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Chemical Substances and Biological Agents

Studies and Research Projects

REPORT **R-516**

Risk of Cancer of the Colon and Rectum in Firemen

Douglas McGregor

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Cancers of the Large Intestine

The large intestine is part of the lower gastrointestinal track that includes the caecum, the colon and the rectum. Anatomically, the colon is further subdivided into ascending colon, hepatic flexure, transverse colon, splenic flexure, descending and sigmoid colon. Most of the tumours of the large intestine are of epithelial origin and are considered malignant when the tumour penetrates the muscularis mucosae into the submucosa (Hamilton et al., 2000). They include adenocarcinoma (by far the most frequent histological type), mucinous adenocarcinoma, signet-ring cell carcinoma, small cell carcinoma, squamous cell carcinoma, adenosquamous carcinoma, medullary carcinoma and undifferentiated carcinoma. The emergence of most of these malignancies are preceded by tubular, villous, tubulovillous and serrated adenomas (Midgley and Kerr, 1999). Other types of neoplasia also may occur in the colon and rectum, although rarely, and these include lipoma, leiomyoma, gastrointestinal stromal tumour, leiomyosarcoma, angiosarcoma, Kaposi's sarcoma, malignant melanoma and the various malignant lymphomas (Hamilton et al., 2000).

Colorectal cancer is the third most common cancer and the fourth most frequent cause of cancer death world-wide, accounting for 9.4% and 7.9% of all cancer cases and deaths, respectively (Ferlay et al., 2004). In more developed countries, colorectal cancer is the second most frequent cancer type and cause of cancer death, accounting for 13.3% and 11.7% of the cases, respectively (Ferlay et al., 2004). There is up to a 20-fold difference in incidence between the high rates experienced in the economically developed countries of Australia, Europe, Japan and North America versus those of central Africa, the Indian sub-continent and southern Asia (Ferlay et al., 2004). There are also significant differences within geographical regions, with higher incidences occurring in western and northern Europe than in central and southern Europe (Cooper et al., 1998). Temporal changes in the incidence of cancers of the colon and cancers of the rectum differ. Within the USA, the incidence of adenocarcinoma of the colon increased by about 18% during the period from 1973 to 1988 while the incidence of rectal adenocarcinoma and mucinonous adenocarcinoma in the colon remained relatively constant in this period (Thomas & Sobin, 1995).

Approximately 60% of colorectal cancers in high incidence populations arise in the left colon (descending and sigmoid colon), whereas in low incidence regions there is a predominance of right-sided cases (caecum, ascending colon, hepatic flexure, transverse colon, splenic flexure) and rectum (Iacopetta, B., 2002). In Western countries, the incidence of right-side cancers has steadily increased, while that of left side tumours has shown a corresponding decrease (Iacopetta, B., 2002). Colorectal cancer incidences among migrants rapidly approach the incidences of their adopted countries (in the first generation or after more than 20 years of residence), indicating that environmental factors play an important role in the aetiology of the disease (Shottenfeld and Winawer, 1996;WHO, 2003).

Both colonic and rectal adenocarcinoma incidence rates are higher in males than in females. While incidence rates for rectal adenocarcinoma are higher amongst whites than in blacks, the incidence rates for colonic adenocarcinoma are higher in blacks than in whites (Thomas & Sobin, 1995). Most cases of colorectal cancer occur above the age of 60 years (see Figure 1).

The vast majority of colorectal cancer cases are sporadic, but about 5% develop in the setting of defined hereditary cancer syndromes (Weitz et al., 2005). Most of the hereditary colorectal cancers are associated with two main predisposition syndromes: familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (Midgley and Kerr, 1999; Weitz et al., 2005). Inflammatory bowel disease, particularly the ulcerative colitis form, has been associated with 4- to 20-fold higher risk of developing colorectal cancer, depending on disease severity and duration (Shottenfeld and Winawer, 1996; Hamilton et al., 2000; Shelton et al., 1996; Lennard-Jones et al., 1990). Colorectal cancer is also higher, by about 3-fold, in the second subtype of inflammatory bowel disease and Crohn's disease (Gillen et al., 1994; Hamilton et al., 2000). On the other hand, ulcerative proctitis is not associated with risk for carcinoma. Several other medical conditions, such as diabetes (Renehan and Shalet, 2005), acromegaly (Jenkins, PJ, 2004; Terzolo et al., 2005) and, possibly, cholecystectomy (Schernhammer et al., 2003) or less frequent bowel movements (Kojima et al., 2004) have been associated with increased risk of colorectal cancer in some epidemiological investigations.

Diet has long been regarded as the most important environmental influence on colorectal cancer (World Cancer Research Fund, 1997). In general, high meat, fat or overall caloric intake have been associated with adverse effect, while diets rich in vegetables and fruits or fibre have been related to decreased risk. Since most of these dietary components are highly correlated, the dietary data are difficult to interpret with greater precision (Potter, J., 1999; IARC, 2003). A formal meta-analysis and a recent large prospective study indicated that risk of colorectal cancer increases with increasing intake of red or processed meat, while a protective tendency emerged for high intake of poultry and fish (Norat et al. 2002; Chao et al. 2005). On the other hand, despite previous inconsistent results, a large prospective study from Europe showed a protective effect of dietary fibre (Bingham et al., 2003). The beneficial effect of high calcium and selenium intake as suggested by epidemiological studies is currently being evaluated in large randomised clinical trials (Hawk and Levin, 2005).

High body mass index (BMI) is an established epidemiological risk factor for colorectal cancer in both men and women (IARC, 2002; Calle et al., 2003); however, the association appears substantially stronger for cancers of the colon than for those of the rectum. There is an approximately linear trend of colorectal cancer risk from BMI 23 to 30 (kg/m^2), with a risk increase across this range of about 25% among women and 50% among men. The association of BMI with colon cancer is similar for time periods early and late in adulthood, suggesting an effect of factors associated with adiposity on the promotion of colon cancer (IARC, 2002). A recent study estimated that about 11% of colon cancers in Europe are attributed to overweight (BMI > 25) and obesity (BMI > 30) (Bergstrom et al., 2001). It has been suggested that greater height could also confer increased risk of cancer (Hebert et al., 1997; Robsahm and Tretli, 1999; Shimizu et al., 2003). Physical activity on the other hand has been associated with decreased risk of colon cancer (IARC, 2002a).

Other factors frequently investigated in relation to colorectal cancers include use of non-steroidal anti-inflammatory drugs (NSAIDs), alcohol consumption and tobacco smoking. Epidemiological studies have consistently shown a protection associated with use of NSAIDs, especially in regular users and with higher dose (Hawk and

Levin, 2005). Intake of alcohol has been associated with increased risk of colorectal cancer in several epidemiological studies (Potter, 1999; Corrao et al., 2004; Su and Arab, 2004). A recent pooled analyses of 8 prospective studies from Canada, Finland, Netherlands, Sweden and USA showed that intake of more than 45 grams of alcohol per day confers about 40% increase in colorectal cancer risk, with adverse effects being seen on proximal, distal colon or rectum, irrespective of the type of alcoholic beverages consumed (Cho, et al., 2004). Although several studies have indicated an increased risk of colorectal cancer with tobacco smoking (Limburg et al., 2003; Colangelo et al., 2004), the evidence linking smoking with risk of developing colorectal adenomas is much stronger (IARC 2004). Also, according to Doll et al. (2005), since smokers tend to be heavier drinkers than non-smokers, it is possible that the relationship observed with smoking in their study might be an artefact due to confounding with alcohol. In the study of the cohort of British doctors, Doll et al. (2005) found after 50 years of observation that there was a relatively weak relationship with smoking, with an "implausibly strong" relationship for rectal cancer and no evident relationship for colon cancer. The authors were reluctant to accept there findings for rectal cancer because no such limitation to rectal cancer was found in many other studies reviewed by IARC (2004). In general, very few studies of firemen have been able to control for any of these positive or inverse association factors.

