Pesticide cancer risks in perspective

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Cancer is related to age, as are many of the other things you will find out soon enough come along with getting older. If you ask the top epidemiologists what's causing cancer, many had a go at it: Sir Richard Peto and Sir Richard Doll, Brian Henderson, Walter Willett, and they all generally agree. About a third of cancer is due to smoking, a third due to bad diets. I think diet may turn out to be even more than a third. They don't discuss aging, but when we eliminate all of these other things, there still will be this power of age that we have to fight, but we're making progress on that.

What is important about diet? That has been a difficult question. One thing that's becoming very clear is obesity is linked to many different types of cancer and is a big risk for cancer. I make the case here that micronutrient deficiency is very important as a cause of cancer. Micronutrients include the vitamins and minerals you require for cell metabolism. Most people don't get enough of one or more micronutrients and the evidence suggests it gives them cancer. Fibre is very important for health. Where do you get your fibre? From fruits and vegetables. You also get lots of your vitamins and minerals from fruits and vegetables, so they are quite important for health.

When you have a chronic infection, e.g. Hepatitis B virus in the liver, your white cells are fighting the invader. What they do is pour out oxygen radicals: hypochlorite bleach, nitrogen oxide, hydrogen peroxide, they are all mutagens, and they are all designed to kill invading bacteria or viruses. Thus if you have a chronic infection, it leads to cancer. Hormones and occupation may cause some cancer as well. Pollution, e.g. pesticide residues, is the big distraction. That's where we are putting all our money compared to anything else, and there is really not much evidence that it is important. Epidemiology studies do not have the power to find minor risks. They can find big things like smoking or bad diets, but they can't find minor risks. There is no convincing epidemiological evidence, and even if there was a tiny amount, you couldn't find it. Toxicologically, tiny traces of pesticides are implausible as cancer risks.

When Vincent Van Gogh, a neighbour of yours, was in a good mood, he painted sunflowers. He painted this Skull With Cigarette in 1885, possibly when he was depressed. He had a good intuition. Smoking isn't good for you. Smoking causes a third of the cancer, a quarter of the heart disease, and 8 years off your life if you are a 2-pack a day smoker. Each cigarette is about 10 minutes off your life. That's a big killer out there.

People have been saying, there is an epidemic of cancer due to the chemical industry. It's just not true. One must correct the cancer rate for age. You have to do that because the population lives longer and longer, which means there is more total cancer. If you correct for age, that is, look at cancer in a group of 50-year olds now and before, and you adjust for smoking, cancer rates have been coming down, not up. A leading epidemiologist, Sir Richard Peto, has analyzed this extensively. Modern technology is good for us, not bad.

People got cancer in the chemical industry back in the late 19th century, because when the aniline dye industry came in, there were no precautions at all. Workers were dipping their hands in the chemicals, they were breathing in huge amounts, there were enormous doses. Some of the workers working with beta-naphthylamine got bladder cancer, and scientists made that connection, so it was discovered chemicals could cause cancer. That was the first time people realized that, and after it was discovered they said, let's test chemicals on rats and mice, we don't want them tested on our workers, and that was very reasonable.

Now what about animal cancer tests? I think that is where a lot of the problem is. A lot of assumptions were made and they all turned out to be wrong. The first problem was that since a third of the animals are getting cancer anyway just on an ordinary diet, you have the problem of statistics in small numbers of animals. So they decided to use the maximum tolerated dose (MTD) in all the animal cancer tests--you find the level of a chemical that will kill the animal, and then you back off just a little bit so they only lose 10% of their weight. Almost all cancer tests are done at this huge dose, and sometimes also at half the MTD. Now we are trying to protect people at a million times below the MTD. The assumption was made we could go from this high dose to a low dose. Another assumption was made that carcinogens at the MTD were going to be rare and that we could eliminate them all. A third assumption was that they were going to be synthetic industrial chemicals. All of those assumptions have turned out to be wrong. And that's what I'd like to demonstrate.

My colleague, Lois Gold and I, set up a database of every animal cancer test ever done to calculate potencies, so we became experts on animal cancer tests. I wanted to do that because we had developed a mutagenicity test, and I wanted to look at the relation, and nobody had done it, so we just did it.

