



Confirmation that Hermann Muller was dishonest in his Nobel Prize Lecture

Edward J. Calabrese¹

Received: 19 July 2023 / Accepted: 26 July 2023

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Abstract

In his Nobel Prize Lecture of December 12, 1946, Hermann J. Muller argued that the dose–response for ionizing radiation-induced germ cell mutations was linear and that there was “no escape from the conclusion that there is no threshold”. However, a newly discovered commentary by the Robert L. Brent (2015) indicated that Curt Stern, after reading a draft of part of Muller’s Nobel Prize Lecture, called Muller, strongly advising him to remove reference to the flawed linear non-threshold (LNT)-supportive Ray-Chaudhuri findings and strongly encouraged him to be guided by the threshold supportive data of Ernst Caspari. Brent indicated that Stern recounted this experience during a genetics class at the University of Rochester. Brent wrote that Muller refused to follow Stern’s advice, thereby proclaiming support for the LNT dose–response while withholding evidence that was contrary during his Nobel Prize Lecture. This finding is of historical importance since Muller’s Nobel Prize Lecture gained considerable international attention and was a turning point in the acceptance of the linearity model for radiation and chemical hereditary and carcinogen risk assessment.

Keywords Hermann Muller · Nobel Prize · Linear dose–response · Mutation · Scientific misconduct · Cancer risk assessment

Introduction

In 2011 (Calabrese 2011a), I published a provocative paper that claimed that the Nobel Prize recipient, Hermann J. Muller deliberately deceived the Nobel Prize audience and the world with his Nobel Prize acceptance speech when he asserted that the scientific and regulatory communities should no longer follow the threshold model but needed to adopt a linear dose–response model for hereditary and cancer risk assessment for ionizing radiation. This paper and a follow-up (Calabrese 2012) analysis generated a strong reaction that was mostly about trying to preserve or denigrate the reputations of the highlighted scientists (Baskin 2011; Crock 2011). Over the next decade follow-up research has provided considerable documentation for numerous other examples of scientific deception and research misconduct by Muller and other leaders of the radiation genetics community

of the 1940–1960s era, all linked to a desire to establish the LNT model for hereditary and cancer risk assessment (Calabrese 2015, 2017, 2019, 2022a, 2023, b; Calabrese and Selby 2022; Selby and Calabrese 2023). The influence of these deceptive practices, and at times, scientific misconduct, has been institutionalized in the philosophies, policies, and practices of regulatory agencies throughout the world, supporting the disturbing premise that “regulatory” science, in contrast to experimental and observational science, is not self-correcting. The present paper revisits the original assertion that Muller was deliberately deceptive during his Nobel Prize Lecture with new information provided by confirmatory recollection provided by a leading radiation researcher, Robert L Brent, in a paper that was published in 2015 in the journal *Health Physics*, but only recently discovered by the author while reading the Brent paper. The Brent comments provide independent, relevant, reliable, and non-biased confirmatory support for the Calabrese (2011a, 2012) comments that were critical of Muller in his Nobel Prize Lecture.

✉ Edward J. Calabrese
edwardc@umass.edu

¹ Department of Environmental Health Sciences, Morrill I,
N344, University of Massachusetts, Amherst, MA 01003,
USA

Summarization of the Muller Nobel Prize Lecture issue

In August, 1946 Ernst Caspari, a Ph.D. researcher working under the direction of professor Curt Stern as part of the Manhattan Project at the University of Rochester in New York State, USA, reported to Stern that chronic exposure to low doses (52.5 R)/dose rates (2.5 R/day) of ionizing radiation (gamma rays from radium) displayed a threshold dose–response for transgenerational gene mutation in *Drosophila*. It has been now well documented that Curt Stern, a strong supporter of the LNT dose–response model, rejected the Caspari threshold interpretation, asserting that these findings were a type of “false negative” because the Caspari control group values were aberrantly high leading to an incorrect threshold conclusion (Calabrese 2011b, 2013a, b, 2015, 2019). However, Caspari rebutted the assertion of Stern, showing that his control group data were consistent with the published literature of several well-respected *Drosophila* radiation geneticists. Consequently, to his credit, Stern backed down, dropping the aberrant control group argument as a basis to reject the threshold interpretation (Calabrese 2013a, b, 2015).

