CHAPTER 42

Similarities in the IHD and Cancer Findings: Tumors in Both Diseases?

Part 1. List of Epidemiological Similarities Found for IHD and Cancer
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Part 3. The Suspicion of Multiple Mini-Tumors in Ischemic Heart Disease

• Part 1. List of Epidemiological Similarities Found for IHD and Cancer

The nature of epidemiology is such that it supplies circumstantial evidence about causation ("who done it"). Rarely is a single piece of epidemiologic evidence capable of PROVING causation or validating an hypothesis. Like circumstantial cases in criminal law, a case based on epidemiology grows stronger with each additional piece of supporting evidence. "What is the chance that all these observations would occur together, if the suspect is INNOCENT? What other explanation fits the COMBINED observations?"

Below, as a convenience, we list the similar epidemiologic observations uncovered in this book with respect to Ischemic Heart Disease and Cancer.

1a. Positive, Unmistakable Dose-Response with PhysPop at Mid-Century

At approximately mid-century, both IHD and cancer MortRates for each sex separately, by Census Divisions, have a positive and irrefutable dose-response relationship with PhysPops (numbers of physicians per 100,000 population). The maximum relationship occurs for IHD in 1950 (the first year for which we have such data), and occurs for Cancer in 1940 (the first year for which we have such data).

The MortRates used in this book include everyone (no exclusions by color or "race"). We also regressed MortRates for "whites-only" on PhysPops, and the results were barely different from the results presented in this book.

1b. Linearity and Strength of Dose-Response

For both diseases, the dose-response is linear and highly significant (Chapters 6, 7, 40, and 41). Such a dose-response for IHD is what elicited Hypothesis-2 in the first place:

	R-squared Males	Coef/SE Males	R-squared Females	Coef/SE Females
IHD, 1950:	0.95	11.24	0.87	6.75
Cancer, 1940:	0.95	11.63	0.86	6.58

It deserves emphasis that the IHD and cancer dose-responses with PhysPop are NOT HYPOTHETICAL. They are real-world facts, as are the other observations listed below. And all of them arise from neutral, objective databases --- in contrast to some databases in which radiation dosage has been retroactively revised and in which dose-cohorts have been shuffled, pruned, and augmented AFTER follow-up results are known.

1c. High Fractional Causation by PhysPop of the Entire MortRate

For both diseases, the central estimate is high and far from negligible, for the fraction of the entire MortRate due to PhysPop and its co-factors. MortRates are "per 100,000 population."

	MortRate Males	Fraction Males	MortRate Females	Fraction Females
IHD, 1950:	256.4	79%	126.5	97%
Cancer, 1940:	115.0	90%	126.1	58%

1d. Prediction of National MortRates by PhysPop Values of 10–20 Years Earlier

A positive and significant correlation, of the MortRates of 1950 (IHD) and 1940 (Cancer) with PhysPops, begins with PhysPops of much earlier years (Boxes 1 in Chapters 6, 7, 40, and 41).

Indeed, for Cancer, the 1921 PhysPops predict the National 1940 All-Cancer MortRates (male, female) quite closely --- and the 1931 PhysPops predict the 1940 National MortRates even better (Chapter 22, Box 4).

For IHD, since our earliest MortRates are for 1950, we look first at the 1931 PhysPops. How closely do the 1931 PhysPops predict the National 1950 IHD MortRates? Quite closely, as shown below.

• 1931, IHD Males: Best-fit Equation comes from Chapter 40 (Part 2f) and the National PhysPop value comes from Chapter 22 (top of Box 4):

Predicted Male National MortRate 1950 = (Xcoef * Natl PhysPop) + Constant
Predicted Male National MortRate 1950 = (1.8540 * 125.3) + 13.58
Predicted Male National MortRate 1950 = 245.9
Observed Male National MortRate 1950 = 256.4 from Table 40-B.

• 1931, IHD Females: Best-fit equation comes from Chapter 41 (Part 2f), and National PhysPop from Chapter 22, Box 4:

Predicted Female National MortRate 1950 = (Xcoef * Natl PhysPop) + Constant
Predicted Female National MortRate 1950 = (0.9827 * 125.3) + (-5.1)
Predicted Female National MortRate 1950 = 118.0
Observed Female National MortRate 1950 = 126.5 from Table 41-B.

1e. Distinction of IHD and Cancer from All Other Causes of Death

Ischemic Heart Disease and Cancer behave alike, when they "select themselves out" from other causes of death, with respect to their mid-century dose-responses with PhysPop. At mid-century, IHD and Cancer each have a highly significant and POSITIVE correlation with PhysPop. By contrast, the dose-response at mid-century between PhysPop and NonCancer NonIHD MortRates is significant and NEGATIVE (Chapter 25, Box 1; subsets are summarized in Chapter 38, Box 1). In terms of a relationship with PhysPop, Ischemic Heart Disease and Cancer clearly do not belong with the other causes of death. They belong with EACH OTHER.

This is a remarkable finding. In Census Divisions where there were more physicians per 100,000 population, the populations at mid-century fared WORSE with respect to IHD and Cancer than did the populations in Census Divisions with fewer physicians per 100,000. Yet simultaneously, populations in high-PhysPop Divisions fared BETTER than populations in low-PhysPop Divisions, with respect to the combination of all OTHER causes of death.

• Part 2. Which Aspect of Physician-Density Deserves the Blame?

