Mice, Humans, and Cancer

By ACSH Staff — January 4, 2006

A January 04, 2006 post [1] by Derek Lowe on the media blog Corante.com describes an online spat over ACSH's oft-repeated point [2] (the inspiration for our lawsuit against the EPA) that high-dose rodent tests are poor predictors of human cancer risk:

Via Tyler Cowen at Marginal Revolution [3] I came across this post [4] earlier in the year from a blog called EffectMeasure on the use of rodent models to predict human cancer risks. It's a broadside against the American Council on Science and Health and a petition they filed against the use of high-dose rodent carcinogenicity tests...

I've left out (as did the MR post) the part where he called the ACSH "right wing whores," which is the kind of thing that doesn't enhance the statistical arguments very much. Dropping the invective, I want to take up Tyler Cowen's question: is there anything to this critique? My answer: there might be. But there might not be. It's certainly not as clear-cut as the author would like to make it, cancer epidemiologist though he is, which would seem to be one of the criticisms he's making against the ACSH petition.

Here are some complicating details:

1. The effects of high doses of compounds can be due to their effects on cell division. At such levels, test substances cause irritation and inflammation that promotes cell proliferation. The more cells are forced to divide, the more opportunities there are for the defects that lead to cancer. These effects do not scale well to lower doses. It's the opinion of Bruce Ames (inventor of the Ames test [5] genotoxicity screen) that this problem has completely confounded [6] the interpretation of high-dose animal data. (His article in Angew. Chem. Int. Ed. 29, 1197, 1990 is a good statement of this argument).

2. The statement that "most chemicals, given in no matter how high a dose, won't cause the very unusual and specific biological effect of turning an animal cell cancerous" is not accurate. As Revere surely knows, there are many mutations and pathways that can turn a cell cancerous (which is why I keep harping on the idea that cancer isn't a single disease). Somewhere between one-third and one-half of
all synthetic chemicals tested in cell assays or in high-dose animal assays show up as possible carcinogens, depending on your definitions. Interestingly, basically the same proportion of natural products (isolated from untreated foods and other sources) show up as positives, too.

Now, if you want to talk confirmed human carcinogens, then Revere may have a point. There are only some three or four dozen specific chemicals that are confirmed as causes of human cancer. Here's the list. [7] If you read through it, you'll note that many of the 95 agents on it are radioactives or broad categories such as "alcoholic beverages." (Mention should be made of things like nickel, all compounds of which are under suspicion. Check your pockets [8], though, for your most likely exposure). Specific compounds known as human carcinogens are quite rare. But doesn't that fact support the ACSH's point more than Revere's?