# Radiation Hormesis

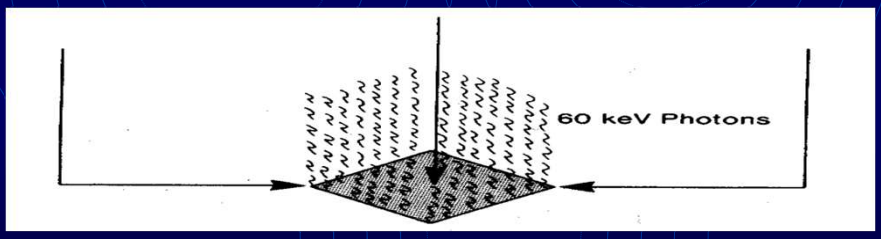
Greg Gibbs

## We Live in a Sea of Radiation:

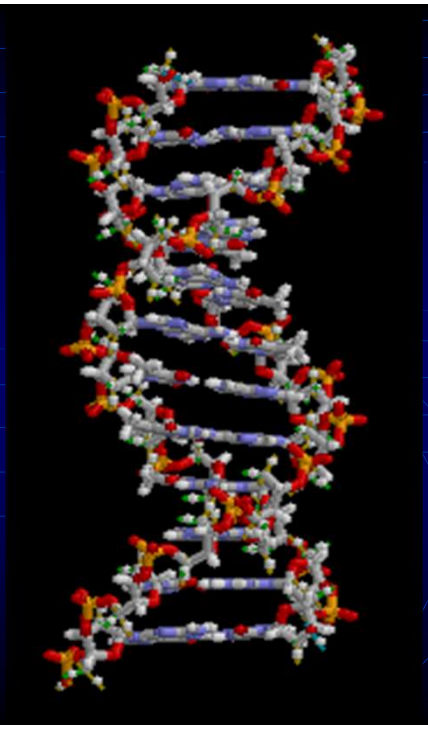
- This is not new
- Background in Colorado 3mSv/year
- Maximum Permissible Dose general public 1mSv/year
  - What this means is that when an entity produces radiation, they are allowed to irradiate the public to 1/3 of the background exposure rate (in Colorado).

# How many photons in a Sv?

Photon Fluence ($3 \times 10^{12}$ photons/cm$^2$) = Exposure (1Gy or 1Sv) = Energy Fluence ($3 \times 10^5$ ergs/cm$^2$)




So – 3 mSv/year = 10,000,000,000 (10 billion) photons/cm$^2$ or ~$2 \times 10^{14}$ (.2peta) photons on your whole body each year!



## DNA

- The carrier of all information pertinent to cell function.
- 23 molecules in each of our 37 trillion cells.
- Each DNA molecule contains between 500 thousand and 2.5 million pairs of bases.
- If the unraveled DNA was expanded to the width of a hair, one cell's worth would be 13.4 miles long.
- A lot of human DNA is shared with worms!

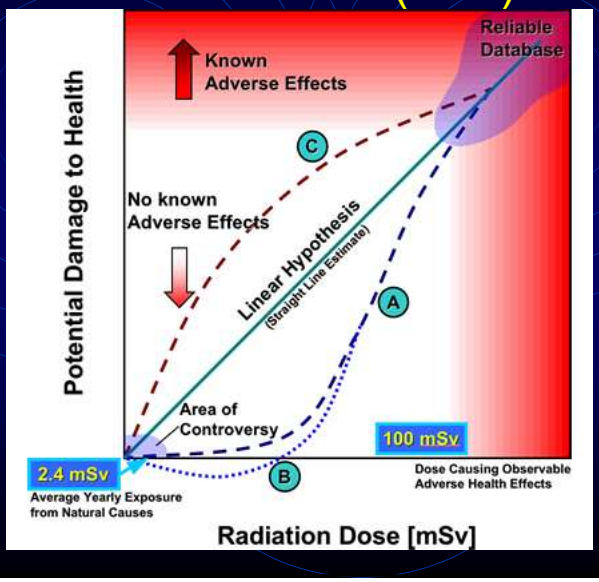
## DNA

- There are lots of things that disrupt DNA
  - Free radicals within our cells
  - Radiation
  - Viruses
- There are as many as 1 million bond breaks in each cell's DNA every day!
- So.....successfully staying alive depends on these breaks being reliably repaired.
- There is an "exercise" effect. When we get DNA breaks, we get better at fixing them

# DNA

- Included in all the information encoded in DNA are instructions on when to STOP growing and reproducing. If this information gets disrupted, CANCER results.

