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# Fluorocarbon 113 Exposure and Cardiac Dysrhythmias Among Aerospace Workers

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We investigated the cardiotoxic effects of 1,1,2-Trichloro-1,2,2-Trifluoroethane (fluorocarbon 113 or FC113) exposures among healthy workers cleaning rocket and ground support equipment for the National Aeronautic and Space Administration (NASA) programs. Exposure and ambulatory electrocardiographic (ECG) monitoring data were evaluated on 16 workers, each of whom was examined on exposed and nonexposed workdays. We examined whether there was a greater rate of dysrhythmias on an exposed workday relative to a nonexposed workday. Overall, we found no within subject differences in the rate of ventricular and supraventricular premature beats (number per 1,000 heart beats), fluctuations in the length of the P-R interval, or heart rate. We found that levels of FC113 exposures below the Occupational Safety and Health Administration (OSHA) 8-hour time-weighted-average (TWA) standard of 1,000 ppm did not induce cardiac dysrhythmias or subtle changes in cardiac activity. However, because fluorocarbons may sensitize the heart to epinephrine, this study's negative findings based on sedentary and fairly healthy workers may not be generalizable to other populations of workers who are not as healthy or engaged in more physically demanding work. © 1992 Wiley-Liss, Inc.

**Key words: arrhythmias, premature ventricular contractions, 1,1,2-trichloro-1,2,2-trifluoroethane**

## INTRODUCTION

Approximately 230,000 U.S. workers are exposed daily to fluorocarbon 113 (FC113) (National Institute for Occupational Safety and Health [NIOSH]). Fluorocarbons are used in refrigerants, foam blowing agents, solvents, anesthetics, and polymer intermediates. Animal studies have shown that FC113 and other fluorocarbons have cardiotoxic effects [Aviado and Belej, 1974; Belej and Aviado, 1975], and lethal arrhythmias have been implicated as the cause of sudden death among occupationally exposed workers [NIOSH, 1989; May and Blotzer, 1984] and aerosol sniffers [Reinhardt et al., 1971; Bass, 1970].

Three human chamber studies have examined the cardiotoxic potential of flu-

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orocarbons. Reduced heart rate was associated with 15–60 seconds of exposure to FC11, FC12, and FC114 among 10 healthy individuals examined by Valic et al. [1977]. Two of the 10 subjects experienced tachycardia and negative T-waves, and one subject developed atrioventricular block at levels reported to be as high as 16,150 ppm. Among 46 healthy volunteers examined by Stewart et al. [1978], an increase in premature ventricular contractions occurred after 1 hour of FC12 exposure at 1,000 ppm in only one subject. No other effects were noted. In a chamber study conducted by Azar et al. [1972], no electrocardiographic (ECG) disturbances were observed in two volunteers exposed to FC12 for 1,000 and 10,000 ppm for 2.5 hours.

Only a few occupational studies have attempted to examine the relationship between fluorocarbon exposure and arrhythmias at the worksite [Antti-Poika et al., 1990; Edling et al., 1990]. Among six refrigerator repairmen, an exposed workday was not clearly associated with an excess in ectopic beats when compared to nonexposed workdays: exposure to FC12 and FC22 ranged from 170–815 ppm for 48–150 minutes. However, in a study of 89 refrigerator repairmen, Edling et al. [1990] found that exposure to fluorocarbons for 5 or more minutes at 750 ppm (with instantaneous peaks exceeding 3,000 ppm) was related to a slightly greater number of ectopic beats and a greater duration of sinus bradycardia than periods of no exposure during the same day among the same individuals. These differences were statistically significant with a one-tailed test among 14 individuals in the medium peak exposure category of 3,000–5,000 ppm, but not among the 5 individuals in the highest peak exposure category which exceeded 5,000 ppm. Although a variety of fluorocarbons were represented in the study, the majority of workers were exposed to FC12 and FC22.

