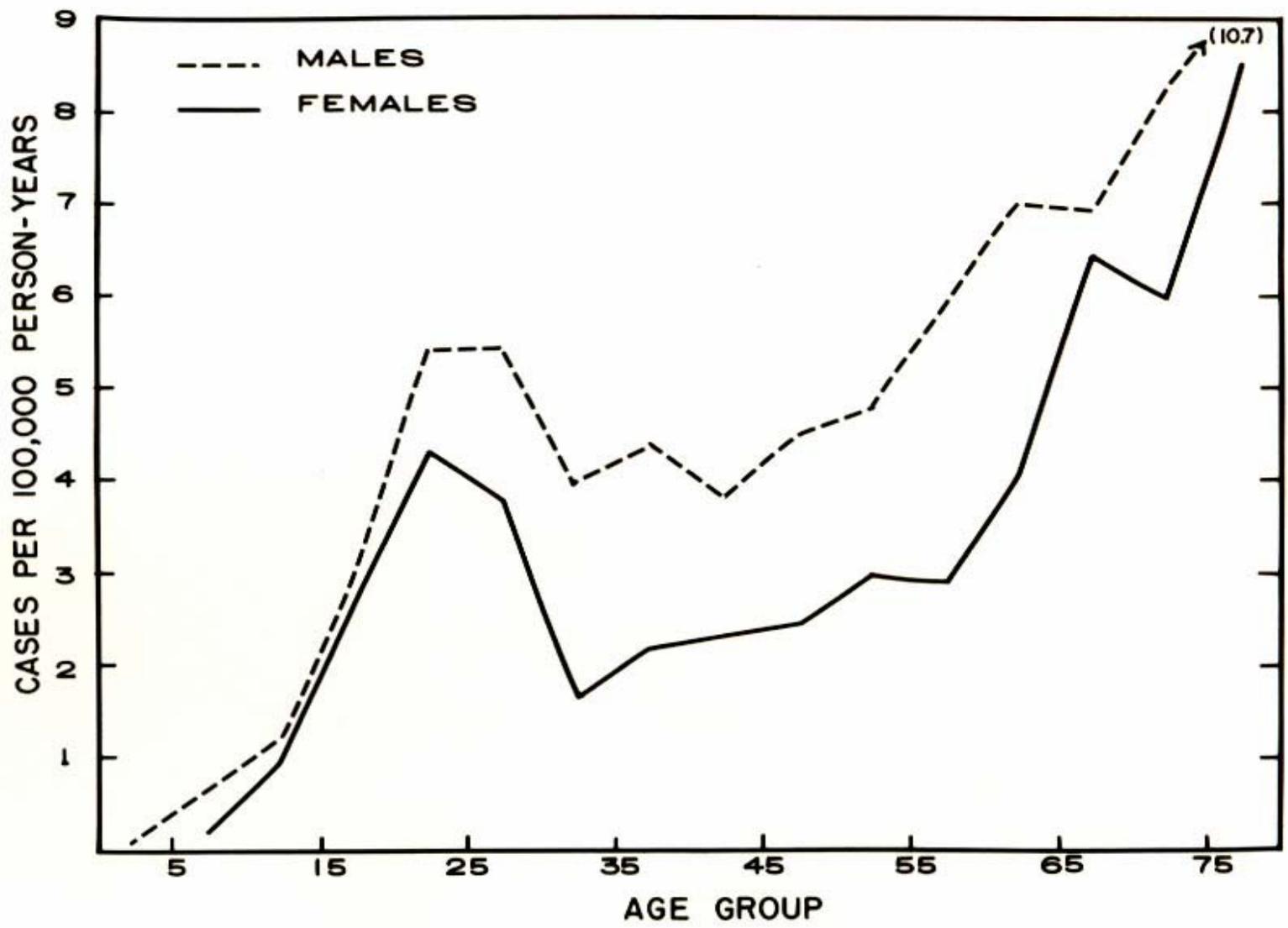