Despite his decision to drop the control group matter, Stern remained committed to minimizing or neutralizing the threshold supportive findings of Caspari. Stern attempted to achieve this LNT-supportive goal, at least in part, with the following strategy. He collaborated with Caspari to write a manuscript for publication that used the manuscript’s discussion to argue that the data should not be used/accepted until it could be determined why these findings disagreed with the single dose/high dose rate exposure-LNT-supportive *Drosophila* results of Warren Spencer who also worked with Stern (Calabrese 2011b, 2015, 2022a, 2023; Spencer and Stern 1948).

This approach of Stern was another type of dishonest, strawman-like strategy as their discussion (Caspari and Stern 1948) failed to report that the Spencer and Caspari studies were methodologically quite different with at least 25 notable differences (Calabrese 2011b). Males, for example, were treated in the Spencer study whereas females were treated by Caspari; gamma rays from radium were used by Caspari while Spencer employed X-rays; diets were also considerably different with the Caspari studies imposing a diet preventing ovulation for 21 days whereas this was not the case with the Spencer study; there was also a large difference in temperature (i.e., 18 versus 25 °C) between the two studies, among other experimental differences. These experimental differences made it practically impossible to properly compare the findings of the two experiments (see Calabrese 2011b). Yet, Caspari and Stern (1948) argued it was necessary to determine why the

results between the studies were different before consideration could be given to the Caspari findings. However, this was not the case with the LNT-supportive Spencer study which had no such restrictions. The approach of Stern was to editorially blunt the utility and influence of the Caspari paper while nonetheless permitting him a journal publication for career advancement purposes.

In addition to the experimental differences between these two studies, the Spencer and Stern (1948) study had fundamental unacknowledged flaws that severely compromised its scientific validity and application for risk assessment. For example, the Spencer and Stern (1948) study in some critical instances combined the data from groups of flies with the same total dose but different dose rates (see Calabrese 2023). This action by Spencer and Stern (1948) was perplexing since this was the principal issue that was being tested. That is, was radiation mutation risk better predicted via total dose or dose rate? By combining different dose rate groups into a single total dose group, Spencer and Stern (1948) effectively invalidated the comparison to be tested. Numerous other experimental limitations have also been documented for the Spencer and Stern (1948) study (Calabrese 2011b, 2022a, b). Yet, one might ask how did this manuscript, therefore, get published in the established journal, *Genetics*. The answer may be found in the fact that Curt Stern was the editor-in-chief at the time and there is strong evidence that the manuscript was never sent out for review (Calabrese 2019).

The challenge of the threshold supporting the Caspari data became highly problematic for the LNT-supportive Stern and colleagues, such as Muller, as these findings could strongly counter their support for the LNT dose–response model for radiation mutation. “The Caspari problem”, as Stern would characterize the situation (Stern Letter to Edward Novitski, March 19, 1948), would compel Stern to attempt to replicate the Caspari findings, requiring additional funding for 2 years of research on this dose–response question. However, such follow-up research activities again came with discouraging outcomes. In fact, the follow-up activities by Stern and a new graduate student, Delta Uphoff, made a fundamental error in the design phase of the research project which led to incorporating two simultaneous variables as they tried to test the Spencer and Caspari research, again resulting in a failed study (Calabrese et al. 2023). The only data that remained unscathed in the Manhattan Project *Drosophila* studies were those of the threshold supporting Caspari study (Caspari and Stern 1948; Calabrese 2023).

Of importance in the timing sequence of the research findings and Muller’s Nobel Prize Lecture is that Stern sent Muller, then at the University of Indiana, the Caspari and Stern manuscript via mail on November 6th, 1946 which Muller acknowledged in a letter to Stern on November 12th, 1946. The November 12th letter of Muller praised Caspari as a researcher and urged Stern to obtain additional grant

funding to test the threshold mutation findings (Calabrese 2015, 2019).