To our knowledge, no study has examined the cardiotoxic effects of FC113 in humans. Because of the widespread industrial use of FC113, we examined whether FC113 exposures within the current Occupational Safety and Health Administration (OSHA) standard elevate the occurrence of cardiac dysrhythmias. The NIOSH-recommended exposure level, and the OSHA 8-hour time-weighted-average (TWA) permissible exposure limit (PEL) is 1,000 ppm, while the 15-minute short-term exposure limit (STEL) is 1,250 ppm [Federal Register, 1990].

In the present study, we simultaneously conducted exposure and ambulatory ECG monitoring. The study is unique in that we examined a wide variety of ECG data, including ventricular premature beats (VPBs) and supraventricular premature beats (SVPBs), A-V block, t-wave inversion, ST segment depression, and more subtle indices of an effect, such as fluctuations in heart rate and length of the P-R interval.

## MATERIALS AND METHODS

### Work Population

FC113 is used to clean rocket and ground support equipment for the National Aeronautic and Space Administration (NASA) programs. Because FC113 is highly volatile (vapor pressure of 285 mm Hg at 20°C) [ACGIH, 1980], high ambient exposures occur as a result of FC113 vaporizing during the washing process. Parts go through a precleaning phase, where FC113 exposures are minimal, and a final cleaning phase in a clean room, where exposures could potentially approach OSHA's PEL. In the precleaning phase, parts are disassembled and then dipped in a series of detergent and acid baths, and in an FC113 vapor degreaser. Parts are then moved to

the clean room, where they are washed with FC113. Once sufficiently cleaned, the parts are reassembled, checked, and packaged in heat-sealed polyethylene bags.

We monitored workers at two contractor-operated, NASA-owned facilities. Both facilities are subject to the same NASA cleaning specifications. Both clean rooms are maintained under positive pressure to prevent migration of dust into the room, and both clean rooms utilize a laminar air flow scheme. Facility A uses a vertical laminar air flow scheme, while facility B uses a horizontal air flow scheme. Both clean rooms provide about 10% fresh make-up air and recirculate 90% of the air.

At Facility A, workers rotate between the precleaning (low exposed) area and the clean room (exposed) area every 2 weeks. Workers at Facility B are assigned to one area, but may be requested to move into the other work area depending on workload demands. Thus, we were able to conduct ECG monitoring on many of the workers during an exposed workday in the clean room and during a low or nonexposed workday in the precleaning area. The physical activity level was minimal in both areas. All workers permanently or temporarily assigned to the clean room were eligible to participate.

Workers at Facility B are given pre-employment physical examinations that include an electrocardiogram and questions concerning palpitations and heart disease. No pre-employment physical, however, is required at Facility A. Workers at both facilities receive periodic physical exams which include electrocardiograms.

## Environmental Sampling and Dysrhythmia Monitoring

We simultaneously collected environmental exposure and ambulatory ECG monitoring data. We attached an ambulatory ECG Holter monitor (CircaMed Workstation Holter Recorder) to each study participant prior to the beginning of the workshift, and removed the ECG monitor at the end of the workshift. The ECG monitor had a timing track and recorded two channels, using four leads and one ground electrode. We tested the conductance of the electrodes, and calibrated the readings by checking a live data strip obtained on each participant from a portable office ECG machine. The ECG tapes were sent to the ECG laboratory at the University of Minnesota, Division of Epidemiology, where a trained technician reviewed the tapes for VPBs and SVPBs, A-V block, t-wave inversion, ST segment depression, heart rate, and P-R interval length. The ECG data were provided to us in 15-minute intervals for each person's total period of monitoring. All questionable readings were reviewed by a cardiologist.

For each individual wearing an ECG monitor, we concurrently measured airborne exposures by collecting a series of short-term personal exposure samples during the entire workshift using charcoal tubes and vacuum pumps. Airborne concentrations of FC113 near each individual's breathing zone were evaluated by drawing air at a rate of 50 $cm^3$ per minute through coconut-shell charcoal tubes using NIOSH analytic method 1020 [NIOSH, 1990]. Samples were collected for periods ranging from 30–60 minutes. The median time for collection of the short-term samples was 44 minutes. The average duration of simultaneous exposure and ECG monitoring was 7 hours per day of monitoring.

