BLOOD NPX LEVELS IN ACCIDENTAL DEATHS

According to both Dr. Larry Lewman, Deputy Coroner of Oregon, and Dr. Boyd Stevens, Coroner of San Francisco, most of the Darvon deaths are not suicides but accidents. One of the criteria for making this decision is an NPX blood level as high or higher than the PX level, often suggesting chronic use of PX.

Blood NPX levels in such accidental deaths are often slightly less than 1, 1, 2, 3 or 4 micrograms per ml. of blood with PX levels often less than 1.

DARVON MARGIN OF SAFETY IS TOO LOW

The margin of safety or therapeutic index of a drug is the ratio between the amount needed to achieve the therapeutic effect (in this case alleged relief of pain) and the amount causing toxicity. According to Danish toxicologist Dr. J. Simonsen [5], Darvon has a "narrow therapuetic index": He says that "just four times the ordinary therapeutic dose can produce highly serious poisoning."

San Francisco Chief Coroner Dr. Boyd Stevens told me that "if you double the Darvon dosage and take just 1 to 2 (bar) drinks, you can get into the toxic or lethal range." Dr. Stevens points out that partly because of its relative weakness as a painkiller, patients may well be inclined to take 2 pills (or more) instead of 1. He says, therefore, that many of the Darvon accidental deaths are not abuse—in the strict sense.

This very low margin of safety is very likely related in many cases to the accumulation, as described above, of the toxic metabolite norpropoxyphene (NPX) in people regularly using the drug. In the above-mentioned study by Simonsen, he discusses the fact that we may be just seeing the tip of the iceberg as far as Darvon deaths. The study describes 2 elderly people found dead with no evidence of suicide whose deaths would otherwise have been attributed to natural causes but for a Danish law requiring autopsy on those dying alone. Subsequent toxicologic analysis showed both to be Darvon deaths.

DARVON VS. MORE EFFECTIVE PAIN-RELIEVERS

Since Darvon's effectiveness in relieving pain is somewhere between that of aspirin (or acetaminophen as in Datril, Tylenol) and a placebo and substantially less than that of codein (in Schedule II and III), it is of interest to look at the number of deaths and the death rate of these preferable analegsics in comparison to Darvon.

Drug and Deaths: 1977 [6]	*Deaths Per Million Prescriptions* [7]
Darvon—590	19
Codeine—255	5
Aspirin [8]—150	<1
Acetaminophen [8]—77	<1

PREDICTABLE INADEQUACY OF SCHEDULE IV

When the possibility of controlling Darvon by putting it into the weak control of Schedulue IV, was first raised in 1973, Lilly responded by saying that if the drug should wind up in Schedule IV, despite its protests, "we believe it wouldn't have any material effect on sales of the product." [9]

In the year before Darvon was put into Schedule IV March 1976–February 1977, there were 459 deaths related to its use. In the first year of Schedule IV (March 1977–February 1978), the number was 510. Although there appears to be a decrease in deaths during the latter part of 1978, these data underestimate the eventual number of reported deaths since all 1978 reports are not completed and sent to DEA until well into 1979.

Although there has been an apparent but slight decrease in emergency room visits involving Darvon, this is not accompanied by any evidence yet of a decrease in fatalities.

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[5] Ugeskr. Laeg. *137*(44) 2605–2609, 1975.
[6] DAWN Quarterly Report January–March 1978.
[7] 1977 Prescriptions filled from National Prescription Audit, I.M.S.
[8] 1977 Retail sales of Aspirin of $500 million and acetaminophen, $130 million—assume average cost of $1 for aspirin, $1.50 for acetaminophen and use death per million bottles.
[9] Wall Street Journal, Aug. 6, 1973.