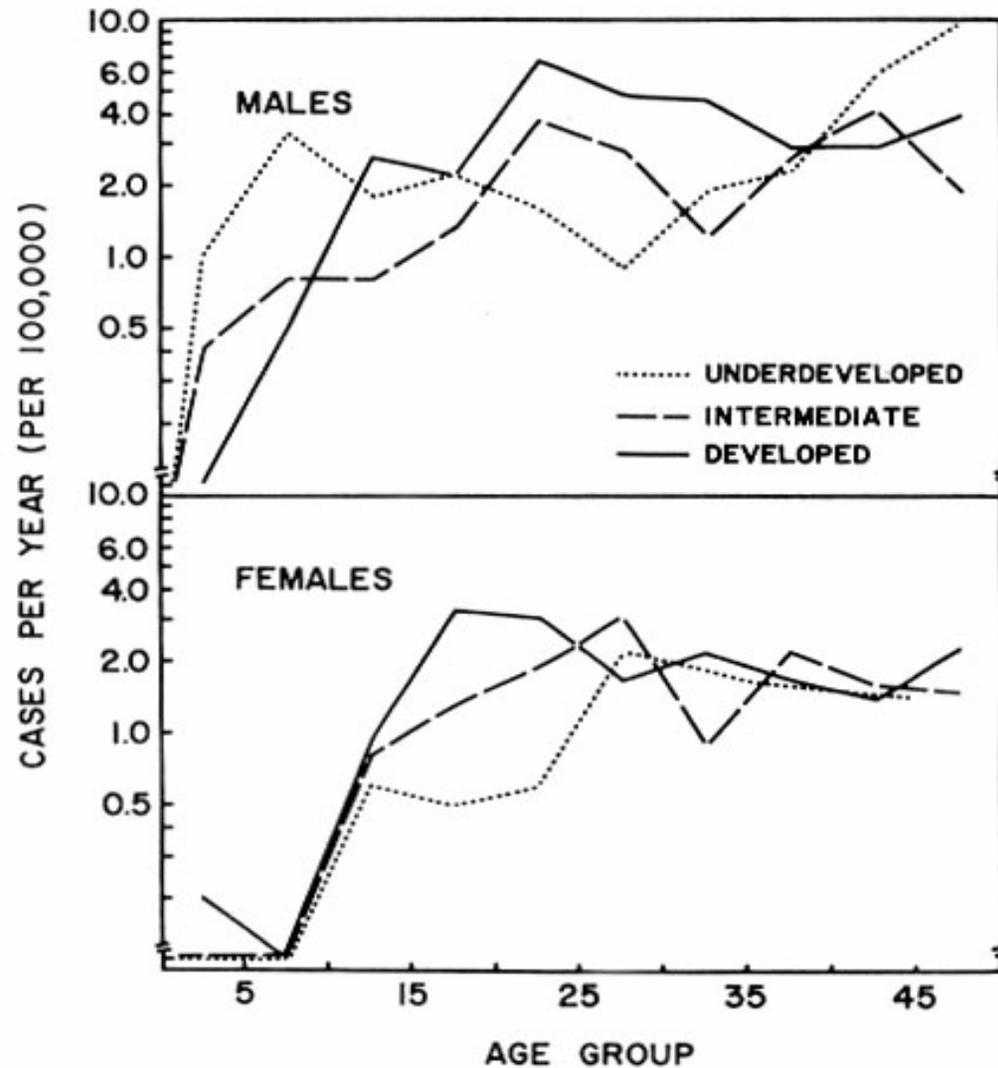