In addition to the exposure and ECG monitoring, we queried workers regarding the timing and amount of smoking, caffeine intake, medication usage, and symptoms during the days that they participated in the study. This information was collected prior to the start of the workshift, after each break, and at the end of the workshift.

**TABLE I. Personal Time-Weighted Average (TWA) FC113 Exposures (ppm) on Exposed and Low Exposed Days for the Paired Comparison (N = 16)**

| | Exposed day | Low exposed day | Paired difference |
|---|---|---|---|
| Mean TWA (SD) | 442.1 (300.2) | 64.4 (59.5) | 377.7 (289.1)[a] |
| Range | | | |
| Minimum | 247 | 0 | 201 |
| Maximum | 1,476 | 200 | 1,370 |

[a]$p < .001$, paired t-test for differences in means.

## Data Analyses

The dependent variables examined included the number of VPBs and SVPBs per 1,000 heart beats, and fluctuations in the P-R interval and heart rate. To determine whether there was a greater number of VPBs and SVPBs on an exposed workday relative to a comparable low or nonexposed workday among the same individuals, we conducted a nonparametric (signed rank) test on the mean difference in the number of events between the 2 days. Parametric (paired t-test) tests were used to compare the mean P-R interval and heart rate between exposed and nonexposed workdays. Because some workers had greater exposures on the exposed day, we examined whether the magnitude of the change in exposure between low and high exposed workdays was related to greater changes in the dependent variables. We compared the change in the rate of VPBs and SVPBs relative to the change in exposure using Spearman's rank correlation coefficient. We used linear regression analysis to examine the relationship of the change in the full-shift TWA exposure with the change in P-R interval and heart rate.

## RESULTS

Thirty-one workers, representing 88.6% of the exposed workers, were monitored on an exposed day. Of the 31 exposed workers, we were able to monitor 21 workers on a low or nonexposed work day. Five of the 21 workers were excluded from the exposed and nonexposed workday comparison, because exposure monitoring found only small differences (<100 ppm) in the TWA FC113 exposure level between the 2 days.[1] The average age of the study participants was 41.7 years, and the average length of employment was 7.8 years. Eight of the workers smoked, and ten were male.

The mean full-shift TWA exposure (not including break periods) was 442.1 ppm during the exposed day and 64.4 ppm during the low exposed day ($p < .001$). The highest full-shift TWA exposure (not including break periods) was 1,476 ppm on the exposed day (Table I). When we calculated the 8-hour TWA on the exposed day,

[1]The clean room was shut down during monitoring of several workers for most of one shift so that exposures were minimal during the exposed day. Also, exposure monitoring on one individual in the precleaning area showed exposure levels comparable to that of the clean room, which may have been due to a problem with the vapor degreaser in the precleaning area or undocumented movement into the clean room.

**TABLE II. Mean Frequency of Premature Beats and Mean Intraindividual Differences Between the Exposed and Low Exposed (FC113) Workday (N = 16)***

| | Exposed day | Low exposed day | Mean of paired differences | Signed rank |
|---|---|---|---|---|
| Type of event | Mean (min, max) | Mean (min, max) | Mean (min, max) | p value |
| VPB total count | 2.19 (0,23.00) | 7.19 (0,78.0) | −5.00 (−75,3.0) | .28 |
| VPB rate | 0.21 (0,0.62) | 0.60 (0,2.19) | −0.15 (−2.1,0.1) | .20 |
| SVPB total count | 1.89 (0,16.00) | 1.45 (0,12.0) | 0.44 (−8.0,14.0) | .85 |
| SVPB rate | 0.07 (0,0.63) | 0.04 (0,0.34) | 0.03 (−.19,0.6) | .66 |
| | Mean (min, max) | Mean (min, max) | Mean (SD) | Paired t-test p value |
| Heart rate | 88.09 (64.8,116.2) | 91.22 (64.2,113.6) | −3.13 (8.06) | .14 |
| P-R interval | 0.13 (0.10,0.17) | 0.13 (0.10,0.18) | 0.001 (0.01) | .75 |

