THE THALIDOMIDE OF GENETIC 'ENGINEERING'

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By the end of the 1980s some millions of people, mostly in North America, were supplementing their diet with L-tryptophan, an essential amino-acid present in proteins of any normal diet. Amino-acids such as tryptophan are routinely produced in micro-breweries using suitable microbial cultures. One producer, Showa Denko K.K., artificially inserted genes into a bacterial species to increase its production of tryptophan.

Then in late 1989, some 5,000 - 10,000 in North America fell ill with a highly unusual illness, EMS (eosinophilia-myalgia syndrome), caused by Showa Denko tryptophan. Within months, dozens had been killed by EMS and thousands maimed. Today thousands continue to suffer permanent nasty effects, and a trickle of them continue to die early (totalling at least 80 by now in the USA). The epidemic ceased when over-the-counter tryptophan was severely restricted.

Two cases were reported in Australia, and one in NZ. The tryptophan those patients took was not traced to manufacturer.

The total killed is not exactly known but may be in the region of a few hundred. Showa Denko has paid out approximately US $2,000,000,000 to avoid damages trials.

We emphasize that if thalidomide had happened to cause a type of birth defect that was already common, *e.g.* cleft palate or severe mental retardation, we would still not know about the harm, and pregnant women would have kept on taking it for its undoubted benefits. The fractional addition to figures that were already relatively large would not have been *statistically* significant. But as it turned out, the damage noticed was of a kind that most doctors never see in a whole career - drastic malformations of the arms & legs - so although the numbers were not huge these cases were picked up.

Similarly, impurities in Showa Denko's genetically 'engineered' (GE) tryptophan happened to cause an illness - EMS - which was novel. The surge of numbers therefore stood out and got noticed. If SDKK's poison had caused the same numbers of a common illness instead, say asthma, we would still not know about it. Or if it had caused delayed harm, such as cancer 20 - 30 years later, or senile dementia in some whose mothers had taken it early in pregnancy, there would have been no way to attribute the harm to the cause.

This reminds us of the need for extreme caution with GE foods. They must be assumed guilty until thorough tests have suggested they are, if not innocent, at worst guilty of only minor dangers. Such is nowhere near the case today as large companies rush to market their GE foods.

It is very disappointing to find a leading physician writing on behalf of the RSNZ about this disaster thus: "Rare cases of EMS were known before the introduction of the genetically engineered bacterium, which further supports the hypothesis that EMS is not due to the genetic engineering event." An exact analogue of that argument would run: "Rare cases of seal-limb were known before the introduction of thalidomide, which further supports the hypothesis that seal-limb is not due to thalidomide."

But even more important is the fact that the trickle of about 100 early EMS cases, years before the epidemic of late 1989, were due to (early versions of) Showa Denko GE bacterial cultures.

None of the half-dozen other manufacturers' tryptophan caused EMS. No other manufacturer used gene-splicing to produce tryptophan.

The contrast is startling with the elaborate procedure before registration of a new drug. It has taken a decade to get legal approval for supplementing humans with (a modified version of) the human hormone amylin, for treating diabetics. Yet GE foods are urged for legal distribution in great haste and with only extremely scanty testing, and the main discussion so far has been whether they should be labelled.

Labelling would not in itself be wrong, but can of course not substitute for the careful lengthy testing that would be needed before any GE food should be approved for human consumption. Labelling of GE food would imply acceptance by authorities, as does the ingredient list of any labelled food.

The Showa Denko disaster is crucial to understanding GE food. If a purified single chemical - the natural amino-acid L-tryptophan, better than 99% pure and definitely satisfying the notorious 'substantial equivalence' test - can turn out when GE'd to kill a hundred or so and cripple thousands, what will it take to check properly a potato containing a synthetic 'exact' copy of a gene for a toxin from the African clawed toad?

And most urgently, the attempt to count purified amino-acids, sugars, oils etc. as 'substantially equivalent' is shown by the Showa Denko disaster to be a gamble. The assumption that soy oil from GE soybeans is exactly equivalent to ordinary soy oil requires the most careful scientific measurements to check it. Merely assuming 'substantial equivalence' will not do.

Those who search the Internet on this topic will soon discover the claim by apologists for GE that the problem was only decreased purification of tryptophan. We disagree for several reasons - mainly, the first three GE strains had been causing EMS (about 100 cases) for years before this slackening of purification procedure in Jan 1989 when also the 'superproducer' strain went into production and caused the epidemic. But this question cannot be settled with finality unless Showa Denko releases the GE microbes for detailed examination.

Whether you believe the impurities were due to incompetent purification & monitoring, or to deviant metabolism in the GE-bugs, or both, you had better believe that the fabled 'substantially equivalent'

assumption flopped in that epidemic of crippling & lethal illness.

Although GE proponents claim that the EMS epidemic was caused solely by faulty filtering, it is possible to question their seriousness. None of them has publicly argued that the Health Food supplement industry should be subject to legal controls for purity & efficacy comparable to those applied to the pharmaceutical industry; yet this would be logical if indeed such a deadly epidemic occurred solely as a result of inadequate purification in manufacturing.

Either way, biotechnology - which includes GE but also includes other processes such as purifying the mixture "lyprinol" from mussels - requires much-enhanced scrutiny.

Main sources

1. L-Tryptophan Puzzle Takes New Twist, *Science 249* 988, 31 August 1990

2. Does Medical Mystery Threaten Biotech? *Science 250* 619, 2 November 1990

3. EMS and Tryptophan Production: A Cautionary Tale, *Trends in Biotech 12* 346-352, Sept 1994

4. Eosinophilia-myalgia syndrome. Results of national surveillance, *J Am Med Assoc 264* 1698-703 1990

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