**“My 30-year *love affair* with
Hodgkin’s lymphoma:
Lessons learned”**

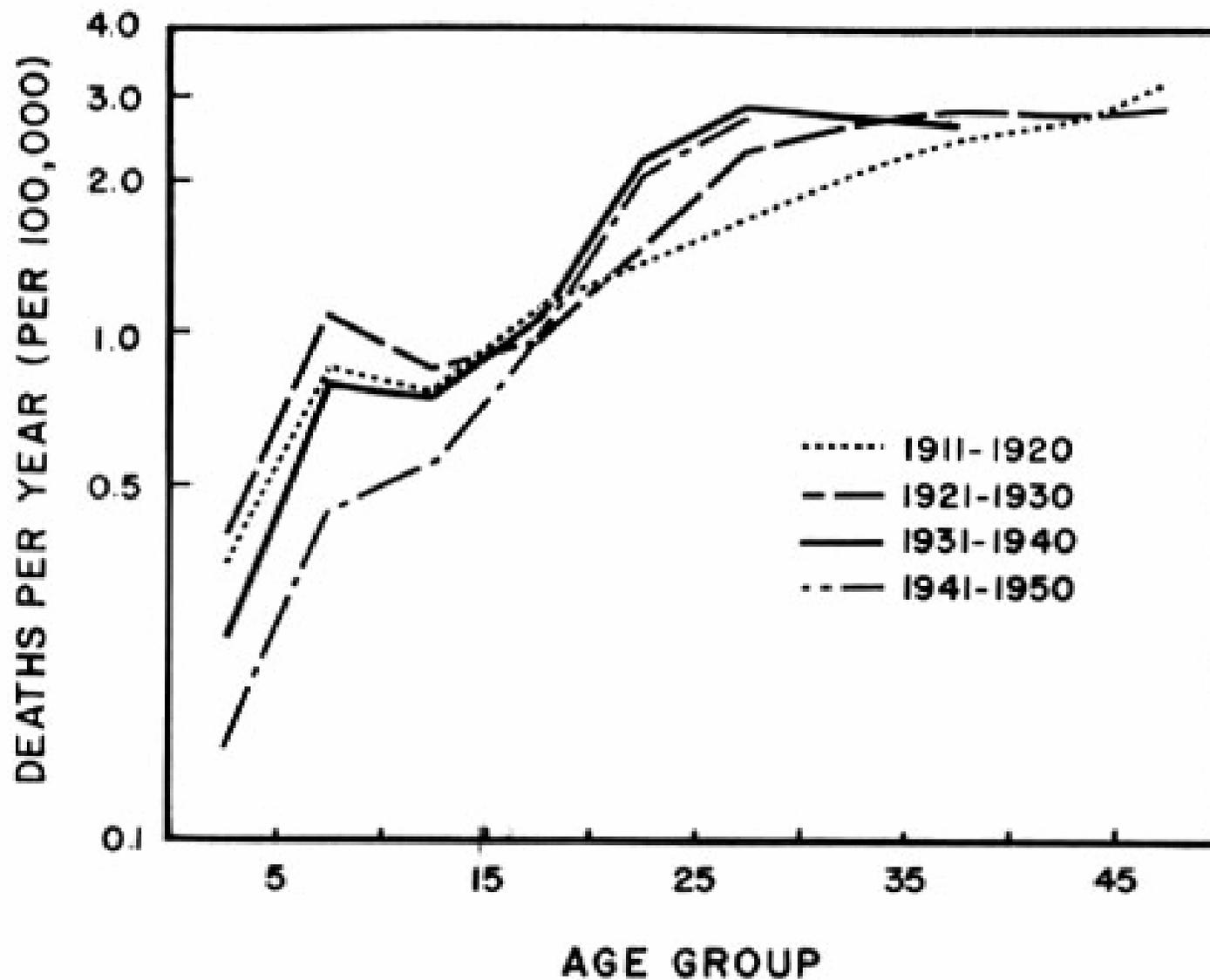
Nancy Mueller, ScD
Harvard School of Public Health



Third National Cancer Survey: US Incidence Data (1969 - 1971)



Age-specific incidence rates of HL by level of economic development by gender. Developing – Cali, Columbia (1962-1966); intermediate – Slovenia (1961-1965); developed – Connecticut (1960-1962). (Correa & O'Connor)



Age-specific mortality rates of HL for successive 10-year birth cohorts of males in England and Wales.

Serendipitous Finding

Sibship size modified the association between tonsillectomy and HL in a case-control study.

Hypothesis

- HL is associated with age of infection with a common oncogenic infection
- EBV was the prime candidate

Funded Research

- 1970s: Population based case-control study
 - Established inverse association with sibship size and young adult HL
- 1980s: International collaboration of serum banks with pre-diagnosis specimens
 - Established that abnormal EBV antibody profile preceded diagnosis years before diagnosis

Conclusions

- Hodgkin's lymphoma was caused by a "delayed" severe infection with the EBV in young adults, while HL in early childhood was due to early severe infection with EBV,

BUT

- No molecular evidence of EBV in HL tissue had been reported.