Colorectal cancer is generally not viewed as an occupational disease (Shottenfeld and Winawer, 1996); however, a weak association between asbestos exposure (especially chrysotile and amosite fibres) and colonic cancer has been suggested (Morgan et al., 1985), which, if correct, could have implications for firemen. This possibility is brought into question by the study of Spiegelman and Wegman (1985), who found that after controlling for diet and physical activity the odds ratio was not elevated for work-related asbestos exposure and colonic cancer. Since then, there have been many studies that have included consideration of effects of asbestos exposure on the incidence of colorectal cancer. Results have been mixed and, where they have suggested an effect, this has been small. An early meta-analysis of 20 cohorts suggested that exposure to amphibole asbestos may be associated with colorectal cancer, but according to the authors the findings could have reflected an artefact of miscertification of cause of death. The study also suggested that serpentine asbestos was not associated with colorectal cancer (Homa et al., 1994). A review of 30 cohort studies published through 1993 found that the overall relative risk (as standardised incidence or mortality ratios) was 0.99 (Weiss, 1995). A recent study, which included smoking information, (Reid et al., 2004) of former workers from a crocidolite (blue asbestos) mine in Western Australia did not show an association between cumulative asbestos exposure and cancers of the stomach, colorectum or upper aerodigestive region.

Firemen: General Characteristics and Exposures

The task of fire fighting consists of two phases: (1) *knockdown*, during which the fire is brought under control, and (2) *overhaul*, when the fire is extinguished and clean up begins. Approximately 90% of structural fires are either extinguished or abandoned and fought from outside within 5 – 10 min., the average duration of heavy physical activity being 10 min. (Gilman & Davis, 1993). Although self-contained breathing apparatuses (SCBA)s are available, these are seldom worn from the time the firemen arrive at the scene until the time that they leave. In a study of exposures in the City of Montréal fire department, Austin et al. (2001a), found that SCBAs were worn about 50% of the time at structural fires, but they were worn for only 6% of the total time spent at all types of fires. Masks are generally put on when the firemen enter a fire or "see smoke," but it is difficult for them to judge when the mask can be safely removed and they are rarely worn during the smouldering phase of a fire or during mop-up operations. Furthermore, communication is essential and this is difficult with the mask in place. The largest category of non-fatal fire fighter injuries associated with fires has been reported to be contact with flames and smoke (39%) and the leading cause of non-fatal injury among younger firemen is related to smoke inhalation (FEMA, 1990).

In a study of municipal structural fires, Austin et al. (2001b) found that just 14 different compounds accounted for about 75% of the total volatile organic materials measured (Table 2). These same compounds constituted approximately 65% of all volatile organic compounds in experimental fires burning various materials commonly found in structural fires (Austin et al., 2001c). The spectra of volatile organic compounds were dominated by benzene along with toluene and naphthalene. They also found that propylene and 1,3-butadiene were present in all of the fires and that styrene and other alkylated benzenes were frequently identified. Other materials that have quantified with some regularity include acrolein, carbon monoxide, formaldehyde, glutaraldehyde, hydrogen chloride, hydrogen cyanide and nitrogen dioxide (Bolstad-Johnson et al., 2000; Caux et al., 2003). There may also be exposure to asbestos and various metals, such as cadmium, chromium and lead. In addition, there is almost certainly exposure to diesel exhaust and fumes and to polycyclic aromatic hydrocarbons (PAHs).

During overhaul, recommended ceiling or short-term exposure levels can often be exceeded, e.g., for acrolein, benzene, carbon monoxide, formaldehyde, glutaraldehyde, nitrogen dioxide and sulphur dioxide (Bolstad-Johnson et al., 2000) and several of these, e.g., carbon monoxide and benzene, were found to be present at appreciable concentrations in the atmosphere at real fire scenes when SCBAs were only used part of the time or not at all, owing to the impression that there was low smoke intensity (Brandt-Rauf et al., 1988, 1989).

<u>Possible risk factors for colorectal cancers associated with fighting fires.</u>

The following discussion is focused on the substances listed in Table 1 that could be risk factors for colorectal cancers. Possible confounders that are not necessarily associated with fighting fires (e.g., tobacco smoking, diet) have been discussed above.

There is very little indication that either benzene or 1,3-butadiene exposures are associated with colorectal cancers. Authoritative evaluations of these compounds did not mention these cancers (IARC, 1987; 1999). Studies of benzene exposure more recent than those reviewed in IARC (1987) also do not normally mention either colon or rectum as sites at elevated risk for cancer. However, a case-control study in Montréal, Canada, did report an elevated odds ratio for colon cancer (1.9) associated with "substantial" exposure to benzene (Goldberg et al., 2001). Nevertheless, in a study of exposure of firemen to benzene in Toronto, Canada, the main conclusion was that while there is indeed exposure to benzene, even with modern protective equipment, the exposure was rather low, based on *t,t*-muconic acid measurements in urine (Caux et al., 2002).

Toluene and the xylenes have been evaluated by the IARC much more recently than benzene. There were eight epidemiological studies in which *toluene* was mentioned as an exposure (IARC, 1999). In two of these studies, one of rotogravure printers in Sweden and one of shoe-manufacturing workers in the U.S.A., it was believed that toluene was the predominant exposure. Cancers at most sites were not significantly associated with toluene exposure in any study. Mortality from cancers of the colon or rectum were significantly elevated only in the study of Swedish rotogravure printers (and with no dose related response). Furthermore, incidence of these cancers was not significantly elevated in either study. This suggests that there could have been bias in the mortality data for cancers of the colon and rectum in the Swedish study. Exposures to *xylenes* were mentioned in four epidemiological studies summarised by IARC (1999). Cancers at most sites were not significantly associated with exposure to xylenes in any study. An exception was colorectal cancer in one case-control study, but in none of the others. There are no epidemiological studies in which *ethylbenzene* (IARC, 2000), *propylene* (IARC, 1994) or *naphthalene* (IARC, 2002b) could be implicated in any of the cancers discussed here. In addition, *styrene*, which is produced mainly by the catalytic dehydrogenation of ethylbenzene, has not been implicated as a risk factor for colorectal malignancies (IARC, 2002b).

A study involving 3730 cancer cases of the possible association between occupational exposure to PAHs and 14 different kinds of cancer was conducted in Montréal (Nadon et al., 1995). Among the PAH exposures considered were benzo(a)pyrene and five categories of PAHs defined on the basis of the source material, which were wood, petroleum, coal, other sources and any source. Each PAH source was subdivided into unexposed, low and high exposure sub-groups (based on duration, concentration and frequency of exposure). There were no significantly increased risks of cancers of either the colon or rectum.

Cancer risk from occupational exposure to PAHs has been reviewed (Boffetta et al., 1997). High occupational exposure to PAHs occurred in aluminium production, coal gasification, coke production, iron and steel foundries, tar distillation, shale oil extraction, wood impregnation, roofing, road paving, carbon black production, carbon electrode production, chimney sweeping and calcium carbide production. In addition, workers exposed to diesel engine exhaust are exposed to PAHs and nitro-PAHs. It was concluded that heavy exposure to PAHs entails a substantial risk of cancer in the lung, skin and urinary bladder, but there was no mention of possible risks for cancers of either the colon or the rectum.. As part of the study mentioned above of firemen exposed to PAHs in Toronto, Canada, the main conclusion was that while there is exposure, even with modern protective equipment, the exposure appears low in comparison to that observed in many industrial workers (Caux et al., 2002). Additionally, unlike industrial workers, the exposure of firemen is not repeated 8 h per day, 5 days per week. Shortcomings of this study noted by the authors were the small number of fire types encountered during the study and the possibility that volunteer firemen may well have used their protective equipment more extensively than others. PAHs are believed to be partly responsible of the association of colorectal cancer with meat consumption (Norat et al., 2002)..