# Linear No Threshold (LNT) Model



## Where did this data come from?

- Lots of populations
  - A-bomb survivors
  - Radium dial painters
  - TB patients
  - Chernobyl

## Statistical Dilemma

- If an effect is seen with 10,000 exposed people at 1 Gy
- It will take 1,000,000 exposed and 1,000,000 controls to see that effect at .1Gy
- It will take 100,000,000 exposed and 100,000,000 controls to see that effect at .01 Gy (1 rad)

## Atomic Bomb Data

- We all know about inverse square law
- We know about shielding
- They did not really know enough about measuring radiation to do this well in 1945 or take the time, there was a war to win.
- The estimate of neutron dose changed BY A FACTOR OF 5, in 1990.

## One more thing

- The cancer incidence after Chernobyl is completely different from Hiroshima/Nagasaki
  - Dose rate (AKA repair)
  - Isotopes are different (I-131 in milk)

## Atomic Bomb Data

RADIATION RESEARCH 177, 229–243 (2012)
0033-7587/12 $15.00

DOI: 10.1667/RR2629.1

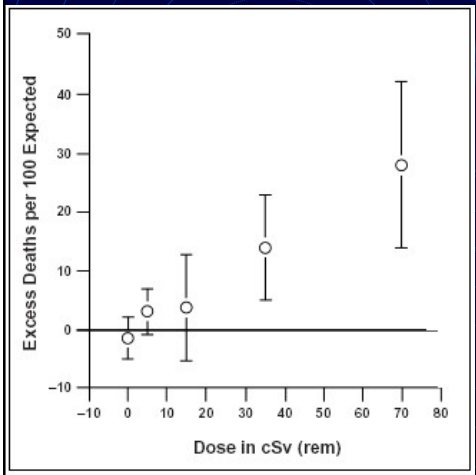
Studies of the Mortality of Atomic Bomb Survivors, Report 14, 1950–2003: An Overview of Cancer and Noncancer Diseases

Kotaro Ozasa,[a,1] Yukiko Shimizu,[a] Akihiko Suyama,[a] Fumiyoshi Kasagi,[a,b] Midori Soda,[a] Eric J. Grant,[a] Ritsu Sakata,[a] Hiromi Sugiyama[a] and Kazunori Kodama[c]

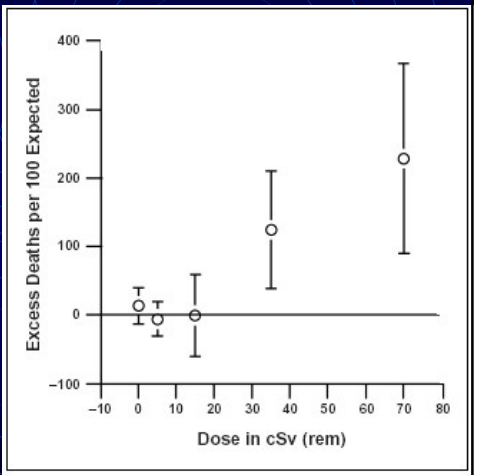
not exposed.

- Of the 11,000 people in the exposed population who have died of cancer, 527 of these deaths were caused by radiation. (4.8% increase)
- Most recent publication is 2012.

## Actual A Bomb Data




Solid Tumors




Leukemia

## Actual A Bomb Data

- Error bars are 95% confidence intervals
- For bottom three points, error bars include 0
- If you only consider the three lowest dose points,there is a 20% chance that the slope is negative
- No evidence of increased risk below .25 Gy!!

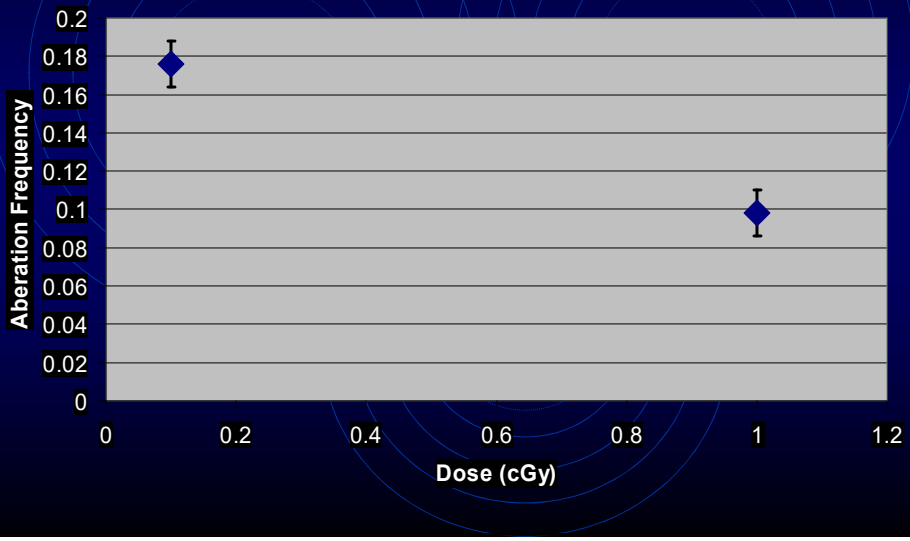
## Convincing Data

- Hanford Nuclear Shipyard workers who received .005 -.05 Gy had 85% of the cancer incidence rate as non exposed workers in same facility
- Numbers of participants was large
- Difference is highly significant (D>4SD)