One month later, on December 12, 1946, Miller gave his Nobel Prize Lecture, during which he failed to mention the findings of Caspari which challenged the LNT model hypothesis. However, Muller prominently cited a 1939 dissertation he directed at the University of Edinburgh by Ray-Chaudhuri which has now been discredited (See Calabrese 2023) due to a series of experimental failings, possibly due, at least in part, to the fact that Muller was unavailable to the student, being in the United States (US) the entire time that the dissertation research was conducted. Muller (1946) used the Nobel Prize Lecture to proclaim that the data of Ray-Chaudhuri: "...leave, we believe, no escape from the conclusion that there is no threshold". This pronouncement and subsequent presentations by Muller made it clear that the threshold dose–response model was scientifically compromised while the LNT model should now become the accepted approach, finally fulfilling such a proposal that had made some 16 years earlier when he offered his version of the LNT model with the articulation of his Proportionality Rule (Muller 1930).

The Robert Brent perspective: the Stern telephone call to Muller

In light of these historical developments and their scientific implications, significant new insight has been shed on why Muller failed to cite the threshold supporting Caspari data. This insight comes from recently discovered comments in a 2015 paper by Robert L. Brent, professor at Thomas Jefferson University, a highly accomplished physician researcher on the effects of radiation on the embryo and fetus. Set within a major review of the literature on the effects of radiation on the embryo/fetus, the 88-year-old Brent (2015) stated that:

“as an undergraduate student at the University of Rochester, I worked at the university’s radiation embryology and genetics division of the Atomic Energy’s facility and was fortunate to have attended elective genetics seminars with Donald Charles, Ph.D., a mathematician and geneticist and with Curt Stern, Ph.D., a famous geneticist...

I met once a week on Friday morning for an hour with either Dr. Charles or Dr. Stern...During one session with Dr. Stern, he related an interaction that he had with Hermann Muller who received the Nobel Prize in 1964 [1946] for discovering that X-irradiation could produce inherited mutation in *Drosophila*. Muller was to receive the Nobel Prize in 1964 [1946] and he sent a copy of his letter of acceptance to Dr. Stern which contained important new information; namely, that protraction or fractionation of X-radiation did not reduce the genetic risk [i.e., presumably the Ray-Chaudhuri study].

Dr. Stern immediately called Dr. Muller and said that he had completed fractionation experiments (i.e., the recently completed Caspari study) and that Muller was incorrect. Stern asked Muller to remove that new information from his acceptance speech; Muller refused...”.

This statement of Brent (2015) indicates that in mid-November/early December, 1946 Curt Stern supported the findings and conclusions of the Caspari study. That is, he felt that the Caspari findings were more reliable than the more limited and problematic research of the Ray-Chaudhuri study (1944). The Caspari study was the strongest and largest study to date on the topic, having made use of an array of high-level technical support staff and available scientific leadership and guidance, as well as more technical resources, important collective features that were lacking in the Edinburgh study.

Several months later in 1947, Stern engaged Muller in a series of letters concerning the validity of the Caspari control group. These letters clearly show that Muller’s extensive control group data closely matched those findings of Caspari but not those of Uphoff (Calabrese 2013a, b). In addition, multiple publications by Muller at the University of Indian during the early to mid-1950s strongly reaffirmed these 1947 statements (Calabrese 2013a, b).

Based on the Brent (2015) statement, there is now new insight indicating that Stern tried to educate and influence Muller on the content of his forthcoming Nobel Prize Lecture but failed. Muller would use the now discredited Ray-Chaudhuri dissertation data (Calabrese 2023) and support the LNT model for radiation risk assessment while ignoring the Caspari data (Caspari and Stern 1948) which strongly supported the threshold model. Why Muller chose to ignore the strong suggestions of Curt Stern for whom he served as a consultant on the Manhattan Project remains an important question. The comments of Brent provide significant new insight into the views and character of Stern concerning the credibility of the Caspari study and the decision of Muller to ignore this advice of Stern.