We have been doing this for 20 years. The first conclusion is carcinogens aren't rare. Over half of all the chemicals ever tested at the MTD, whether natural or synthetic, turn out to be positive, they give cancer to rats or mice at these huge doses. Half of the naturally occurring chemicals were carcinogens at the MTD, exactly the same as synthetic chemicals. Plants make natural pesticides to kill off insects, and other predators. Every time you eat a plant you get 50 to 100 natural toxic chemicals or so. Each plant is different. Half of all chemicals tested come out positive, in high dose cancer tests, whether nature's pesticides in our veggies, mould toxins, or natural chemicals in coffee. I think the problem is these high-dose animal cancer tests are a high-dose artefact. And I'll give you the evidence why I think that.

Chemicals tested in both rats and mice	
All Chemicals	**377/636 (59%)**
Naturally-occurring chemicals	**86/152 (57%)**
Synthetic chemicals	**291/484 (60%)**
Chemicals tested in rats and/or mice	
All Chemicals	**748/1430 (52%)**
Natural pesticides	**39/73 (53%)**
Mold toxins	**15/24 (63%)**
Natural chemicals in roasted coffee	**21/30 (70%)**
Commercial pesticides	**79/196 (40%)**
Mutagens	**287/382 (75%)**
Non-mutagens	**200/428 (47%)**
INNES negatives chemicals retested	**16/34 (47%)**
PDR drugs with reported cancer tests	**117/241 (49%)**
FDA database of drug submission	**125/282 (44%)**

Figure 1. Proportion of Chemicals Evaluated as Carcinogenic

Back in the 60's, a scientist named Innis took a few 100 industrial chemicals and said, let's test all of these chemicals in mice and see what percentage of chemicals are carcinogenic. And he found 9% were positive and everybody said, okay, carcinogens are rare, we'll identify and eliminate them, and then we won't get any more cancer. But in fact, the tests were only done on mice; they killed them after 16 months instead of letting them go to the full lifetime they do in a modern test; and they weren't using the maximum tolerated dose. So we went back and we took all the Innis negative chemicals and asked had any been retested in a modern test, and when you do that, half of them are positive. So carcinogens aren't rare, half of all the chemicals ever tested at the MTD are positive. And it doesn't mean anything for extrapolating to low doses. You can't eat anything in the grocery store that doesn't have natural carcinogens as defined in this way.

Why do plants have natural pesticides to kill off the insects. Plants don't have teeth, they don't have immune systems, they can't run away. All plant evolution is chemical warfare, cyanic compounds, all sorts of things like that. Should we worry about eating cabbage? No. Cabbage is good for you, but it's filled with carcinogenic chemicals, as defined by rodent tests at the MTD. Nature's pesticides. Nobody ever bothered asking, well, what happened if you test these things in an animal cancer test? Well, the Japanese have been testing lots of natural chemicals, and in fact, half of them come out positive, just like synthetic chemicals. And the amounts of nature's pesticides we eat are huge compare to the amounts of synthetic pesticides. The natural pesticides are in parts per thousand or million, where synthetic chemicals are in parts per billion. There is nothing you can eat that doesn't have chemicals in it, and when you test them in high doses in rats or mice, half of them cause cancer. Some of these are known mutagens, the psoralens, the hydrazines, as well as carcinogens. Mushrooms are full of hydrazines, the mushrooms we eat. Mustard is parts per thousand in allyl isothiocyanate, which is a mutagen and carcinogen. Nobody cares. But we are told to worry about some incredibly low level of a synthetic chemical.

And the modern human diet is completely different than a hunter-gatherer's diet. A European diet is completely different than it was 500 years ago. The potato came from the New World, the tomato came from the New World. Every new plant you eat has 50 different chemicals in it. Humans are designed to deal with toxic chemicals because that's what's in our diet. The largest source of poisoning in children is from eating some plant in the garden. We bred plants to be not quite so toxic; we eat a little bit of a lot of things. We made a comparison, synthetic pesticides, you eat 0.05 milligrams a day, and there are about 100 chemicals in the parts per billion range, while natural pesticides are 5,000 or so chemicals in the parts per million range. A part per billion is an awfully tiny amount, it's 1 person in all of China. Unless it's Mao, you just don't want to worry about it. Aflatoxin, a mould toxin, is active at microgram levels, and alcohol is a carcinogen at gram levels. So in order to compare things, you have to do how much humans are getting as a percent of what gives half the rodent's cancer, we set up a scale like that. Natural chemicals completely dominated the list. Synthetic chemicals, like DDT at its highest level, was very tiny compared to those. And there is no evidence DDT ever really hurt people. When you get down to regulation, regulatory agents were regulating parts per hundred or parts per thousand. Now they are trying to regulate at parts per trillion, because that's what regulatory agencies do, they try and expand their turf. That's their incentive, as a monopoly. But whether it has anything do with human cancer, I very much doubt it, there is really no good evidence. Besides pesticides lower the price of fruits and vegetables, which is a good thing. And you get more food out of less land which is a good thing for the environment. So I think pesticides are a good thing.

