Cancer clusters

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Contents

It would be helpful for you to have read the document From radiation dose to cancer risk.

Introduction

There is anecdotal evidence of rare cancers among those who lived [1] downwind of the Rocky Flats plant during its operations, as indicated by the health survey health survey solicitation from the Rocky Flats Downwinders: "If you were a resident of the areas circumscribed by the boundaries of Highway 7/168th/Arapahoe Avenue on the north, I-25 on the east, Colfax Avenue on the south, and Highway 93 on the west (see map) from 1952 to the present day we invite you to take the health survey." Assuming this means continuously from 1952 through the present and not at *any* time in this period, respondents have lived through the 1957 and 1969 fires and whatever blew off the Rocky Flats plant during its period of operation (through 1989 for Pu production).

It is worth examining briefly the issue of 'cancer clusters' and how they are identified since imagined (or possibly disingenuous) uncertainty about this issue is being used as a delaying tactic by those opposing public access to the Rocky Flats National Wildlife Refuge:

- "What is safe? What is an allowable level of plutonium," asked Alesya Casse, an outspoken activist

against projects surrounding Rocky Flats. 'Test first for plutonium': Denver CBS affiliate, May 2017

- "There are no studies to review the effects of plutonium exposure on the residents of surrounding towns while Rocky Flats was producing plutonium triggers . . . a formal health study has not been conducted since Dr. Carl Johnson's report in the 1980s (which states that workers and local residents had higher than normal rates of cancer, brain tumors and leukemia)." STOP the building. . . : www.change.org; 2014?
- "The area around Rocky Flats, the buffer zone, has not been adequately assessed. . . There is a need to test for fresh data with independent oversight by knowledgeable public."—Paula Elofson-Gardin, quoted in Denver Post, June 2017.

Those who have already read the documents on this website are in a good position to assess whether the area around the Wildlife Refuge (and within it) are well-characterized or not, and whether or not the health effects of plutonium are understood.

Cancer clusters

A 17-page 2012 article [2] entitled *Cancer clusters in the USA: What do the last twenty years of state and federal investigations tell us?* surveyed 428 investigations (including 567 distinct cancers) in all 50 states (and Washington DC).

They conclude

> At a time when cancer research funding is scarce, it is time to pose the following questions: Given the outcomes of community cancer clusters investigations over the past 40 years, is it appropriate that we devote more resources to staying the same path we have been following, using the same hypotheses and tools? Based on what we know about the likelihood of confirming a cancer cluster and then identifying a cause looking only at environment—defined in the same way that it has generally been defined over the previous 40 years—without broadening our thinking, can we expect a different outcome when we look back 10 or 20 years from now? We suggest that the answer to these questions is "no" and that simply using the same approach, but with

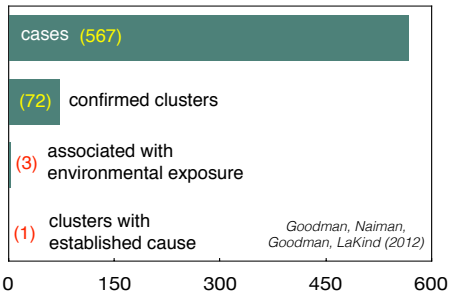

Figure 1: Number of cancer clusters whose cause was established; data of [2]

> expending more resources will not get us closer to understanding cancer etiology. Certainly the results of this review indicate that despite the large number of geographic or community cancer cluster investigations and the amount of resources already expended, the likelihood of a successful cancer cluster investigation where the etiology of disease is discovered is extremely small. With four decades' worth of cancer cluster investigations revealing little regarding cancer cluster etiology and prevention, it is time to recognize the shortcomings of the current approach to investigating cancer clusters investigations that originate with a perception of increased rates of cancer in a community and to begin a multidisciplinary national dialogue on more creative, innovative approaches towards understanding when and why cancer and other chronic diseases may cluster in time and space. In our view, the dialogue will need to include a focus on testable hypotheses based on well-defined measurable environmental exposures (e.g. concentrations of halogenated chemicals rather than "groundwater contamination"), specific disease outcomes (e.g., glioblastoma multiforme as opposed to "brain cancer"), methods for improving current and historical estimates of exposures and a broader examination of "environment" that would include biological, socioeconomic and lifestyle related factors.

In short: based on 40 years of experience, it is so difficult to identify cancer clusters that money is better spent elsewhere. Much more precise specification of cancers based on testable hypotheses is needed.

Although clusters of high *cancer mortality rates* [3] do exist, they have been documented at a regional level (*e.g.*, clusters of counties in Kentucky West Virginia, Alabama, or along the Mississippi River) and for fairly common cancers (*e.g.*, breast cancer or lung cancer).

Characteristics of cancer clusters

Sir Austin Bradford Hill proposed [4] in 1965 a set of 9 criteria to (quoting Wikipedia) "provide epidemiological evidence of a causal relationship between a presumed cause and an observed effect." Again quoting Wikipedia,

1. *Strength* (effect size): A small association does not mean that there is not a causal effect, though the larger the association, the more likely that it is causal.
2. *Consistency* (reproducibility): Consistent findings observed by different persons in different places with different samples strengthens the likelihood of an effect.

3. *Specificity:* Causation is likely if there is a very specific population at a specific site and disease with no other likely explanation. The more specific an association between a factor and an effect is, the bigger the probability of a causal relationship.

4. *Temporality:* The effect has to occur after the cause (and if there is an expected delay between the cause and expected effect, then the effect must occur after that delay).

5. *Biological gradient:* Greater exposure should generally lead to greater incidence of the effect. However, in some cases, the mere presence of the factor can trigger the effect. In other cases, an inverse proportion is observed: greater exposure leads to lower incidence.