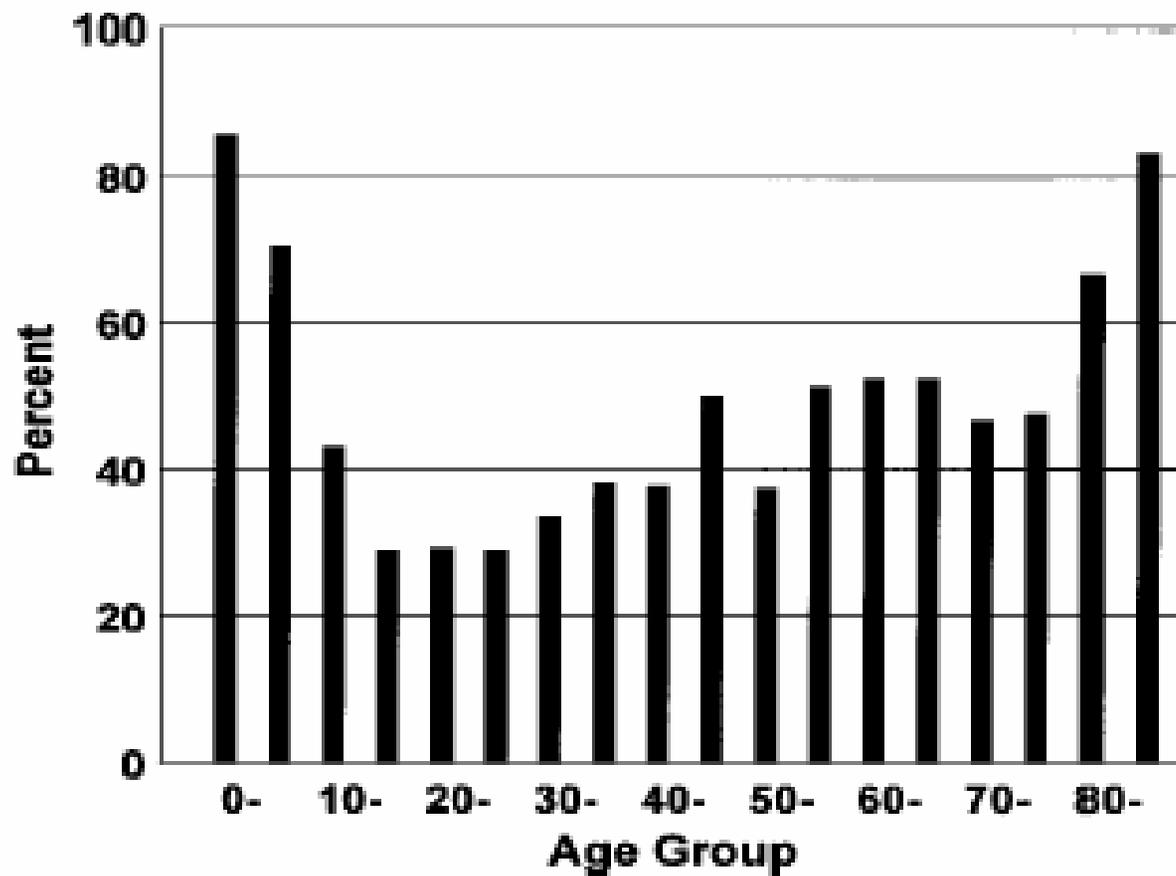
Breakthrough

- Weiss et al (NEJM, 1989) demonstrated that clonal EBV genome was present in about 30% of HL cases

BUT

Paradox:

The characteristics of EBV-genome-positive HL cases are almost the mirror image of that predicted by HL epidemiology.



Percentage of EBV-positive patients in each 5-year age group. (Glaser et al, Int J Cancer, 1997)

Hypothesis

- EBV plays a causal role in all HL, but is selectively lost in patients with adequate immune function.

Funded Research

- Mid-1990s- : Program Project with population-based case-control study, cohort study on pre-diagnosis specimens, and functional immunologic analyses to EBV infection in EBV(+) and EBV(-) cases.

Conclusions

- We found no evidence that EBV plays a role in the etiology of EBV(-) HL.
- EBV(+) and EBV(-) younger cases do not appear to differ in their susceptibility to late infections, including EBV.
- EBV (-) HL may be due to another viral infection with a similar transmission pattern to EBV, and with a greater oncogenic potential in immune competent persons.

Why devote one's scientific energy to a rare cancer?

- They cause human suffering
- They are seductive, intriguing problems to be solved

What are the difficulties?

- Few epidemiologists in field
- Few basic scientists interested in collaboration
- Small number of cases
- \$\$ -Low priority in peer review/
few advocates

Lessons Learned

Lesson 1

- Network with other epidemiologists in the field
- Network with epidemiologists working on similar/related diseases

Lesson 2

- Collaborate!
 - with basic scientists
 - with clinicians
 - with pathologists

Lesson 3

- Do parallel research on similar diseases

Warning!

- Case-control studies are increasingly difficult to carry out
- AND they may impede your academic health

The Role of NCI

- Foster networking among epidemiologists
 - “Interlymph”
- Foster interdisciplinary research
 - Comprehensive Cancer Centers
 - SPOREs
- Target \$\$\$

What's the reward?

- The opportunity to make a difference

It's a labor of love!