Dr. Gold and I published a paper listing all the natural pesticides that have been tested around the world in animal cancer tests. They are present in apple, apricot, banana, basil, beer, broccoli, Brussels sprouts (sorry), cabbage --- rutabaga, soybeans, tomatoes, turnip, and everything in-between. Chocolate also (sorry). There is nothing you can eat that doesn't have natural carcinogens as defined by high-dose rodent tests. You don't want to scare people about a thousand minor hypothetical risks, because then you are lost; no one knows what is important any more. And that's where we are now, the public doesn't know what's important anymore because they've been scared about too many hypothetical implausible risks. There are more carcinogens in one cup of coffee than pesticide residues you get in a year. But we don't worry about coffee and I don't think there is any reason to worry about coffee, there is no good evidence that it hurts us.

Carcinogens:
N=37
Acetaldehyde methylformylhydrazone, allyl isothiocyanate, arecoline.HCL, benzaldehyde, benzyl acetate, caffeic acid, capsaicin, catechol, clivorine, coumarin, crotonaldehyde, 3,4-dihydrocoumarin, estragole, ethyl acrylate, N2- γ -glutamyl-p-hydrazinobenzoic acid.HCL, hydroquinone, 1-hydroxyanthraquinone, lasiocarpine, d-limonene, 3-methoxycatechol, *8*-methoxypsoralen, N-methyl-N-formylhydrazone, 4-methylcatechol, methylhydrazine, monocrotaline, pentanal methylformylhydrazone, petasitenine, quercetin, reserpine, safrole, safrole, senkirkine, sesamol, symphytine

Noncarcinogens:
N=34
Atropine, benzyl alcohol, benzylixothiocyanate, benzyl thiocyanate, biphenyl, d-carvone, codeine, deserpidne, disodium glycirrhysinate, ephedrine sulphate, epigallocatechin, eucalyptol, eugenol, gallic acid, geranyl acetate, β-N-[γ-/(+)-glutamyl]-4-hydroxymethylphenylhydrazine, glycyrrhetirric acid, p-hydrazino-benzoic acid, isosafrole, kaempferol, *dl*-menthol, nicotine, norharman, phenethyl, isothiocyanate, pilocarpine, piperidine, protocatechaic acid, rotenone, rutin sulfate, sodium benzoate, tannic acid, 1-trans-δ9-tetrahydrocannabinol, turmeric oleoresin, xinblastine

These rodent carcinogens occur in: absinthe, allspice, anise, apple, apricot, banana, basil, beer, Broccoli, Brussels sprouts, cabbage, cantaloupe, caraway, cardamom, carrot, cauliflower, celery, cherries. Chili pepper, chocolate, cinnamon, cloves, coffee, collard greens, comfrey herb tea, corn, coriander, currants, dill., eggplant, endive, fennel, garlic, grapefruit., grapes, guava, honey, honeydew, melon, horseradish, kale, lemon, lentils, lettuce, licorice, lime, mace, mango, marjoram, mint, mushrooms, mustard, nutmeg,m onion, orange, paprika, parsley, parsnip, peach, pear, peas, black pepper, pineapple, plum, potato,radish, raspberries, rhubarb, rosemary, rutabaga, sage, savory,

Figure 2. Carcinogenicity Status Of Natural Pesticides Tested In Rodents

Now I'd like to talk about what's really important. To run your metabolism, you need about 15 minerals and about 15 vitamins and some essential fatty acids and amino acids. These are the micronutrients you need in addition to fuel. And the argument I'm going to make is whenever you are short of a micronutrient, it's likely to shorten your life span and increase cancer risk, and damage your brain.

Are we getting enough micronutrients? The answer is "NO." Look at iron: menstruating women are losing iron, about 16% of them in the United States are more than 2 standard deviations below the RDA. The RDA is the Recommended Dietary Allowance. Two standard deviations below that is the EAR which is a measure of population inadequacy. About 16% of menstruating women in the United States are < EAR and too low.