An authoritative evaluation of possible carcinogenic effects of diesel exhausts and fumes found that there was *limited evidence* for the carcinogenicity in humans of diesel engine exhaust, a conclusion that was based on moderate increases in lung cancer risks, colorectal cancers having played no role in the evaluation. Increased risks for other malignancies were not identified (IARC, 1989). Similar findings were the outcome of a review of work with exposure to diesel engine exhaust in the transport industry (Boffetta et al., 1997).

Epidemiological Studies Reviewed.

In the epidemiological literature on risk of cancer among firemen that has been reviewed, 10 publications were suitable for examination of cancers of the colon (Vena & Fiedler, 1987; Sama et al., 1990; Grimes et al., 1991; Demers et al., 1992, 1994; Aronson et al., 1994; Tornling et al., 1994; Ma et al., 1998; Baris et al., 2001; and Bates et al., 2001) or of the rectum specifically (Vena & Fiedler, 1987; Heyer et al., 1990; Sama et al., 1990; Beaumont et al., 1991; Demers et al., 1992, 1994; Aronson et al., 1994; Burnett et al., 1994; Baris et al., 2001; and Bates et al., 2001) and 2 publications reported colon and rectal cancers combined (Giles et al., 1993; Guidotti, 1993). One study combined rectal with anal cancers Tornling et al., 1994), but since anal cancer is infrequent in comparison with rectal cancer (see Figure 1), any bias introduced by combining these cancers is likely to be small. In addition, six studies examined risk of cancers of the whole digestive tract (Musk et al., 1978; Feuer & Rosenmann, 1986; Deschamps et al., 1995), of the intestine (Eliopulos et al., 1984), or the intestine except the rectum (Heyer et al., 1990; Beaumont et al., 1991) (Table 3). In these latter five studies, no significantly increased risks of cancer of the digestive tract or intestine were recorded. Apart from Heyer et al. (1990), which contains separate data on rectal cancer, they will not be considered further because of the unknown effect of classifying all intestinal or digestive tract tumours together, when a specific effect on colorectal cancers is being examined. If occupational exposures to firemen are affecting all gastrointestinal tract tumours to the same extent then risk ratio changes would be reliable, but in the event of a specific effect on colorectal cancers, then the bias would be towards the null. Those studies that examined either colorectal cancers together or cancers of the colon and rectum separately are summarised below. Very similar data have been reviewed recently (http://www.worksafebc.com/regulation_and_policy/archived_information/policy_discussion_papers/pdf/FirefightingOccupationReport.pdf).

Vena and Fiedler (1987) studied the mortality experience of 1867 male white firemen in Buffalo, NY, USA who had been employed in this capacity for at least one year, from 1950 to 1979. Death certificates were obtained for 94% of the 470 deaths that occurred in this period. Risk of death from cancer of the colon (ICD- code 153) was statistically significantly increased: SMR = 1.83 (CI 1.05-2.97), based on 16 cases, whereas cancer of the rectum (ICD- code 154) was not: SMR = 2.08 (CI 0.83-4.28), based on 7 cases. When analysed for year of first employment as a fireman, calendar year of death and for years worked as a fireman, risk of cancer of the colon remained significantly increased ($p < 0.05$) in the groups first employed before 1930 and from 1930-1939: SMRs = 2.27 and 2.35, based on 10 and 4 cases respectively, the most recent category of calendar year of death (1970-1979): SMR = 2.20, based on 9 cases, and with 40 or more years employment: SMR = 4.71, based on 4 cases. Clearly these are not independent analyses, since they may indicate that latency plays a role, but this factor is not independent of these subgroups being surrogates for exposure. No significantly elevated risks were observed in any other categories of any of these analyses.

Heyer et al. (1990) studied a cohort of 2289 firemen in Seattle, WA from 1945 through 1983 by which time there were 383 deaths. Overall, 105 (4.6%) were lost to follow-up. As mentioned earlier, deaths from intestinal cancers were not elevated: SMR = 0.79 (CI 0.32-1.64), based on 7 cases, but it cannot be known from the publication how much of the intestine was included in the analysis, except for the rectum, which was analysed separately. There was a lower than expected risk of death from rectal cancer: SMR = 0.65 (CI 0.08-2.37), but this is based on only 2 cases. With such a small number of cases, subgroup analysis serves no purpose and was not pursued by the authors.

Sama et al. (1990) examined associations between fire fighting and cancer incidence in Massachusetts, cancers of the colon and rectum being two of nine malignancies that were studied. Subjects were identified through the state cancer registry files for 1982-86. Disease classification was made on the basis of primary site and histology according to the International Classification of Diseases for Oncology (ICD-O) system (WHO, 1976). Occupation and industry were coded according to the 1980 U.S. Bureau of the Consensus (BC) system (U.S. Bureau of the Consensus, 1982). Male cancer cases included were firefighter (BC code 417) and fire chief (BC code 413). Two "unexposed" reference populations were used: Massachusetts policemen and white Massachusetts men. Police were selected as a reference group because of their probable similarity to firemen with regard to socio-economic factors. Standardised morbidity odds ratios (SMOR) were not increased for either cancers of the colon (ICD-O code 153) or rectum (ICD-O code 154) among firemen compared with police referents colon, SMORp = 1.04 (CI 0.59-1.82), based on 33 cases; rectum, SMORp = 0.97 (CI 0.50-1.88), based on 22 cases, and were not significantly increased when Massachusetts white men were used as the reference population: colon, SMORm = 1.20 (CI 0.80-1.82); rectum, SMORm = 1.35 (CI 0.84-2.19). Incidence data (as used in this study) have the advantage over mortality data in that cancer registry information provides better diagnostic information than death certificates. Over 96% of the cases were pathologically confirmed. Limitations of the study were that occupational information was available for only about 50% of the cases and misclassification of occupation in the cancer registry records could have occurred. Both of these limitations, however, are likely to be random. Another issue is that there was no sub-classification of firemen according to their actual duties, so no assessment of likely exposures is possible. This is likely to dilute effects of exposure and bias risk estimates towards the null, in this study.

Beaumont et al. (1991) calculated mortality rates for 3066 firemen who had been employed in San Francisco, CA between 1940 and 1970. Vital status was ascertained until 1982 and rate ratios calculated using USA death rates for comparison. The rate ratios were standardised for age, year, sex and race. Amongst 1186 deaths there were 236 cancer deaths, approximately as expected, RR = 0.95 (0.84-1.08). There was a statistically significant excess of digestive system cancer, RR = 1.27 (CI 1.04-1.55) based on 99 cases, but this was mainly due to a statistically significant excess of oesophageal cancers, RR = 2.04 (CI 1.05-3,57), based on 12 cases. For rectal cancer, there was an excess, but it was not significant, RR = 1.45 (CI 0.77-2.49), based on 13 cases. There was no separate mention of cancer of the colon, but intestinal other than rectal cancers were not increased, RR = 0.99 (CI 0.63-1.47), based on 24 cases. For rectal cancers, there was no response directly related to either time since first employment (3-19 years, RR = 2.64; 20-29 years, RR = 1.05; 30-39 years, RR = 1.04; 40+ years, RR = 1.77) or length of employment (3-9 years, RR = 0.00; 10-19 years, RR = 2.19; 20-29 years, RR = 1.45; 30+ years, RR = 1.42). Study limitations include the use of the US general population rates for comparison, the lack of tobacco smoking data (but this is not a clear risk factor for rectal cancer) and the multiple comparisons made (92 in all).

Grimes et al. (1991) made a small, proportional mortality study of 58 firemen who died of cancer between 1969 and 1988 employed in the Honolulu fire service in Hawaii, USA using reference rates for men in Hawaii. For all cancers combined, the PMR = 1.19 (CI 0.96-1.49) and for cancer of the colon, PMR = 0.91 (CI 0.37-2.20).

