

# Review of New Evidence Regarding the Relationship of Gasoline Exposure to Kidney Cancer and Leukemia

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Four new or updated epidemiologic studies were presented at a meeting on the health effects of gasoline exposure held in Miami, Florida, November 5-8, 1991. A focus of these studies was whether there is a relationship between gasoline exposure and kidney cancer and leukemia. For gasoline distribution workers, who have a relatively high exposure, there was some evidence for a kidney cancer relationship in three studies but none in the fourth. There was evidence for an acute myelocytic leukemia relationship in three studies. The fourth study dealt only with kidney cancer. It is possible that the benzene content of gasoline was responsible for the leukemia findings. It is uncertain whether gasoline exposure is a cause of kidney cancer.

## Introduction

At a meeting in Miami, Florida, November 5-8, 1991, on the health effects of gasoline, a panel was formed to evaluate the evidence and express an opinion. Presented at the meeting were four new or updated sets of epidemiological data that dealt with deaths from kidney cancer and leukemia. These data are important in that all relate to some extent to gasoline distribution workers who have a relatively high exposure to gasoline. They are the only data that report kidney cancer and leukemia deaths for large populations with gasoline exposures as high as gasoline distribution workers and represent the best effort to date to answer the question as to whether gasoline exposure is associated with kidney cancer and leukemia. To fairly review and evaluate the new evidence, it was necessary to examine the reports on which the meeting presentations were based, including revisions of these reports and other reports. Of the four sets of epidemiological data presented, one dealt mainly with gasoline refinery workers but contains some limited data on distribution workers, one dealt only with gasoline distribution workers, and the other two dealt with both refinery and distribution workers.

## Kidney Cancer

For refinery workers, the data provide little or no support for an excess in kidney cancer. A case-control study by Poole et al. shows no dose-response relationship (100 cases: relative risk [RR] = 1.00) (1). According to the

authors, the finding most consistent with a causal interpretation was for workers hired at 35 years of age or older where there was a relative risk of 2.5 (9 cases). However, in the light of other findings in their study, the authors felt that this finding could not be accorded a great deal of weight. A cohort mortality study presented by Rushton shows no elevation in the SMR (56 cases: SMR = 101) (2). There is also a new mortality study of refinery workers that shows no excess (9 cases: SMR = 91) (3). A meta-analysis by Wong and Raabe shows no overall excess in kidney cancer in a large number of refinery worker studies (4).

For gasoline distribution workers, who have higher exposure levels than refinery workers, there is mixed evidence of a kidney cancer excess. Data that suggest a kidney cancer excess in distribution workers include the study of refinery workers by Poole et al., in which there was a relative risk of 2.5 for workers whose longest job was in receipt, storage, and movement of petroleum products (1) (9 cases). Poole et al. commented on the value of studying gasoline distribution workers (1). Rushton found an SMR of 121 in distribution workers (53 cases) in contrast to the SMR of 101 in refinery workers (2). For distribution workers, the SMR < 20 years since first exposure was 102 (9 cases), 20 years or more since first exposure was 126 (44 cases), and 30 years or more since first exposure was 148 (36 cases). For tank truck drivers, whose gasoline exposure is believed to be highest, the SMR was 141 (25 cases); however, there was only a weak relationship with time since first exposure. Rushton believed there may have been underreporting of kidney cancer in her study of distribution workers. Schnatter et al. reported an SMR of 135 in marketing and transportation workers (9 cases) in contrast to the SMR of 91 in

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refinery workers (3). For distribution workers exposed to gasoline, Schnatter et al. reported an SMR of 158 (7 cases) (5). For workers with daily exposure, the SMR was 208 (5 cases). For tank truck drivers, the SMR was 210 (2 cases). Twenty years from first exposure, the SMR was 181 (6 cases). For workers with 20 years or more employment, the SMR was 175 (5 cases). Schnatter et al. believed their patterns of risk were consistent with a possible risk of kidney cancer due to gasoline exposure (5).