Nutrient	Population Group	% Ingesting < EAR * From Food
Minerals		
Iron	Women 14 - 50 years	16 %
Magnesium	All	56 %
Zinc	All	12 %
Vitamins		
B6	Women > 70 years	49 %
Folate	Adult Women	16 %
E	All	93 %
C	All	31 %

* USDA What we Eat in America (NHANES 2001-2002) Sept. 2005

Figure 3. Micronutrient undernutrition in Americans

Low iron is bad in many ways. Magnesium, 56% of the U.S. population is low (< EAR) for magnesium. Where do you get magnesium? It's in the centre of the chlorophyll molecule. So anytime you eat something green, you are getting some magnesium. You also get some from whole grains. And people just aren't eating enough; about 90% of teenagers are below the EAR for magnesium. Much of the population is too low in zinc, vitamin C, vitamin B-6, folate; they add folates to flour, and even with that, half of all women are too low in folate. Vitamin E, practically everybody is too low. I got interested in micronutrients because Dr. Jim McGregor came on sabbatical to my lab. He had just shown that folic acid deficiency in mice, causes broken chromosomes. He irradiated mice and found broken chromosomes, but he found the same thing by a deficiency of folic acid. *Folia* is the Latin word for "leaf." You get folic acid from your spinach and things like that. What does folic acid do? It moves one-carbon units around. My graduate student, Ben Blount, worked out why a deficiency of folic acid breaks chromosomes. Methylene-THF helps to methylate uracil to thymine, when you don't have enough folic acid, you put uracil in your DNA. Your DNA repair enzymes are always taking out the uracil, so you are breaking the DNA. It's just like radiation; radiation gives you clusters of electrons to create nearby lesions on opposite strands, and the 'repair' causes the chromosome to fall apart. That's the dangerous part of radiation. Folic acid deficiency does the same thing to DNA and works in a very similar way. We had a paper comparing folic acid deficiencies and radiation.

People are worried about incredibly tiny levels of radiation, but they did not appreciate that half the poor had broken their chromosomes because they just didn't eat enough folic acid. So it's lack of

micronutrients that's likely to be important, not a trace of synthetic chemical. McGregor did a study in humans showing folic acid breaks chromosomes, and we did some studies together. And when I realized that half the poor were at the level of folic acid where they had broken chromosomes, I had an epiphany and gave up worrying about minor risks. Folic acid doesn't cost anything, less than a penny for a daily dose. All of the vitamins and minerals are inexpensive. Two billion women in the world are short of iron: iron is rusty nails. The cost is trivial. It's a matter of paying attention to important things instead of spending all our time on unimportant things. Fenech in Australia showed folate deficiency and vitamin B-12 deficiency, both cause chromosome breaks. We looked at iron and too little iron, the mitochondria pour out oxygen radicals. You're aging faster. About 2 billion women and children eat too little iron. Too much iron is bad for you, also. A lot of men eat too much meat, and they are getting the same problem with their mitochondria because they eat too much iron. So there is a balance. Low iron in pregnant women causes low birth rate babies, and pre-term babies.

Dr. Joyce McCann and I have just written four big reviews on the developing brain. When you are a foetus and in the first 2 years of your life, you make almost a trillion neurons, and each neuron has a 100 or so connections. If you don't have enough iron, the brain doesn't develop well. Kids don't do well in school, it's irreversible. Same thing with DHA, an omega-3 fatty acid, which is 30% of the brain fatty acids. Everybody is short of omega-3 fatty acids. We are not paying enough attention to the shortage. They weren't even adding DHA to baby formula in the United States until recently. They do it in Europe.

Now we have submitted a review on vitamin D. Vitamin D deficiency may cause 30% of the cancer in the United States, particularly in dark-skinned people, as they need 6 times as much sunshine as light-skinned people to make the same amount of vitamin D. Dark-skinned people in northern climates, in Europe, in northern United States, are in trouble. They have such low levels of vitamin D. It's not only a big risk factor for cancer, but the brain is full of vitamin D receptors, it's doing something important in the brain.

We are using human cells in culture, and making them slightly deficient in one micronutrient after another, and every time we do this, we see DNA damage. Micronutrient zinc deficiency gives you DNA damage, as does magnesium deficiency, vitamin B6 deficiency and biotin deficiency. Magnesium, B6, or biotin deficiency also shortens the lifespan of human cells in culture. Those are the only three we have tested in cells for senescence acceleration and all three shorten their lifespan. So I looked in the literature, and anytime anybody tested a, deficiency caused DNA damage or was associated with cancer.