Demers et al. (1992a) studied the mortality of 4546 men employed as firemen in Seattle and Tacoma, WA, and Portland, OR, USA for at least one year between 1944 and 1979. This study, like most others on firemen, relied upon death certificates for cause of death information. The standardised mortality ratios (SMRs) were calculated using reference rates for the USA as a whole and incidence density ratios (IDRs) were calculated for firemen relative to police in the same cities with standardisation by five-year age groups and time periods. Between 1945 and 1989, there were 1169 deaths in the study population, 291 being cancer deaths. There was no excess risk of overall cancer mortality: SMRm = 0.91 (CI 0.85-1.07), IDRp = 0.97 (CI 0.67-1.33). There was no increased risk of either cancer of the colon (ICD-9 codes 152, 153) or of the rectum (ICD-9 code 154) when compared with U.S.A. national rates for men: colon SMRm = 0.85 (CI 0.54-1.26), based on 24 deaths; rectum SMRm = 0.95 (CI 0.41-1.87) based on 8 cases. Also, there was no significant increase in risk for either cancer when firemen were compared with policemen from the same cities: colon IDRp = 1.58 (CI 0.73-3.43); rectum IDRp = 0.89 (CI 0.30-2.66). The latter comparison is likely to be the better comparison, in terms of socio-economic factors that could influence risk. However, the higher (although non-significant) risk of colon cancer in the comparison of firemen with policemen was in part due to the statistically significantly reduced risk of death from colon cancer observed when policemen are compared with overall USA rates: SMR = 0.50 (CI 0.22-0.99), based on 8 cases. Analyses were also conducted for possible dose response relationships based on duration of exposed employment, years since first employment and age at death. No significant increases in risk were found and there were no indications of dose response relationships.

In a study comparing the relative advantages of tumour registry and death certificate information in the U.S. cities of Seattle and Tacoma, WA, Demers et al (1992b) analysed cancer incidence and mortality in a cohort of 4528 firemen and policemen followed between 1974 when all were alive and 1989. For cancer of the colon the standardised incidence ratio (SIR) = 1.00 (CI 0.68-1.43) based on 31 cases and the standardised mortality ratio (SMR) = 0.68 (CI 0.33-1.26) based on 10 deaths. For cancer of the rectum SIR = 0.95 (CI 0.55-1.52) based on 17 cases and the SMR = 1.48 (CI 0.48-3.45) based on 5 cases.

Giles et al. (1993) studied the cancer incidence in a cohort of 2865 firemen employed in Melbourne, Victoria between 1980 and 1989. The cancer incidence in the cohort was compared with that of men in the state of Victoria. There were 20853 person-years of follow-up. The incidence of all cancers combined was not elevated, SIR = 1.13 (CI 0.84-1.48), based on 50 cases, whereas the incidence of colorectal cancers was higher, although not statistically significant, SIR = 1.36 (CI 0.62-2.59).

Guidotti (1993) studied mortality among firemen in Edmonton and Calgary, Alberta, Canada between 1927 and 1987. The cohort consisted of 3328 firemen, amongst whom there were 92 cancer deaths. Follow-up of 96% of the cohort was possible and this provided 64983 person-years of observation. Expected mortality was derived from the corresponding age- and time-specific mortality rates for men residing in Alberta. Comparisons were made over 5-year intervals. Analyses were conducted based on age and on time from entry to the fire service. In addition, to assess the fit of mortality trends to a presumed exposure profile, job categories were weighted as follows: fireman lieutenant and captain = 1, safety or straining officer = 0.2, district chief or volunteer fireman = 0.1, desk job and other designations not involving active fire fighting = 0.0. There was a statistically significant increase for all cancers combined, SMR = 1.27 (CI 1.02-1.55), but the increase in risk of colorectal cancers (ICD-9 codes 152-154) was not statistically significant, SMR = 1.61 (CI 0.88-2.71), based on 14 cases. Some subcategories did show significant increases in risk, but the numbers of cases were never more than 3 in each age or time of entry category. Consequently, the data are unstable and there was no clear correlation with entry cohort. For analysis according to exposure, the cancer mortality category analysed was changed to “intestine and rectum”. The results from the three exposure categories containing data were: exposure index (EI) >0 - <1, SMR = 2.83, based on 2 cases; EI 1 – 9, SMR = 4.58, based on 6 cases; and EI 10, SMR = 0.92, based on 6 cases. Thus, analysis based on exposure opportunity also showed no clear dose response.

Aronson et al. (1994) conducted a cohort study in metropolitan Toronto, Ontario on all 5414 employees who had worked as firemen for at least 6 months at any time between 1950 and 1989. Deaths and causes of deaths were obtained by computerised record linkage. There were 114008 person-years of follow-up. The average years of follow-up and years of employment were 21 and 20, respectively. The incidence of all cancers combined was not elevated, SMR = 1.05 (CI 0.91-1.20) based on 199 cases. The SMR for cancer of the colon (ICD-9 code 153) was 0.60 (CI 0.30-1.08) based on 11 cases and the SMR for cancer of the rectum and rectosigmoid junction (ICD-9 code 154) was 1.71 (CI 0.91-2.93). Because of the increased, but non-significant risk observed for the latter, rectal cancers were further analysed according to years since first employment, years of employment and age at death from the disease. Except for the subgroup employed for < 15 years, all showed elevated risks, but none was statistically significant. Importantly, there was no clear dose response according to years of employment, the SMRs being: < 15 years, 0, no cases; 15-29 years, 2.35 (CI 0.76-5.48), 5 cases; ≥ 30 years, 1.74 (CI 0.75-3.43), 8 cases.

Demers et al. (1994) studied cancer in 2447 firemen in Seattle and Tacoma, WA, USA, with reference to tumour registry data. Incident cancer cases were identified through the population-based registry of the Cancer Surveillance System (CSS) of the Fred Hutchinson Cancer Research Center. Unlike their 1992 study, death certificates were not used as a source of cancer information. Duration of active duty was assignable for Seattle firemen and used as a surrogate measure of cumulative exposure to combustion products from fires; no exposure was assigned for years spent in administrative duties or support services. Total years of employment had to be used for Tacoma firemen because records identifying the start and end dates of specific duties were not available for all of them. The study population was followed for 16 years (1974-89) and the cancer incidence compared with that among 1878 policemen from the same cities. There were 244 cancer cases in the study population. There was no excess risk of overall cancer: SIRm = 1.1 (CI 0.9-1.2), SIRp = 1.0 (CI 0.8-1.3), nor was there a statistically significant excess risk of cancer of either the colon (ICD-9 code 153) or of the rectum when compared with local county rates for men: colon SIRm = 1.1 (CI 0.7-1.6), based on 23 cases; rectum SIRm = 1.0 (CI 0.5-1.8) based on 12 cases. Also, there was no significant increase in risk for either cancer when firemen were compared with policemen from the same cities: colon IDRp = 1.3 (CI 0.6-3.0); rectum IDRp = 1.3 (CI 0.5-3.9). SIRs were also calculated according to duration of exposed employment, but in neither active duty as a fireman (Seattle) nor total employment (Tacoma) was there any significant underlying relationship of risk with increasing surrogate for exposure, although there was a tendency for the risk increase with duration for colon but not for rectum. The SIRs for cancer of the colon were: < 10 years, 0.8 (CI 0.1-2.9), 2 cases; 10-19 years, 0.7 (CI 0.1-2.6), 2 cases; 20-29 years, 1.1 (CI 0.6-1.9), 15 cases; 30+ years, 1.5 (CI 0.4-3.9), 4 cases. Duration of active fire fighting employment (Seattle) represents an improvement over total duration of employment (Tacoma) as a surrogate index of exposure to specific agents. Thus, there was almost certainly misclassification of exposure in the Tacoma segment, which is likely to bias risk estimates towards the null (as in the Sama et al., 1990 study). Finally, analysis by years since first employment relative to local county rates showed no significant increase or clear indication of an increasing trend in risk with time for either cancer of the colon or the rectum.

