mouse. Indeed, when we surveyed the possibility of LDHV contamination in the human tumor lines that we maintained as xenografts (using a method based on the elevating effect of serum LDH activity in which mice were inoculated with test samples [sera from tumor-bearing nude mice]), six (11.8%) of 51 human tumor xenografts tested were contaminated with LDHV. These LDHV-positive tumors included human lung cancer xenograft LX-1, which is widely used in various fields. All six human xenografts had been introduced to our laboratory from other research institutions, but it is unclear when and where they were contaminated.

LDHV is considered to infect only Mus musculus and M. caroli but not rats. Therefore, there is the possibility that this virus can be eliminated from contaminated tumors by transplanting these tumors into nude rats that are insensitive to LDHV and can accept xenogeneic tumor cells. In our study, ICR mice inoculated with serum samples from nude mice bearing LDHV-contaminated tumors showed an increased serum LDH activity that was threefold higher than the control level. In contrast, serum samples from nude rats bearing LDHV-contaminated tumors or from nude mice bearing the tumors after passage in nude rats did not increase the serum LDH activity in ICR mice. No virus was detected by the above bioassay method after subsequent passage of this tumor in nude mice, which suggests that the virus is eliminated after passing in nude rats. We succeeded in eliminating the virus by using this method in all six tumors in which LDHV contamination had been confirmed.

LDHV-infected mice generally show no clinical symptoms. Rather, attention should be paid to the modification of experimental results by this infection. In addition, the virus elimination method described here is very simple. This information may be more useful for researchers in the fields of experimental cancer than laboratory animal scientists.

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Case Report of a Lethal Cardiac Toxic Effect Following High-Dose Cyclophosphamide

The potentially lethal cardiac toxic effect of high-dose cyclophosphamide has been reported previously (1-4) and even studied prospectively (5), but this toxic effect has not occurred at doses lower than 180 mg/kg given over a 4-day period. We recently observed a patient who died as a result of acute toxicity following the first dose of doxorubicin-cyclophosphamide given to her on protocol B25 of the National Surgical Adjuvant Breast and Bowel Project (NSABP).

A 30-year-old, well-educated, previously healthy woman underwent mastectomy for a locally advanced breast cancer. Involvement of intramammary lymphatic ducts and a single intramammary lymph node was observed. The metastatic work-up was negative, and the ejection fraction was 62%. The patient received doxorubicin (60 mg/m²) as an intravenous bolus and cyclophosphamide (2400 mg/m²) as an intravenous infusion over a 4-hour period. Ondansetron, dexamethasone, and lorazepam were given concurrently as antiemetics, and 1000 mL of 5% glucose in half normal saline was infused over an 8-hour period before and after chemotherapy. The patient developed nausea and vomiting several hours after chemotherapy, so she returned to the outpatient facility the following morning; her weight was stable. Additional intravenous fluids were administered, but she became hypotensive within 4 hours. She was transported to the inpatient facility for monitoring of cardiac rhythm and vital signs. Her blood pressure remained low, despite fluid administration, and the electrocardiogram revealed low voltage. Twenty-four hours after chemotherapy, she experienced severe chest pain, which was partially relieved by administration of morphine. Under the direction of a cardiologist experienced in the management of this syndrome, the patient was given fluids and pressors over the ensuing 6 hours, but her condition deteriorated, and she died. Autopsy revealed diffuse myocardial edema and congestion with ischemic degeneration. In addition, there were focal cardiac muscle necroses and hemorrhaging, which are associated with injury to the capillaries and are consistent with cyclophosphamide-induced cardiomyopathy; the patient's death was consequently attributed to cardiogenic shock.

Of the 2548 women enrolled in NSABP Protocol B25, 1698 have received the same dose of cyclophosphamide, and only our patient experienced acute lethal cardiac toxicity. Nonetheless, we believe that this fatal syndrome should be studied extensively, particularly if high-dose cyclophosphamide therapy is found to be effective adjuvant therapy for patients with aggressive malignant diseases. Clinicians prescribing similar doses of cyclophosphamide should be aware of this rare complication and should advise patients of it as part of the pretreatment consent process.

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References


Correction: Prior Annotation of B. Fisher's Papers Incorrect

Medline, CancerLit, and PDQ erroneously annotated certain articles authored or co-authored by Dr. Bernard Fisher with the phrase "scientific misconduct—data to be reanalyzed." All such annotations have been removed or are being removed. However, the Journal published the incorrect annotation in the reference lists of papers that cited those articles. We apologize for any problems or concerns this may have caused. Readers should disregard the erroneous annotations in the papers named below:


Note

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Beat the Smokeless Habit

Game Plan for Success

Smokeless tobacco represents a serious health risk. Beat the Smokeless Habit: Game Plan for Success provides the facts about smokeless tobacco and a nine-step plan for quitting. Baseball stars comment on their experiences with quitting and how the sport and smokeless tobacco have been historically linked.

Single copies of this booklet are available at no charge from the National Cancer Institute. Please write to: National Cancer Institute, Beat the Smokeless Habit: Game Plan for Success, Bldg. 82, Rm. 123, Bethesda, MD 20892 or fax your request to 301-231-6941.