I started thinking, why is nature causing DNA damage when there is a micronutrient deficiency? I realized nature wants it this way. Think of the 15 minerals. Every living creature requires about 15 minerals. Magnesium, calcium, copper, iron, and all the usual metals that are used in biochemistry. Are they spread evenly through the world? No. Organisms throughout evolution were often becoming deficient in iron, or magnesium, or some other metal. What does nature want? It wants survival so that maybe it can reproduce a bit. And any metabolism that affects the long term gets cut out. Well, DNA damage is long term, it doesn't show up as cancer for 20 years. On shortage nature will lose the magnesium from DNA repair enzymes and keep it in places like the mitochondria and the heart. The adaptive immune system goes out, there are papers that if you don't have enough vitamin B-6, the adaptive immune system goes out. That's long term. You might die of an infection in 3-4 years, but that isn't important if it's a matter of survival. I call all of this triage, and elaborate it in a recent paper in P.N.A.S.

To summarize, if you don’t eat right or take supplements, you may look perfectly fine, but if you are not getting your magnesium or you are not getting your omega-3 fatty acids you're likely to be getting long term damage. Your immune system isn't working as well, your DNA is getting damage, your brain, all these things that don't show up right away in your biochemistry.

Now what about obesity? A third of the children at Children's Hospital where I work now are obese, mainly blacks and Hispanics, it tends to be the poor. And you look at their numbers, they are deficient in everything. The diet of the obese is amazingly deficient in vitamins and minerals. It's as we heard from several speakers, refined food that's cheap and high in calories, fat and carbohydrate, is very low in vitamins and minerals. And being fat is associated with 40 different diseases, including cancer, and heart disease, and diabetes. And the cost is going to be astronomical.

These are the 10 leading sources of calories in the United States. A sugary soft drink, is an abomination. It’s 40 grams of sugar and no nutritive value. A doughnut is an abomination, it's all this sugar and no nutrients. You can go down the list, there are not a lot of veggies on this list. People that are obese are short of fibre, they are short of all these vitamins and minerals. And I suspect it's making them hungry all the time. If you are not getting your magnesium, which obese people aren't, maybe the body is craving that magnesium. I suspect that nature would rather have you fat and fertile than thin and nonfertile. So you keep on eating trying to find that missing magnesium, but it's scarce in your diet because you are eating the wrong kinds of food. We are trying to prove that. That's still very hypothetical.

Obesity is likely to be due to the bad diet, not just calories in and exercise out. Exercise is important, too, and people aren't getting enough.

There still is a lot to learn about obesity, and about diet and cancer. If we are going to have any impact on public health, you have to work on important issues and not on unimportant things like traces of pesticides. No company would survive that spent all its time on unimportant things, and didn't address the important things. The important things, if we really want to improve public health, are smoking and getting people on good diets. And all this fuss about pesticides is a distraction. We are spending *incredible* amounts of money on trivia and it hurts the economy. It isn't helping public health to worry about a part per billion of this and that.

Thank you

Q&A

Q: Can you satisfy your micronutrient requirement through vitamin pills?

A: I think everybody in the world should take a multivitamin mineral pill as insurance. The nutrition community dislikes that, but they've been telling the poor to eat more fruits and vegetables for 30 years with little success. Maybe we should tell the poor to take a multivitamin as insurance, and also to eat a good diet. We don't understand everything about diet, and we shouldn't just take a pill and forget about a good diet, as you won't get your fibre from a pill, and you won't get your omega-3 fatty acids, or your potassium, but the multi will help. I think a supplement should be an adjunct to telling people about eating a good diet. I have an Italian wife and I eat a wonderful Mediterranean diet, but I take my multivitamin mineral pill every day as insurance.

Q: You said tiny residues of synthetic chemicals are a distraction. What is the cost of this distraction? Economic cost, I mean, globally speaking, in the world?

A: I don't know the cost in Europe. In the U.S., people estimate that the Environmental Protection Agency cost $10 billion a year, and that's not salaries to them, but it's the cost to society. I suspect it's much larger than that. We are spending far more money worrying about a part per billion of some chemical, than we are on teaching people about large risks, such as obesity, bad diets, or the hazards of smoking. It's just misplaced priorities. It doesn't mean you don't want rules; you don't want every chemical company dumping all their garbage out the back door into the local river. You need rules. But you just don't want to shoot yourself in the foot by spending all of your efforts on minor hypothetical risks.