Tornling et al. (1994) studied the incidence and mortality in firemen employed for at least one year in Stockholm, Sweden between 1931 and 1983. An index of the number of fires fought has calculated for each individual. The final study population for the mortality analysis consisted of 1116 people, 316 of whom had died between 1951 and 1986. Cancer incidence data collection began in 1958, when the National Cancer Register was established, and collection was stopped in 1986. At the beginning of this period 1091 cohort members were alive. Most (69%) of the firemen began this work before the age of 25 and 61% continued until retirement. Cancer of the colon (ICD-8 code 153) resulted in SMR = 0.85 (CI 0.31-1.85), based on 6 cases, and SIR = 0.90 (CI 0.39-1.77), based on 8 cases. Cancer of the rectum and anus (ICD-8 code 154) resulted in SMR = 2.07 (CI 0.89-4.08), based on 8 cases, and SIR = 1.70 (CI 0.81-3.12), based on 10 cases. No significant increases in risk were observed for either cancer.

Burnett et al. (1994) conducted a particularly large investigation into the occurrence of cancer death in firemen that was reported as a brief communication (although full details are available from the authors). This was a proportionate mortality study of white firemen in 27 states of the USA from 1984 through 1990, using data collected from the National Occupational Mortality Surveillance system. There were 5744 deaths, 1636 being due to cancer. The proportionate mortality ratio (PMR) was statistically significantly increased for all cancers combined, PMR = 1.10 (1.06-1.14) and for that portion of the cases who died at < 65 years of age, PMR = 1.12 (1.04-1.21). Deaths from cancer of the rectum (ICD code 154) significantly increased amongst firemen of any age, PMR = 1.48 (1.05-2.05) based on 37 deaths and for those that died at age <65 years, PMR = 1.86 (1.10-2.94) based on 18 deaths. The strength of this study is its relatively large numbers of cancer deaths. Its weaknesses (shared by other studies of this type) are its reliance on death certificate information, which may be inaccurate, especially for occupation, and give no information on duration of occupation and possible exposures involved, or on possible confounders. In addition, the PMR method of estimating risk will over estimate risk if the overall death rate for the occupational group is low, as might be the case among firemen (DeCouflé et al., 1980).

Ma et al. (1998) used a database overlapping that of Burnett et al. (1994) to examine possible racial differences in susceptibility to cancer mortality. Although the database was extended by three years to 1993, some data were not included because three states were removed from consideration (Alaska, New York and Pennsylvania). There were 6607 deaths, 1817 being due to cancer. Although the stated objective was a racial comparison, there was a large numerical imbalance of deaths between the races. For all cancers combined amongst whites, the mortality odds ratio (MOR) = 1.1 (CI 1.1-1.2) based on 1817 deaths, while amongst blacks the MOR = 1.2 (CI 0.9-1.5) based on 66 deaths. For deaths from cancer of the colon amongst whites, the MOR = 1.0 (CI 0.9-1.2) based on 149 deaths, while amongst blacks the MOR = 2.1 (CI 1.1-4.0), based on 9 deaths. Deaths from cancer of the rectum amongst whites, the MOR = 1.1 (CI 0.8-1.6) based on 27 deaths, while among blacks there were no deaths from this cause. The likely large degree of overlap with the Burnett et al., 1994 study indicates that these cannot be considered as completely independent investigations of cancer of the rectum in the white population. For this reason it is remarkable that there were no colon cancers reported by Burnett et al. (1994). The same study limitations as described for Burnett et al., 1994 apply to Ma et al. (1998).

Baris et al., 2001 studied an historical cohort of firemen in Philadelphia, 1925 to 1986. From the point of view of measures of exposure, length of the historical cohort and length of follow-up, this was a particularly valuable study. Comparison was made against the general white male population of the USA. The 7789 firemen were normally employed in their late 20s and worked for an average of 18 years, with an average of 26 years follow-up. This provided 204821 person-years of follow-up in which there were 2220 deaths, of which 500 were due to cancer. The measures of exposure that were used were:

1. duration of employment (≤ 9 years; 10 – 19 years; ≥ 20 years);
2. type of company employment (engine only; ladder only; engine and ladder);
3. year of hiring (before 1935; 1935-1944; after 1944);
4. cumulative number of fire runs (low, ≤ 3323; medium, ≥ 3323 & ≤ 5099; high, > 5099, i.e., less than the median, ≥ median and ≤ 75th percentile, and ≥ 75th percentile);
5. accumulation of fire runs (low, ≤ 3191; high, > 3191);
6. fire runs during first 5 years as a fireman (low, ≤ 729; high, > 729);
7. life time fire runs with diesel exposure (non-exposed; low exposed, 1 – 259 runs; medium exposed, 260 – 1423 runs; high, ≥ 1423 runs).

The overall risk of mortality from cancer of the colon (ICD-9 code 153) was increased among firemen, with SMR = 1.51 (CI 1.18-1.93) based on 64 deaths, whereas cancer of the rectum (ICD-9 code 154) was not increased, with SMR = 0.99 (CI 0.59-1.68) based on 14 deaths. Mortality from colon cancer was significantly increased among firemen with ≤ 9 years or with ≥ 20 years duration of employment (SMR = 1.78, CI 1.12-2.82, 18 deaths and SMR = 1.68, CI 1.17-2.40, 30 deaths), but not with 10-19 years employment (SMR = 1.11, CI 0.68-1.81, 16 deaths), so the dose response is not clear. Increased risks of colon cancer were observed among firemen hired between 1935 and 1944 (SMR = 2.00, CI 1.38-2.90, 28 deaths) and among those hired after 1945 (SMR = 1.60 CI 1.03-2.49, 20 deaths) whereas hiring before 1935 was not associated with any increased risk (SMR = 1.00, CI 0.61-1.63, 16 deaths). Increased risk of colon cancer was also associated with working exclusively in an engine company (SMR = 1.94, CI 1.38-2.73, 33 deaths), but not with working in either a ladder company exclusively (SMR = 0.59, CI 0.15-2.35, only 2 deaths) or with working in both ladder and engine companies (SMR = 1.19, CI 0.81-1.77, 25 deaths). This could be interpreted as a dose response, with higher risks being associated with engine companies. On the other hand, when numbers of runs was used as an indicator of exposure, simple associations were not found; significant excess risk of colon cancer was found in groups having participated in low and medium cumulative numbers of runs (low, SMR = 1.93, CI 1.29-2.91, 23 deaths; medium, SMR = 2.22, CI 1.36-3.62, 16 deaths), but not high cumulative runs (high, SMR = 1.22 CI 0.64-2.35, 9 deaths). Comparison of subjects with high cumulative runs (> 3191) and high number of runs during the first 5 years (> 729) as a firemen with subjects with low values showed reductions in risk in the high run number categories (high cumulative runs, RR = 0.80 CI 0.44-1.47, 26 deaths; high number of runs during first 5 years, RR = 0.50 CI 0.27-0.92, 16 deaths). This study provides a complex result analysis of the data, there being several indications of an association between occupation as a fireman and risk of cancer of the colon, yet indicators of actual exposure do not provide a clear dose related response. The study also found no association between any of the chosen parameters and cancer of the rectum.