Placing the actions of Stern and Muller in perspective

In the case of Stern, there is the observation that he first challenged the validity of the Caspari control group. However, when Caspari presented evidence that refuted this assertion that the control group was aberrantly high, Stern appropriately reversed that initial position. However, the actions of Stern to develop a discussion for the Caspari paper that used the flawed Spencer study as the gold standard and being not willing to challenge his support for the LNT perspective until one could determine why the Spencer and Caspari studies differed suggests a high degree of

editorial bias. Yet, the inconsistent Stern saw value in the Caspari study and tried to educate Muller to its merits for possible inclusion in the Nobel Prize Lecture, replacing the Ray-Chaudhuri perspective. Even though the Caspari data supported a threshold response, and Stern strongly favored the linear dose–response model, he appeared capable of following the data, not ideology. Furthermore, several years later, Robley Evans sent Stern a final draft of his Caspari and threshold supporting paper (Calabrese 2023). Stern was highly supportive of the Evans and Caspari positions (Calabrese 2023). Nonetheless, it is apparent that Stern did not publicly challenge Muller on this most critical issue on the nature of the dose–response in the low-dose zone for radiation-induced gene mutation, even though, according to Brent (2015), Muller made a double error (i.e., retaining the Ray-Chaudhuri data while dropping the Caspari findings) during his Nobel Prize Lecture.

With respect to Muller, his interactions with Stern were consistent with his ideological obsessions concerning the LNT model. Muller also deceived the scientific community when he attacked the Caspari control group as being aberrantly high in several papers in the 1950s after sharing with Stern that Caspari’s control matched closely with his while Uphoff’s data were aberrantly low (Muller 1950a, b, 1954). These developments indicate that Muller had a strong ideological bias while Stern was able to follow the data but probably not in the presence of Muller.

The comments of Brent (2015) were stimulated by several earlier papers (Calabrese 2011a, b, 2012) that raised the question that Muller was deliberately deceptive during his Nobel Prize Lecture as he was aware of the Caspari findings and many of the limitations of the Ray-Chaudhuri dissertation (Calabrese 2022a, b). The newly discovered insights of Brent (2015) support this earlier finding.

Was the Brent perspective credible?

Finally, how accurate was the memory of Brent as he published this paper in 2015, nearly 70 years after the event. The only clear mistake by Brent in the section of relevance was stating that Stern “became the chairman of genetics at California Institute of Technology”. However, the institution was the University of California at Berkeley. He accurately remembered both Charles and Stern, their areas of expertise and that the key scientific issue related to dose rate versus total dose. He recalled that Muller planned to cite a study that did not show a dose rate effect (i.e., the Ray-Chaudhuri dissertation that Muller directed) while the Stern directed the study of Caspari that showed a dose rate effect and a dose-related threshold. From the perspective offered here, the statements of Brent were accurate for the people identified, their scientific expertise, the scientific issues, components of

the story that can be validated. Brent also related the experience to a specific class and on a specific day of the week and that the communication between Stern and Muller was via a phone call and that Muller refused the Stern suggestions. All these specific conditions persisted and were recalled. The confirmation of the event and its consistency add important credibility to the information written by Brent. Furthermore, over the course of a 70 year highly visible professional career in the area of radiation health and medicine, there is no evidence that Brent had personal, professional, or other disputes with Muller or with the content of Muller’s Nobel Prize Lecture. Thus, the statement of Brent (2015) is seen as valuable and insightful concerning key aspects of Muller’s Nobel Prize Lecture and how it occurred.

Acknowledgements EJC acknowledges longtime support from the US Air Force (AFOSR FA9550-19-1-0413) and ExxonMobil Foundation (S1820000000256). The U.S. Government is authorized to reproduce and distribute for governmental purposes notwithstanding any copyright notation thereon. The views and conclusions contained herein are those of the author and should not be interpreted as necessarily representing policies or endorsement, either expressed or implied. Sponsors had no involvement in study design, collection, analysis, interpretation, writing and decision to and where to submit for publication consideration.