On the other hand, some of the data presented do not support a kidney cancer excess in distribution workers. A large study by Wong et al. of land-based distribution workers had an SMR for kidney cancer of only 65 (12 cases) (6). For tank truck drivers the SMR was 61 (8 cases). For marine distribution workers the SMR was 83 (14 cases). This is the only study where a quantitative estimate of gasoline exposure was made. There was no relationship between kidney cancer and length of exposure, time since first exposure, year of first exposure, job, and for land-based workers, peak exposure and cumulative exposure or cumulative frequency of peak exposures. There was some support, however, for the observation by Poole et al. of an association with exposure for workers first exposed at older ages. The SMR for workers first exposed at ages 45 and over was 148 for land based workers (2 cases) and 113 for marine (4 cases). A paper presented by Rodgers and Baetcke indicates that it now seems highly unlikely that the study of male rats, which largely stimulated current concern regarding a relationship between gasoline exposure and kidney cancer, applies to humans (7).

## Leukemia

As to whether gasoline exposure is a cause of leukemia, this would seem to depend on the benzene content, because gasoline contains benzene and benzene is a known cause of leukemia in humans. All three of the new or updated studies of gasoline distribution workers presented at the meeting suggested excesses in leukemia—particularly acute myelogenous leukemia (AML), the type of leukemia most likely to be related to benzene exposure. However, none of these studies attempted to relate benzene exposure to leukemia. For AML, Rushton reported an SMR of 121 (25 cases) (2). For tank truck drivers the SMR was 155 (13 cases). Schnatter et al. reported a significantly elevated SMR of 335 for tank truck drivers (5 cases) (5). One of these deaths was a definite AML and two were possible. All were hired before 1972. Wong et al. reported an SMR of 150 for AML (13 cases) for land-based distribution workers but no increase in marine employees (6). The excess was limited to workers hired before 1948. There was, however, no trend in AML when data were analyzed by various gasoline exposure indexes. While it is possible that the excesses are related to the benzene content of gasoline, they need further study in the light of actual benzene exposure levels. Also, there are new data relating to the magnitude of the leukemia risk from benzene that need consideration (8).

## Comment

The Wong et al. study (6) of distribution workers is important because of its size and because it deals with gasoline exposure in a quantitative fashion. Overall, this is a negative study for kidney cancer and perhaps for leukemia as well. There is some question, however, as to selective factors in the study population and the possibility that health-related covariates were quite different from those in the reference population used in calculating SMRs. For land based workers the SMR for all causes was only 51 (2066 deaths), in contrast to an SMR of 91 in the Rushton study (2) (8743 deaths) and 88 in the Schnatter et al. study (5) (1154 deaths). According to Wong et al. (6), the low SMR was probably due to selection at time of hire and, when compared to the general population, better health maintenance, less smoking, less drinking, and higher socioeconomic status. It is not clear, however, why these same factors were not operative in the Rushton (2) and Schnatter et al. (5) studies of distribution workers. Certainly they help explain the very low SMRs in the Wong study. They also raise a question as to the kind of inferences that can be made from such an atypical population. Examination of dose-response relationships in the Rushton (2) and the Schnatter et al. (5) studies may help answer this question.

The Poole et al. study (1) deals with gasoline exposure in a semiquantitative fashion and is also negative for kidney cancer. The Poole et al. study relates to refinery workers, however, where gasoline exposure is lower and for whom other studies are also negative. The Rushton study (2) tends to be positive for both kidney cancer and leukemia and is particularly important because of the large number of deaths and the fact that the new follow-up confirms findings on kidney cancer reported earlier for the same group of workers. Unfortunately, analysis of these data was incomplete at the time of the Miami meeting. The results of the Schnatter et al. study (5) are, in my opinion, consistent with both a kidney cancer and a leukemia excess.

## Conclusion

The question as to whether or not gasoline exposure is associated with kidney cancer has not been answered by the four new or updated sets of epidemiological data presented at the Miami meeting. On the other hand, there is evidence of a relationship between gasoline exposure and acute myelogenous leukemia, and it is possible that this is due to the benzene content of gasoline.

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