Bates et al., 2001 studied a cohort of all paid and volunteer firemen in New Zealand, 1977 to 1995. The final cohort contained 4305 firemen (4221 males and 84 females). To the end of 1995 the total follow-up time was 59322 person-years, comprising 58709 for males and 613 for females. Because of the low numbers of feamales, they were not included in this review. There was no significant increase or decrease in the incidence of cancer of either the colon (ICD-9 code 153) or rectum (ICD-9 code 154) (SIR = 0.60, CI 0.2-1.2, 7 colon cancers; SIR = 1.15, CI 0.5-2.2, 9 rectal cancers). The data were analysed separately for the period from 1990, because cancer registry data were considered to be more complete from that time, but no important differences in SIRs emerged (SIR = 0.58, CI 0.2-1.5, 4 colon cancers; SIR = 1.08, CI 0.3-2.5, 5 rectal cancers). Years of service was used as a measure of exposure divided into 0-10 years, 11-20 years and > 20 years for all firemen and for paid service firemen only. Low numbers limited the value of this procedure and in no category was there a significant increase in risk of either of these cancers. During the study period there were 6 colon cancer deaths and 4 rectal cancer deaths, neither of which was significantly different from the expected numbers (SMR = 1.19, CI 0.4-2.6 for colon cancer; SMR = 1.21, CI 0.3-3.1 for rectal cancer).

Discussion

1. *Problems in the interpretation of epidemiological data.*

a. *Healthy worker effect.*

Fighting fires is a mentally and physically demanding occupation in which burns, falls and crush injuries are commonplace and exposure to smoke and other airborne organic and inorganic substances is part of the job (Gochfeld, 1995). Nevertheless, firemen tend to have a lower mortality rate than the general population, at least during the earlier years of employment. It may be, therefore, that front line firemen are a work population particularly prone to a healthy worker effect, since it appears that many firemen who develop symptoms early in their careers may be moved to other, non-fire-fighting roles (Guidotti & Clough, 1992). This suggestion is supported by the higher prevalence of non-specific respiratory disease amongst firemen who do not actually fight fires (Peters et al., 1974). The healthy worker effect is important during the earlier years of employment, due in large part to a reduction in cardiovascular disease, but the effect tends to disappear with longer employment (Guidotti, 1995). Any effect in late employment could be due to the removal of workers (because they become unfit) from exposure to risk factors predisposing them to early mortality. Bias of this kind, should it occur, is more likely to affect disease categories other than cancer. In the study of Baris et al. (2001) the SMR for all causes of death was significantly reduced during the first 9 years and after 20 years of employment, but not in the employment range 10 – 19 years. These changes seemed to be largely due to changes in SMRs for circulatory disease and ischaemic heart disease and so they are consistent with the suggestions made by Guidotti (1995).

b. *Study size*

Most of the studies reviewed here are based on small numbers of cases of cancer of the colon and rectum. The four larger colonic cancer studies (the white population in Ma et al., 1998, Baris et al., 2001, Sama et al., 1990 and Demers et al., 1992a) had 149, 64, 33 and 31 cases, respectively, the remainder relying upon 24 or fewer cases. The two larger rectal cancer studies (Burnett et al., 1994, Sama et al., 1990) had 37 and 22 cases, respectively, the remainder relying on 14 or fewer cases. Thus, most of the studies lacked sufficient statistical power to detect a possible moderate association (e.g., a 2-fold increase in risk).

c. *Occupational classification*

There have also been concerns in several studies based on cancer registry data that information about occupation was missing or that misclassification of the reported occupation could have occurred. The probability of such misclassification is even higher for studies based on death certificates. This is because firemen belong to an occupational group that routinely retires early and then pursues another occupation and it is the last occupation that is recorded; however, it was judged that the effect of such misclassification would be to reduce the strength of the observed association, because it is expected that the misclassification would be non-differential, i.e., it is independent of the cancer diagnosis.

d. Exposure assessment

Generally few studies could address the issue of actual fire-fighting experience among workers employed as firemen, because a fireman might have been fighting fires, or he might have been assigned purely administrative tasks. Such a lack of sub-classification could influence risk ratios, biasing them towards the null. In addition, the small numbers of cases available in most studies precluded meaningful analysis according to a fireman's actual or likely exposure.

A general problem affecting studies with firemen is that reliance by the investigators upon the number of years employed as a surrogate for actual exposures at fires, which probably resulted in misclassification and might not form a sound basis for describing dose-response relationships. Austin et al., 2001a provide such evidence, as only 66% of fire department personnel were in fact 1st line combat fire fighters and many of these combat firemen moved into non-exposed jobs before the end of their careers. In the same study there was a good correlation between the number of runs to fires and the time spent at fires, and they concluded that the number of runs would be a better surrogate for exposure than years worked as a fireman. However, it was also found that the number of runs may seriously over- or under-estimate the time spent at fires for individual crews, so that time spent at fires is the preferred surrogate. In one example, two crews had almost identical numbers of fire runs, but one spent 1.72 times longer at fires than the other. These results are contrary to the opinion of Guidotti & Goldsmith (2002) who specifically do not advise that job assignments or cumulative number of fire alarms to which firemen were assigned be used as measures of exposure (the only practical basis being, in their estimation, duration of employment). Within the studies reviewed here, Demers et al. (1994) used duration of active duty fighting fires and Baris et al. (2001) used not only duration of employment, but also estimated cumulative number of runs and number of runs during the first 5 years as a fireman. The last estimate of exposure was divided into two groups, low and high, and the relative risk was lower in the high number of runs category. Year of first employment as a fireman, which was used in several of the studies, is more a measure of latency than exposure, since job categories are likely to have changed over the years. Interpretation of dose-response associations between fire fighting and cancers of the colon and rectum is difficult, however, taking into account the very small numbers of cases available in sub-group analyses, even when only two categories of exposure were compared.

e. Adjustment for confounders

Most of the studies relied on death certificates as the main source of information and consequently no information about possible confounders (e.g. diet, alcohol consumption, physical activity, intake of non-steroidal anti-inflammatory drugs) was available. Policemen would be expected to share many socio-economic factors with firemen and this proximity could make for a more sensitive comparison. This factor had no significant effect on the risk of cancer of either the colon or rectum in those studies where the issue was addressed (Sama et al., 1990; Demers et al., 1992a, b, 1994).

f. Design weaknesses

Proportional measures can be misleading because their denominator is the total number of cases or deaths from all causes within the same population. The PMR method of estimating risk, as used by Grimes et al., (1991) and Burnett et al. (1994), will overestimate risk if the overall death rate for the occupational group is low, as might be the case for firemen (DeCouflé et al., 1980). To obtain Mortality Odds Ratios (MOR), as used by Ma et al. (1998), the expected numbers were calculated using all causes of death except cancers from the same occupational mortality database from which the firemen's deaths were obtained. As noted for PMRs, this measure relies on death certificate information and is therefore prone to bias because of misclassification of both the cause of death and the exposure. These two studies are interesting, however, because their study populations are overlapping (which would detract from their significance) and have used different analytical methods - which would add to the significance of their common conclusion.

Generally speaking, incidence data obtained from cancer registries form a more reliable and more detailed source of information on which to base analyses (Demers et al., 1992b). In any of these analyses, the characteristics of the reference population is important; it being an advantage to select a reference population as close to the study population as possible. This advantage was maximised in those studies (Sama et al. (1990); Demers et al. 1992a; 1994) that selected police as a reference group in addition to a more general population.

2. *General Discussion*

Consistency and the strength of the observed associations are important factors in the identification of causality. No single study can provide definitive evidence for a relationship and the strength of the association (the size of the relative risk) must be taken into consideration.

In eight of the studies listed in Table 3, there was some indication of increased risk of cancer of the colon, but risks were significantly increased in only three studies (Vena and Fiedler, 1987; Baris et al., 2001 and for black but not white cases in Ma et al., 1998). Six studies reported some indication of increased of cancer of rectum but risk was significantly increased in only in the Burnett et al. (1994) proportional mortality study. Thus, it is possible that there is a small adverse effect of employment as a fireman, especially, as risk factors have been shown to differ for cancers of the right and left colon and for the rectum and none of the studies could address such a possibility. However, bias and confounding cannot be ruled out since none of the studies controlled for diet, which is a recognised risk factor for cancer of the colon. On the other hand, is it not known if the firemen had lower BMI values than the referents (which would tend to lower risk of colon cancer in firemen, but would have no effect of rectal cancer). If so, then any small increases in risk amongst firemen would have greater aetiological significance. Smoking habits also were not considered, but this is probably not very important, since it seems that tobacco smoking has a small effect at most.