Data availability Not applicable.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

References

- Baskin P (2011) Seeing value in poisons, a toxicologist takes on a late laureate. *The Chronicle of Higher Education*, October 2.
- Brent RL (2015) Protection of the gametes embryo/fetus from prenatal radiation exposure. *Health Phys* 108:242–274
- Calabrese EJ (2011a) Muller’s Nobel lecture on dose-response for ionizing radiation: ideology or science? *Arch Toxicol* 85(12):1495–1498
- Calabrese EJ (2011b) Key studies used to support cancer risk assessment questioned. *Environ Mol Mut* 52:595–606
- Calabrese EJ (2012) Muller’s Nobel Prize lecture: when ideology prevailed over science. *Toxicol Sci* 126(1):1–4
- Calabrese EJ (2013a) Origin of the linearity-no threshold (LNT) dose response concept. *Arch Toxicol* 87(9):1621–1633
- Calabrese EJ (2013b) How the U.S. National Academy of Sciences mislead the world community on cancer risk assessment: new findings challenge historical foundations of the linear dose response. *Arch Toxicol* 87(12):2063–2081
- Calabrese EJ (2015) On the origins of the linear no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith. *Environ Res* 142:432–442
- Calabrese EJ (2017) Flaws in the LNT single-hit model for cancer risk: an historical assessment. *Environ Res* 158:773–788
- Calabrese EJ (2019) The linear no-threshold (LNT) dose response model: A comprehensive assessment of its historical and scientific foundations. *Chem-Biol Interact* 301(SI):6–25

- Calabrese EJ (2022a) Key historical study findings questioned in debate over threshold versus linear non-threshold for cancer risk assessment. *Chemico-Biol Interact* 359:109917
- Calabrese EJ (2022b) Linear non-threshold (LNT) fails numerous toxicological stress tests: implications for continued policy use. *Chemico-Biol Interact* 365:110064
- Calabrese EJ (2023) Thresholds for radiation induced mutation? The Muller-Evans debate: a turning point for cancer risk assessment. *Chemico-Biol Interact* 382:110614
- Calabrese EJ, Selby PB (2022) Cover up and cancer risk assessment: prominent US scientists suppressed evidence to promote adoption of LNT. *Environ Res* 2010:112973
- Calabrese EJ, Agathokleous E, Giordano J, Selby PB (2023) Manhattan project genetic studies: Flawed research discredits LNT recommendations. *Environ Poll* 319:120902
- Caspari E, Stern C (1948) The influence of chronic irradiation with gamma-rays at low dosages on the mutation rate in *Drosophila melanogaster*. *Genetics* 33:75–95
- Crock M (2011) Attack on radiation geneticists trigger furor. *Science*, October 11, <https://www.science.org/content/article/attack-radiation-geneticists-triggers-furor#:~:text=In%20two%20recent%20papers%2C%20Calabrese,Nobel%20acceptance%20speech%20in%20Stockholm>.
- Muller HJ (1930) Radiation and genetics. *Am Nat* 64:220–257
- Muller HJ (1946) Nobel Prize Lecture. Stockholm, Sweden
- Muller HJ (1950a) Some present problems in the genetic effects of radiation. *J Cell Comp Physiol* 35(suppl 2):9–70
- Muller HJ (1950b) Radiation damage to the genetic material. *Am Sci* 38(1):32–59 (**126**)
- Muller HJ (1954) The manner of production of mutations by radiation. In: Hollaender A (ed) *Radiation biology*, vol 1. Mac Graw Hill, New York, pp 475–626 (**Chapter, 8**)
- Ray-Chaudhuri SP (1944) The validity of the Bunsen-Roscoe law in the production of mutations by radiation of extremely low intensity. *Proc Royal Soc Edinburgh* 62:66–72
- Selby PB, Calabrese EJ (2023) How self-interest and deception led to the adoption of the linear non-threshold dose response (LNT) model for cancer risk assessment. *Sci Tot Environ* xx:165402
- Spencer WP, Stern C (1948) Experiments to test the validity of the linear R-dose/mutation at low dosage. *Genetics* 33:43–74
- Stern C (1948) Letter to E. Novitski. American Philosophical Society, Stern Files, March 19

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