6. *Plausibility:* A plausible mechanism between cause and effect is helpful (but Hill noted that knowledge of the mechanism is limited by current knowledge).

7. *Coherence:* Coherence between epidemiological and laboratory findings increases the likelihood of an effect. However, Hill noted that "... lack of such [laboratory] evidence cannot nullify the epidemiological effect on associations".

8. *Experiment:* "Occasionally it is possible to appeal to experimental evidence".

9. *Analogy:* The effect of similar factors may be considered.

In the context of radiation-induced health problems, for example, these criteria (which bear on the evaluation of cancer clusters as well) would suggest (i) no cancer until the latency (incubation) period for a given cancer type, (ii) a higher cancer rate in areas with higher demonstrated contamination levels, because cancer is a 'stochastic' rather than a 'deterministic' effect of radiation exposure, (iii) a plausible connection (*e.g.*, employment at Rocky Flats or enough years living downwind to have accumulated a significant dose), (iv) cancers or birth defects

demonstrated via other work to correlate with radiation exposure.

Latency times for cancers

As mentioned above, a 'latency time' or incubation period separates [5] the first exposure to a carcinogen from the diagnosis of cancer. Most studies must 'look back' in time to follow the development of cancers in a large population unless the cancer is extremely well understood. Table 1 shows commonly-accepted approximate latency times for broad classes of cancers.

cancer	minimum latency (y)	radiation-induced latency (y)
leukemias and lymphoma	0.4	4-8
thyroid cancer	2.5	4-5
solid cancers	4	15-60

Table 1: Range of latencies (in years) for classes of cancers. Minimum latencies from [6]; leukemias from [7], others from [8].

It is important to note that *minimum* latencies are often determined by exposure to volatile organic compounds such as vinyl chloride, formaldehyde, or other toxic chemicals rather than due to radiation exposure. (This may be an important factor to those who lived downwind of Rocky Flats.) The document Recent developments in low-dose radiation response should be consulted to understand the confounding effects of very low-dose radiation, which may *increase* the latency period for some cancers. For example, in experiments on cancer-prone, radiation-sensitive mice it was found that [9]

> All tumors are therefore assumed to be of spontaneous origin. However, a 10 mGy exposure reduced the risk of both lymphomas and spinal osteosarcomas by significantly increasing tumor latency, indicating that the main in vivo effect of a low-dose exposure is a reduction in the rate at which spontaneously initiated cells progress to malignancy. The effect of this adaptive response persisted for the entire life span of all the animals that developed these tumors. Exposure to 100 mGy delayed lymphoma latency longer than the 10 mGy exposure. However, the 100 mGy dose increased spinal osteosarcoma risk by decreasing overall latency compared to unexposed control mice.

Resources for identifying cancer clusters

The CDC maintains [10] a page of links [11] including others maintained by the National Cancer Institute and other agencies. A communications 'toolkit' targeting various audiences and providing literature resources, sample cancer cluster scenarios, and case studies is available [12]. A recent NSF-sponsored project resulted in a guide [13] to assist citizens in assessing cancer trends in their areas and determining whether more formal study is warranted.

There is a software package (freely downloadable on registration) intended to facilitate identification of cancer clusters, at the SaTScan website [14]. A case study [15] used SaTScan© to assess a brain cancer cluster alarm in Los Alamos, NM (where most of the workforce is employed at Los Alamos National Laboratory). The authors concluded "The excess of brain cancer in Los Alamos falls well within the realm of chance. This finding coincides with the final conclusions of the New Mexico Health Department, which used a statistically less formal approach".)

Another 2014 article [16] examined pediatric cancers in Florida over the 2000-2014 period; cancer clusters in south Florida in regions of populations from 515,000 (for leukemias), 670,000 (for lymphomas), to 1.22 million (for brain cancers) were identified. The second document describes in some detail how SaTScan© is used. A cautionary tale [17] from 2017 indicates that 'citizen science' "often lacks the careful critical analysis that can identify with more precision and certainty what the real threats actually are. Citizen science tends to be the product of the instinctive way we perceive the world in our fundamental and constant drive to avoid danger. It's a hint, a clue, and often an important first step, but it is not the answer. . . . Most of the time, though, quick conclusions about disease clusters and their causes don't hold up to careful scrutiny. They are based on the leaps and assumptions we

are programmed to make quickly and instinctively. They are a first reaction to the initial evidence, which must then be assessed using more careful critical thinking. That takes time and effort and open minds–not the default way the brain prefers to operate."

For better or for worse, radiation exposure policy is *not* set by the experiences of relatively small numbers of possibly sensitive people; it is (and of necessity needs to be) set by epidemiology–the response of large numbers of people.

Even though cancer clusters (even for common cancers unrelated to radiation)) are very hard to prove, under the right circumstances they can provide detailed information about very low-dose radiation and its impact on humans. "Whatever you do will be insignificant [statistically], but it is very important that you do it."–Mahatma Ghandi.

Takeaway messages

- There is anecdotal evidence of exotic cancers among people who lived downwind of the Rocky Flats plant during its operation (through 1989).
- Arguments by some who object to public use of the RF Wildlife Refuge continue to maintain that 'not enough is known' about the effects of Pu exposure on those living downwind, or that the buffer zone has not been adequately assessed are, in the light of the documentation available for Rocky Flats, a delaying tactic.
- Epidemiologists acknowledge that the search for cancer clusters is not an effective use of personnel or government funds.
- The signatures of cancer clusters were briefly reviewed.
- Resources for identifying cancer clusters were discussed.

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bibliographic entry will fire up our Web browser and take you to where the original file is available.