Because of the generally low numbers of cases the examination of dose-response relationships was not usually possible, although attempts were sometimes made. Baris et al. (2001) examined dose-response relationships, but there was no consistency in their results: duration of employment showed no relationship, a high number of runs during the first 5 years of employment reduced the risk and cumulative number of runs was associated with a significantly increased risk only in the low number category.

Other important factors in establishing causality are the existence of a biologically plausible mechanism and the demonstration of a dose-response relationship. Currently, there are no identified occupational risk factors for cancer of either the colon or rectum and there is a lack of a mechanistic basis that could link colorectal cancer with fighting fires.

Diet is by far the most important exogenous risk factor so far identified for these diseases (Tomatis et al., 1990) and it has been estimated that 70% of colorectal cancers could be prevented by nutritional intervention (Honda et al., 1999). Given the apparent strength of nutritional influences, it would always be difficult to implicate any occupational factor in the absence of control for detailed nutritional factors. In none of the studies described was such control exercised. Lack of adequate adjustment for other confounders, particularly alcohol intake, NSAIDS, supplement use and smoking could have also influenced study results

Conclusion

The available epidemiological data do not provide sufficient evidence for an aetiological role of the occupation as a fireman in the incidence or mortality from cancer of cancer of either the colon or the rectum.

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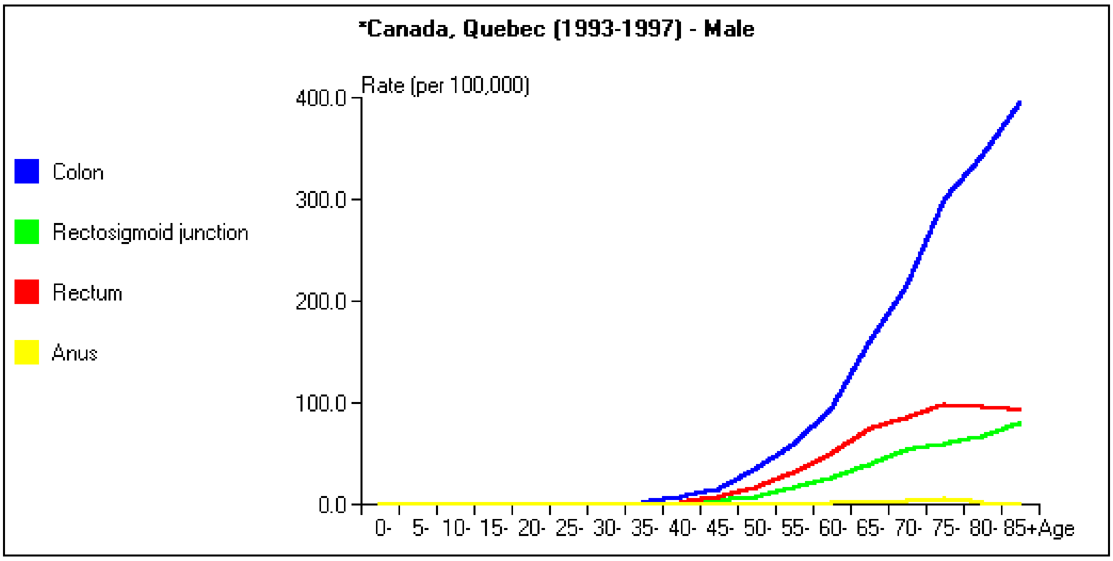
Figure 1. Age-Standardised Incidence of Cancers of the Colon, Rectum and Anus among Men in Canada and Quebec (1993-1997)



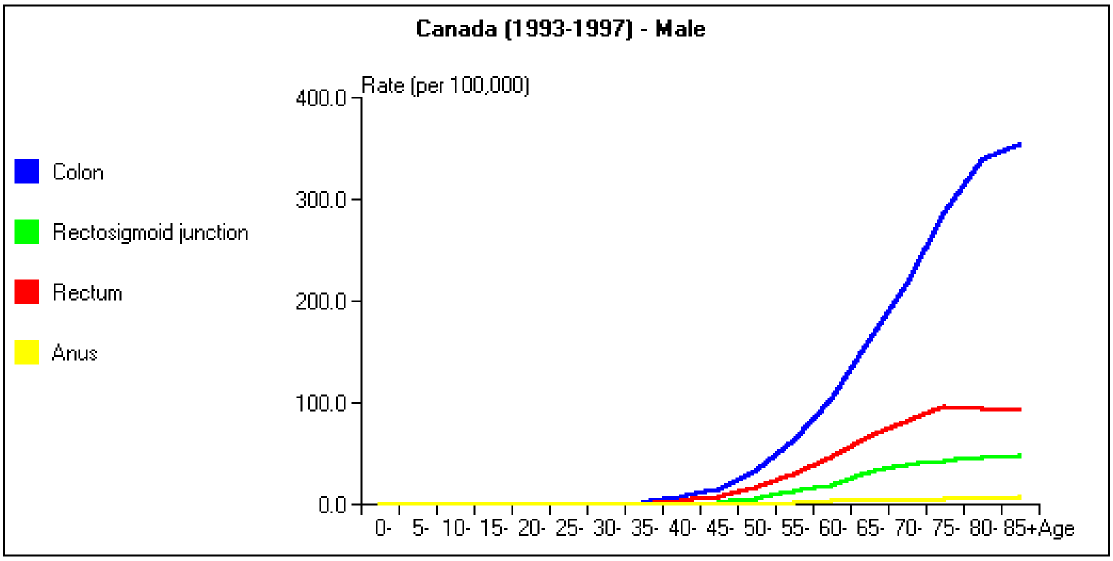


Table 1. Volatile Organic Compounds Consistently found in 9 Municipal Structural Fires.

Chemical	Concentration Range Found (ppm)
Propene	0.22 – 21.64
Benzene	0.12 – 10.76
Xylenes (*o*-, *m*-, *p*-)	0.06 – 9.19
1-Butene/2-methyl propene	0.03 – 4.08
Toluene	0.05 – 5.52
Propane	0.03 – 3.63
1,3-Butadiene	0.03 – 4.84
2-Methylbutane	0.004 – 0.43
Ethylbenzene	0.01 – 5.97
Naphthalene	0.01 – 2.14
Styrene	0.003 – 2.01
Cyclopentene	0.002 – 3.29
1-Methylcyclopentene	0.001 – 1.79
Isopropylbenzene	0.0004 – 0.55

***Table 1. Summary characteristics and results of studies on the relation between occupational exposure as a fireman and cancer.**