# More Convincing Data: Iranian Background

- There is widely varying background radiation in Iran. Some areas get 1 cGy/year others get .1 cGy/year.
- When lymphocytes from these two groups are irradiated to 1.5 Gy, the mean frequency of chromosomal aberation is .098+/- .012 for the high dose group, and .176 +/-.017 for the low dose group. A 4 SD difference!

# Chromosome damage from a single dose decreases with increasing background!



## Most Convincing Data

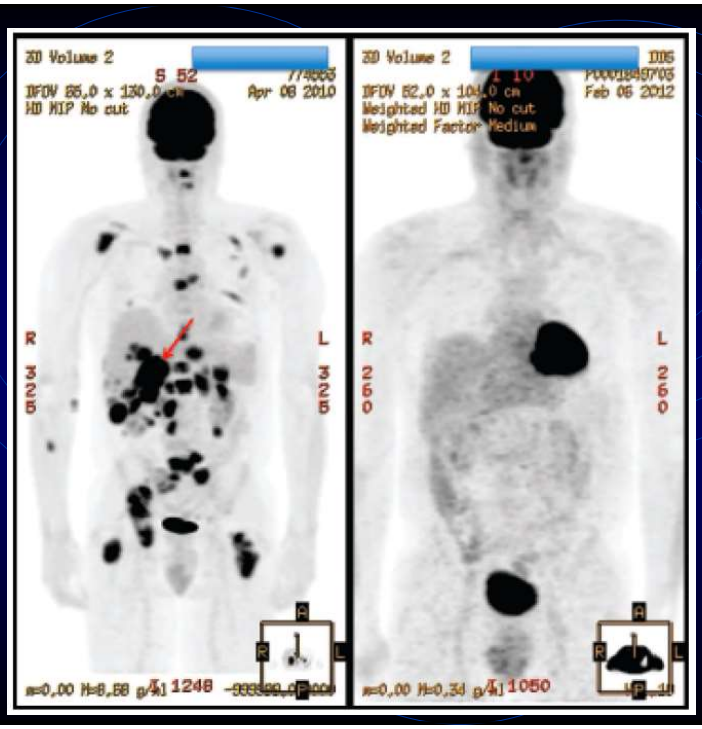
- In Taipei, between 82-84,1700 apartments were built using steel contaminated with Co60 (Oops)
- 10,000 residents received .05 Gy in the first year, .33 Gy over 16 years
- Using Taiwan data, 175 solid tumors and 4.5 leukemias were expected
- However, only 5 solid tumors and 1 leukemia have occurred

## So.. a little radiation is good!

- A few years ago there was activity to change the regulations to increase maximum permissible dose
- Knowledgeable folks pointed out that is is a disservice to protect the public from low doses of radiation
- Petition was rejected

# Bonus Section: Abscopal

- Relating to or being an effect on a nonirradiated part of the body that results from irradiation of another part



## Abscopal Effect

- So... This means that there is communication between the tumors
- Most likely through the immune system

## Abscopal Effects

- Show up between 1 and 24 months after irradiation
- Median time of tumor progression after the effect show up is 13 months (what we know now). Range 3-39 months.
- It appears that the radiation and immunotherapy must be concurrent.

## Immunotherapy 101

- An important part of the immune system is its ability to tell between normal cells in the body and those it sees as "foreign." This lets the immune system attack the foreign cells while leaving the normal cells alone.

## Immunotherapy

- To do this, it uses "checkpoints" – molecules on certain immune cells that need to be activated (or inactivated) to start an immune response.

## Immunotherapy

- Cancer cells sometimes find ways to use these checkpoints to avoid being attacked by the immune system. But drugs that target these checkpoints hold a lot of promise as cancer treatments.

## Researchers from around the world

Anti-Tumour Treatment

The abscopal effect of local radiotherapy: using immunotherapy to make a rare event clinically relevant

Kobe Reynders [a,*], Tim Illidge [b], Shankar Siva [c,d], Joe Y. Chang [e], Dirk De Ruysscher [a]

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## Abscopal Effects

- Happen without immunotherapy, but enhance with it.
- There is promise that immunotherapy and radiation therapy could augment each other for certain tumors.
- It appears that the radiation and immunotherapy must be concurrent.