Strong dose-responses are widely acknowledged to be strong presumptive evidence of causation, unless shown otherwise. For both Ischemic Heart Disease and Cancer, the strong dose-responses between MortRates and PhysPop, by Census Divisions, point to variation in PHYSPOP as the cause of variation in DEATH RATES (Chapter 5, Part 5a).

So we must ask: WHICH aspect of physician-density can be the cause of the observed variation in mortality?

Fortunately, we do not have to guess randomly at the answer. For Cancer, the evidence points clearly to RADIATION from medical procedures as the culprit (Chapter 22, Part 6). Both common-sense and evidence support the premise that the more physicians per 100,000 population, the more radiation procedures per 100,000 population will be ordered (Chapter 3, Part 1a). In addition, there is separate and solid evidence that:

• - Ionizing radiation is a uniquely powerful mutagen, capable of inducing every known kind of mutation, especially the complex types which --- quite unlike routine DNA damage from endogenous free radicals --- often elude successful repair (Chapter 2 and Appendices C and D).

• - There is no threshold dose with respect to the induction of unrepairable genetic damage by ionizing radiation (Chapter 2, Parts 4 and 6, and Appendix-B).

• - Xrays are an even more potent mutagen than gamma rays, per dose-unit (Chapter 2, Part 7).

• - Ionizing radiation is a proven cause of genomic instability, a feature of the most aggressive cancers (Chapter 2, Part 4b, and Appendix-D).

• - Most kinds of human cancer are inducible by ionizing radiation (Chapter 2, Part 4c).

But what about Ischemic Heart Disease?

• Part 3. The Suspicion of Multiple Mini-Tumors in Ischemic Heart Disease

In the epidemiologic features listed above in Part 1, Ischemic Heart Disease and Cancer behave like each other --- and NOT like most other causes of death. Those similarities between the two diseases are so striking that --- even if we knew nothing else about either disease --- we would suggest that the disease called Ischemic Heart Disease is closely related in etiology with the set of diseases called All-Cancers-Combined.

3a. Radiation-Induced Mini-Tumors in the Coronary Arteries

Because solid Cancers are characterized by tumors and generally by multiple genetic mutations (inherited and/or acquired), we propose the second part of Hypothesis-2:

Radiation-induction of mutations in the coronary arteries, resulting in dysfunctional clones (mini-tumors) of smooth muscle cells, is the probable mechanism by which medical radiation contributes causally to Ischemic Heart Disease.

Such a concept ought to be testable by pathologists and molecular biologists. And indeed, long before our study here, a few investigators have done work which leads them to say that multiple mini-tumors DO exist in atherosclerotic lesions of the coronary arteries (Chapter 44, Part 8).

3b. Evidence that Ionizing Radiation Induces Non-Malignant Tumors

A central feature of both malignant and non-malignant tumors is inappropriate proliferation by cells, where proliferation serves no beneficial purpose. If the net balance between cell-division and cell-death is very largely under genetic control, one might expect a potent mutagen, like ionizing radiation, to cause non-malignant tumors as well as malignant ones.

The evidence, that ionizing radiation can induce NON-malignant tumors (as well as malignancies) in humans, is compelling for thyroid nodules and adenomas, and parathyroid adenomas (Gofman 1981, pp.189-197, + BEIR 1990, pp.289-292 and pp.321-323, + Shore 1993, + Wong 1993). For non-malignant tumors of the stomach, a recent analysis of the Hiroshima-Nagasaki LifeSpan Study reveals a positive dose-response between bomb-dosage and such tumors (Ron 1995). For myoma uteri (a non-malignant tumor of the womb), a statistically significant excess in bomb-exposed females has been reported from the Hiroshima-Nagasaki Adult Health Study (Wong 1993). A study of medical xrays finds excess non-malignant skin tumors (as well as malignant ones) in irradiated medical patients (Ron 1991).

It would be hard to assess how many grants have ever been issued to LOOK for radiation-induced non-malignant tumors in various other organs. A lack of evidence may mean simply that there has been little support for such inquiries. With respect to the coronary arteries, we doubt very much that grants have been issued to look for radiation-induced mini-tumors in such arteries.

3c. Hypothesis-2: Its Two Parts Are Independent of Each Other

If tumors are a feature of BOTH Cancer and Ischemic Heart Disease, it would explain why IHD MortRates respond to PhysPop in the same way that cancer MortRates respond to PhysPop, and why the response of both diseases to PhysPop is so different from NonCancer NonIHD MortRates. Such similarity between IHD and Cancer is a "smoking gun" which deserves attention, as a starting point for further inquiry into the second part of Hypothesis-2.

There is a popular adage about similarities. The adage, which is just a variant on Ockham's Razor (Chapter 22, Part 6a), urges human beings not to scorn an obvious explanation: "If it walks like a duck, and if it quacks like a duck, and if it looks like a duck, it probably is a duck."

Ionizing radiation can induce genetic mutations and tumors. These two well-established facts may suffice to explain the findings in this book, that variation in medical radiation controls variation in the MortRates from Ischemic Heart Disease, by Census Divisions. Chapters 43 through 46 discuss how the tumor hypothesis fits into the existing knowledge about the causes of Ischemic Heart Disease. Time will tell if the second part of Hypothesis-2 is valid, but only if appropriate studies are done.

Meanwhile, the epidemiologic observations provided in this book stand independently, on their own, as evidence in favor of the first part of Hypothesis-2: Medical radiation, received even at very low and moderate doses, is an important cause of Ischemic Heart Disease.

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