Reference	Study base & type	Reference group	Numbers	Risk* (95% C.I. or significance level)	Adjustments & Comments
Musk, et al., 1978	Firemen in Boston, MA Cohort 1915-75	Massachusetts men	5655 firemen with 367 cancer deaths	Digestive combined, SMR = 80, n.s.	No dose-response analysis. Based on death certificates. 104561 person-years actively working; 38414 person-years retirees
Eliopulos et al., 1984	Firemen in Western Australia, 1939-78	Western Australia men	990 firemen with 30 cancer deaths	Intestinal, SPMR = 1.59 (0.43-4.07)	No dose response analysis. Based on death certificates. 16876 person-years
Feuer & Rosenman, 1986	Firemen in New Jersey, 1974-80	NJ police NJ men USA men	No. of firemen not clear. 67 cancer deaths, 23 respiratory, 4 leukaemias, 20 digestive system	All cancers, PMR = 1.07, n.s. All cancers, PMR = 1.00, n.s. All cancers, PMR = 1.15, n.s. Digestive, PMR = 0.91, n.s. Digestive, PMR = 1.11, n.s. Digestive, PMR = 1.45, n.s.	Proportional analysis. No indication of a dose-response
Vena & Fiedler, 1987	Firemen in Buffalo, NY, 1950-1979	White USA men	102 cancer deaths	All cancers, SMR = 1.09 (0.89-1.32) Colon, SMR = 1.83 (1.05-2.97) Rectum, SMR = 2.08 (0.83-4.28)	Gradiant in the SMR with years of service for all cancers, colon and urinary bladder. Not corrected for age. 32858 person-years
Heyer et al., 1990	Firemen in Seattle, WA, 1945-83.	White USA men	2289 firemen, 92 cancer deaths	All cancers, SMR = 0.96 (0.77-1.18) Intestinal, SMR = 0.79 (0.32-1.64) Rectal, SMR = 0.65 (0.08-2.37)	Small numbers of cancer cases, resulting in instability of the SMRs. Dose-response analysis inconclusive. 52914 person-years.
Sama et al., 1990	Firemen in Massachusetts, 1982-86	MA police (p) White MA men (m)	315 cancer deaths	Colon, SMORp = 1.04 (0.59-1.82) SMORm = 1.20 (0.80-1.82) Rectum, SMORp = 0.97 (0.50-1.88) SMORm = 1.35 (0.84-2.19)	Case-control study of selected cancers from a cancer registry.
Beaumont et al., 1991	Firemen in SanFrancisco, California, 1940-82.	White USA men	3066 firemen with 236 cancer deaths	All cancers, SMR = 0.95 (0.84-1.08) Intestine (except rectum), SMR = 0.99 (0.63-1.47) Rectum, SMR = 1.45 (0.77-2.49)	Analysis of dose-response inconclusive. Number of person years not stated.
Grimes et al., 1991	Firemen in Honolulu, Hawaii, 1969-88.	Hawaii men	205 deaths, including 58	All cancers, PMR = 1.19 (0.96-1.49) Colon, PMR = 0.91 (0.37-2.20)	Proportionality study.

			cancer deaths.		Small numbers of individual cancers No analysis of dose-reponse
Demers et al., 1992	Firemen in Seattle, Tacoma & Portland, NW USA, 1945-89	Police in the same cities (p). White USA men (m)	4401 firemen with 291 cancer deaths	All cancers, IDRp = 0.97 (0.67-1.33) SMRm = 0.91 (0.85-1.07) Colon, IDR = 1.58 (0.73-3.43) SMR = 0.85 (0.54-1.26) Rectum, IDR = 0.89 (0.30-2.66) SMR = 0.95 (0.41-1.87)	122852 person-years for the 3 cities
Demers et al., 1992b	Firemen and policemen in Seattle & Tacoma WA, U.S.A. 1974-1979	For SIR, male rates for the urban counties of region For SMR, white WA, U.S.A. men	4528 firemen & policemen with 338 cancer cases	Colon, SIR= 1.00 (0.68-1.43) SMR = 0.68 (0.33-1.26) Rectum, SIR = 0.95 (0.55-1.52) SMR = 1.48 (0.48-3.45)	SIR from cancer registry; SMR from death certificates
Demers et al., 1994	Firemen in Seattle & Tacoma, NW USA, 1974-89.	Police in the same cities (p) Men in the same counties (m)	2447 firemen with 244 cancer deaths	All cancers, SIRp = 1.0 (0.8-1.3) SIRm = 1.1 (0.9-1.2) Colon, SIRp = 1.3 (0.6-3.0) SIRm = 1.1 (0.7-1.6) Rectum, SIRm = 1.3 (0.5-3.9) SIRm = 1.0 (0.5-1.8)	Sub-group of the preceding study . Small numbers for some cancers
Giles etal.,1993	Firemen in Melbourne, Australia, 1980-89	Men in Victoria	2865 firemen, 50 cancer cases	All cancers, SIR = 1.13 (0.84-1.48) Colon + rectum, SIR = 1.36 (0.62-2.59)	20853 person-years of observation. Dose-response analysis non-significant
Guidotti, 1993	Firemen in Edmonton & Calgary, Alberta, 1927-87	Men in Alberta	3328 firemen with 92 cancer deaths	All cancers, SMR = 1.27 (1.02-1.55) Colon + rectum, SMR = 1.61 (0.88-2.71)	Follow-up of 96% of the cohort for 64983 person-years. Dose-response analysis inconclusive
Aronson et al., 1994	Firemen in Toronto, Ontario, 1959-89	Men in Ontario	5414 firemen with 199 cancer deaths	All cancers, SMR = 1.05 (0.91-1.20) Colon, SMR = 0.60 (0.30-1.08) Rectum, SMR = 1.71 (0.91-2.93)	114008 person-years of follow-up. Dose response analysis non-significant. No information on smoking habits or diet.
Tornling et al., 1994	Firemen in Stockholm, Sweden, 1951-86	Men in the Stockholm region	1116 firemen with 93 cancer deaths	All cancers, SMR = 1.02 (0.88-1.25) Colon, SMR = 0.85 (0.31-1.85) Rectum + anus, SMR = 2.07 (0.89-4.08)	Tendency for a dose-response relationship between duration of employment and number of fires attended for cancers of the brain and stomach.
Burnett et al., 1994	Firemen in 27 states of the USA, 1984-90	Men who died in the same 27 states of USA	Number of firemen not stated. 1636 cancer deaths	All cancers, PMR = 1.10 (1.06-1.14) < 65 years age, PMR = 1.12 (1.04-1.21) Rectum, PMR = 1.48 (1.05-2.05) <65 years age, PMR = 1.86 (1.10-2.94)	Proportionality study

Ma et al., 1998	Mortality odds ratio study of death certificates of firemen for race-specific cancer risk in 24 states of USA, 1984-93	Men who died from causes other than cancer	6607 deaths of firemen with 1883 cancer deaths (1817 white, 66 black)	**WHITE**: All cancers, 1817, MOR = 1.1 (1.1-1.2) Colon, 149, MOR = 1.0 (0.9-1.2) **BLACK** All cancers, 66, MOR = 1.2 (0.9-1.5) Colon, 9, MOR = 2.1 (1.1-4.0)	Small numbers for some cancers in whites, small numbers for most cancers in blacks, leading to instability of the MORs.
Baris et al., 2001	Historical cohort mortality study of Philadelphia firemen employed 1925-86	Men in the general USA population	7789 firemen with 2220 deaths	See text for SMRs according to exposure indices. All cancers, 500, SMR = 1.10 (1.00-1.20) Colon, 64, SMR = 1.51 (1.18-1.93) Rectum, 14, SMR = 0.99 (0.50-1.68)	204821 person-years of follow-up. Thus, the largest study available to date. Best estimates of exposure because, in addition to duration of employment, the cohort was analysed according to job assignment and – most importantly – number of runs.
Bates et al., 2001	Historical cohort study of all firemen in New Zealand, 1977-96	Men who died from cancer in the same period throughout New Zealand	4221 firemen	Total period: Colon, 7, SIR = 0.60 (0.2-1.2) 6, SMR = 1.19 (0.4-2.6) Rectum, 9, SIR = 1.15 (0.5-2.2) 4, SMR = 1.21 (0.3-3.1) For 1990-1996: Colon, 4, SIR = 0.58 (0.2-1.5) Rectum, 5, SIR = 1.08 (0.3-2.5)	58709 person-years. Cancer Registry database more complete from about 1990 Also analysed by length of exposure (paid service or paid service and volunteer service), but numbers are very low.

*C.I. Confidence Interval

IDR = incidence density ratio; MOR = mortality odds ratio; PMR = proportional mortality ratio; RR = relative risk; SIR = standardised incidence ratio; SMR = standardised mortality ratio; SMOR = standardised mortality odds ratio; Subscripts: m = men; p = police