*Median score of the paired differences for the total count and rate of ventricular premature beats (VPBs) and supraventricular premature beats (SVPBs) was 0.

which included periods of no exposure during breaks, the mean 8-hour TWA was 272.7 ppm, and the highest 8-hour TWA was 935.0 ppm. Thus, this population of workers had an 8-hour TWA exposure level within the 1,000 ppm OSHA 8-hour PEL.

Smoking and caffeine intake among the 16 workers was comparable on the exposed and low exposed workdays: mean of the paired difference was −1.5 for the number of cigarettes smoked, and −0.5 for the number of caffeine drinks consumed ($p > .05$).

As seen in Table II, the mean of the paired differences in VPBs per 1,000 heart beats was −0.15 ($p = .20$), and the mean of the paired differences (delta) in the rate of SVPBs was 0.03 ($p = .66$). No effect of exposure was observed on heart rate (mean delta = −3.13, $p = .14$) or the length of the P-R interval (mean delta = −0.0006, $p = .75$). The Spearman rank correlation coefficient for the rate of VPBs ($r = .17$, $p = .52$) and SVPBs ($r = .31$, $p = .23$) showed no significant dose-response effect. Similarly, the linear regression coefficients for heart rate (beta = −0.002, $p = .82$) and P-R interval (beta = −0.000004, $p = .51$) showed no dose-response effect. One individual, however, had an episode of sinus rhythm bradycardia for less than 15 minutes on the exposed day only, which occurred during short-term exposures of 600 ppm. But, another worker with S-T segment depression had similar ECG patterns on both the exposed and low exposed workdays. There were no events of A-V block or T-wave inversion on either of the 2 days. Also, no workers reported palpitations, dizziness, or lightheadedness.

## DISCUSSION

Overall, an exposed workday was not associated with a greater number of dysrhythmic events than a comparable low exposed workday in this population of aerospace workers exposed to FC113. One strength of this study is that we were able to examine the same workers on comparable exposed and low exposed days. Caffeine intake, tobacco usage, and the physical activity level during work in the exposed and

low exposed areas were very similar. Another strength of the study is that we had sufficient power to detect small differences because of the small within-subject variance in the ECG data. For example, we had 80% power (at an alpha of .05) to detect a 0.34 difference in VPB rates and a 0.10 difference in SVPB rates between the exposed and the low or nonexposed days.

A number of study constraints, however, limit our ability to generalize from these results to other populations of workers. Because fluorocarbons are thought to sensitize the heart to epinephrine [Zachari and Aviado, 1982], this study's negative findings based on sedentary workers may not be generalizable to workers engaged in more physically demanding work. High exposures in this population of workers occurred while the workers were standing at the sinks, dipping or spraying the parts with FC113, which required minimal physical effort.

Another limitation of the study is that we used a cross-sectional study design. Therefore, workers who felt an effect from FC113 exposure may have selected out of the exposed area and would not have been available for recruitment for our study population. Also, healthy individuals may have been selected for the cleaning and precleaning work through mandatory pre-employment physical examinations at Facility B, and periodic physical examinations at both facilities. While medical records are available on all employees, we have no information on the proportion of job applicants that were ineligible for employment on the basis of preexisting health conditions.

Another study constraint was that we observed each participant on only one exposed day. Given that many of the ECG events were relatively rare in this population of healthy workers, and that the magnitude of exposures may vary from day to day, additional days of observation may have been advantageous.

In summary, levels of FC113 exposures below the OSHA standard of 1,000 ppm did not induce cardiac dysrhythmias or subtle changes in cardiac activity. The generalizability of the results to other populations of workers, however, may be limited.

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